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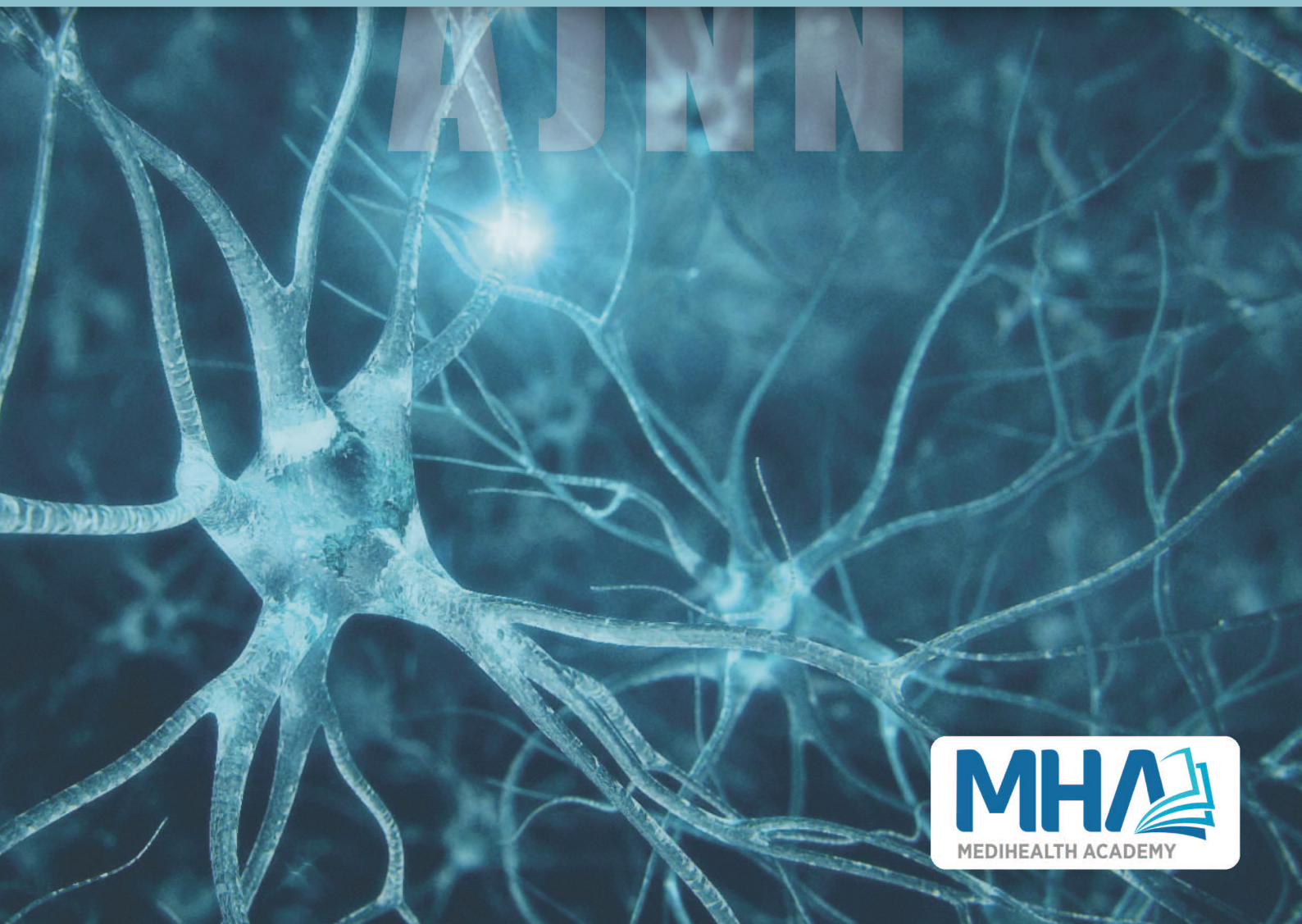

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Original Article

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Investigation of cognitive decline in patients with COVID-19 syndrome within 12 weeks after infection

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ABSTRACT

Aims: Recent findings suggest that COVID-19 may contribute to cognitive decline through neuroinflammatory and vascular mechanisms. To clarify the extent and underlying causes of these effects, we propose a study examining the cognitive outcomes of affected individuals. This study aims to investigate the effect of cognition in patients with COVID-19 within 12 weeks after infection.

Methods: A prospective study included 30 patients with COVID-19 within 12 weeks after COVID-19 and 30 healthy controls. The age, gender and educational status of the participants were recorded. These patients underwent montreal cognitive assessment (MoCA) test. Statistical comparisons were performed using Mann-Witney U test and Pearson Chi-square test.

Results: There was a statistically significant difference in age between the patients with COVID-19 and the control group (p=0.02). No statistically significant difference was found between the two groups in terms of gender (p=0.06). The total MoCA test score of the COVID-19 patient group was found to be statistically significantly lower than the control group (p=0.00). The education level of the patients with COVID-19 was found to be statistically significantly lower than the control group (p=0.05).

Conclusion: The results suggest that cognitive decline is a prolonged effect within 12 weeks after COVID-19. Emerging research suggests that COVID-19 may lead to cognitive impairments, including memory deficits and executive dysfunctions. Neuroinflammatory mechanisms and vascular complications are proposed as key contributors to these changes, highlighting the need for further investigation into the long-term neurological consequences of the infection.

Keywords: COVID-19 syndrome, cognitive decline, cognitive test, post-acute COVID syndrome

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel betacoronavirus that causes a range of symptoms known as coronavirus disease (COVID-19).[1]

The cytokine storm in COVID-19 can cause a series of small punctate ischemias without causing significant neurological deficits. When these patients leave the hospital after an acute SARS-CoV-2 infection, it may present as memory impairment, loss of attention, or slowness of thinking. More than 80% of patients discharged from hospital after COVID-19 reported severe cognitive difficulties in their daily lives even 4 months later.[2] Therefore, if these patients still have cognitive problems, slowness of information processing, or attention deficit even months after hospital discharge, it would be beneficial to see a neurologist or undergo neurocognitive testing. Patients who score low on some cognitive tests may need to undergo brain rehabilitation to return to their baseline cognitive capacity levels. As a result, their risk of developing age-related cognitive decline in later life will be reduced.[3,4] MoCA is the most commonly used tool in the studies reported in reviews, so it may be a relevant screening tool for cognitive assessment after COVID-19. However, the recent development of other digital cognitive screening tools may provide other alternatives.[5]

Some patients develop symptoms such as fatigue, “brain fog,” or cognitive decline after the acute infection phase; this phase is often referred to as “long COVID”.[6]

The post-COVID-19 syndrome (PCS) is divided into two categories: (1) acute or persistent symptomatic acute post-COVID-19, which includes symptoms and abnormalities present 4–12 weeks after COVID-19; and (2) chronic PCS, which includes symptoms and abnormalities that persist or are present beyond 12 weeks from the onset of acute COVID-19.[7]

In this study, we planned to investigate cognitive test in patients with COVID-19 within 12 weeks after COVID-19 and healthy volunteers.

METHODS

Consent was obtained from these participants in accordance with the Helsinki Declaration. Permission to conduct the study was obtained from the Ministry of Health and the Ethics Committee of İstanbul Kanuni Sultan Süleyman Training and Research Hospital, University of Health Sciences (Date: 29.01.2021, Decision No: KAEK/2021.01.29).

For the study, 30 patients whit COVID-19 within 12 weeks after COVID-19 who applied to the Neurology outpatient clinic of İstanbul Kanuni Sultan Süleyman Training and Research Hospital, University of Health Sciences between February 2021 and September 2021 were randomly selected. These patients underwent montreal cognitive assessment (MoCA) test. As the control group, 30 randomly selected people, male and female, over the age of 18, who had never had covid, who applied to the outpatient clinic, were taken and the MoCA test was performed. The age, gender and educational status of the participants were recorded. Patients with other neurological and psychiatric diseases were excluded from the study. The case group and the control group were compared in terms of age, gender, educational status, MoCA test results.

Statistical Analysis

All analyses were carried out using the Statistical Package for the Social Sciences (SPSS), version 24 (İBM Corp., Armonk, NY). All data are presented as mean±standard deviation. Group differences in demographic data and neuropsychological variables were evaluated using the independent sample t-tests. The Mann-Whitney U test was used as a nonparametric equivalent of the Student's t-test for non-normaly distributed data. Catagorical variables were expressed as counts and percentages. The Wilcoxon rank-sum test and Maental-Haenszal X^2 test were used to compare of two groups. All results were quoted as 2-tailed P values, with statistical significance set at $p<0.05$.

RESULTS

The study included 30 patients with COVID-19 and 30 healthy controls. The mean age of the patients with COVID-19 was 43.3±12.9, and the mean age of the control group was 35.6±11.4 (Table 1). There was a statistically significant difference in age between the patients with covit-19 and the control group ($p<0.05$). The age of patients with COVID-19 was found to be statistically significantly higher than the control group (Table 2).

15 (50%) of the patients with COVID-19 were female and 15 (50%) were male. 22 (73.3%) of the subjects in the control group were female and 8 (26.7%) were male (Table 1). No statistically significant difference was found between the two groups in terms of gender ($p>0.05$) (Table 2).

The total MoCA test score average of the patients with COVID-19 was 43.3±12.9, and the total MoCA test score of the control group was 35.6±11.4 (Table 1). A statistically significant difference was found between the patients with COVID-19 and the control group in terms of the total MoCA test score ($p<0.05$). The total MoCA test score of the COVID-19 patient group was found to be statistically significantly lower than the control group (Table 2). In the MoCA test subcategories in the COVID-19 patient group, except for naming, the score of the COVID-19 group was found to be statistically significantly lower than the control group in all categories. No statistically significant difference was found between the two groups only in the naming category.

Of the patients with COVID-19, 1 (3.3%) was uneducated, 15 (50%) were primary school graduates, 11 (36.7%) were high school graduates, and 3 (10%) were university graduates. Of the subjects in the control group, 1 (3.3%) was uneducated, 2 (6.7%) were primary school graduates, 6 (20%) were high school graduates, and 21 (70%) were university graduates. The education level of the patients with COVID-19 was found to be statistically significantly lower than the control group ($p<0.05$) (Table 2).

DISCUSSION

Since the beginning of the coronavirus disease 2019 pandemic, many persistent neurological sequelae, including cognitive decline, have been recognized as part of the post-acute COVID syndrome. The reticular activating system (RAS) in the brainstem controls the sleep-wake cycle and executive attention.[8] The brainstem also houses the raphe nuclei and locus coeruleus, which are the primary source of serotoninergic and noradrenergic neurons in the brain, respectively.[9,10] The ventral tegmental area and substantia nigra are also located in the midbrain of the brainstem, which supply dopaminergic neurons to higher brain regions.[11,12] These neurotransmitters originating in the brainstem have been shown to be associated with a wide range of neurological disorders, including depression, anxiety, sleep and cognitive disorders, headache, fatigue, myalgia, and pain perception.[13,14] Therefore, invasion of SARS-CoV-2 into the brainstem may disrupt neurotransmitter systems in the brain, causing various neurological symptoms.

Long COVID has a wide range of manifestations, including cardiopulmonary complications, persistent fatigue, and neurocognitive dysfunction among various persistent syndromes.[15-21] Although there is no universally accepted definition, in December 2020, the United Kingdom (UK) National Institute for Health and Care Excellence guidelines defined long COVID as the persistence of symptoms for more than 4 weeks after SARS-CoV-2 infection.[22] This term consists of two phases: a ongoing symptomatic post-acute phase (4–12 weeks) that persists according to the duration of symptoms and a chronic phase PCS (>12 weeks). More recently, the World Health Organization has provided a case definition for post-COVID-19 status[23] which is used to refer to the persistence of symptoms for more than 3 months after SARS-CoV-2 infection, lasting at least 2 months, and not explained by another illness.[7]

Post-acute COVID-19 status is defined as persistent symptoms that persist for at least 8 weeks, usually occurring within 12 weeks from onset in individuals with confirmed or probable SARSCoV-2 infection in the past and that cannot be explained by an alternative diagnosis.[24] Fatigue and cognitive

Table 1. Demographic data and MoCA test results of the participants

	COVID (-) (n=30)		COVID (+) (n=30)		Total	
	n	%	n	%	n	%
Gender						
Female	22	73.3	15	50	37	61.7
Male	8	26.7	15	50	23	38.3
Education						
1 uneducated	1	3.3	1	3.3	2	3.3
2 elementary	2	6.7	15	50	17	28.3
3 high school	6	20	11	36.7	17	28.3
4 university	21	70	3	10	24	40
COVID						
1 COVID (-)	30	50	_	_	30	50
2 first month	_	_	9	30	9	15
3 second month	_	_	11	36.7	11	18.3
4 third month	_	_	10	33.3	10	16.7
Age	35.6±11.4 med:30.5 min:24 max:69		43.3±12.9 med:39 min:19 max:65		39.4±2.6 med:26 min:19 max:30	
MoCA	25.7±2.6 med:26 min:19 max:30		17.3±5.9 med:19.5 min:5 max:28		21.5±6.2 med:23 min:5 max:30	

Min: Minimum, Max: Maximum, SD: Standard deviation, Med: Median, Mean±standard deviation, MoCA: Montreal cognitive assessment test

Table 2. Comparison of demographic data and cognitive test score between groups

	Total	COVID (+)	COVID (-)	Test statistic	p*
	n=60	n=30	n=30		
Age	39.4±2.6	43.3±12.9	35.6±11.4	Z: -2.265	0.02[a]
MoCA	21.5±6.2	17.3±5.9	25.7±2.6	Z: -5.61	0.00[a]
Gender					
Male	23 (38.3)	15 (50)	8 (26.7)		
Female	37 (61.7)	15 (509	22 (73.3)	X^2: 3.45	0.06[b]
Education					
1 uneducated	2 (3.3)	1 (3.3)	1 (3.3)		
2 elementary	17 (28.3)	15 (50)	2 (6.7)		
3 high school	17 (28.3)	11 (36.7)	6 (20)		
4 university	24 (40)	3 (10)	21 (70)	X^2: 24.91	0.00[b]

Mean±standard deviation, MoCA: Montreal cognitive assessment test, a: Mann-Whitney U test, b: Pearson Chi-square test

impairment have been reported to be some of the most common complaints of PCS.[25]

In a systematic review and meta-analysis of 81 studies, it was found that approximately one-third of the individuals included experienced persistent fatigue 12 or more weeks after COVID-19 diagnosis and more than one-fifth of the individuals exhibited cognitive decline.[26] In our study, we evaluated cognitive functions in individuals who were within 12 weeks after COVID-19.

Most studies included in the current review used the MoCA instead of the MMSE as a general cognitive screening test.[27,28] These studies reported that the MoCA assessment was more sensitive than the MMSE in detecting cognitive deficits in patients who tended to perform worse on this task compared with uninfected controls. In our study, we used the MoCA test for cognitive function assessment.

Another study showed that cognitive decline (mainly attention and executive function impairments) was reported in 28–56% of patients with mild or asymptomatic COVID-19 and was associated with reduced cortical thickness in the right gyrus rectus and language-related areas.[29] Another published article showed that changes in working memory, set shifting, divided attention and processing speed were not associated with intubation length, psychiatric and clinical diagnosis in a cohort of 57 patients who recovered from moderate/severe COVID-19.[30] In our study, in the MoCA test subcategories in the COVID patient group, the COVID group had a statistically significantly lower score than the control group in all categories except naming. No statistically significant difference was found between the two groups only in the naming category.

Previous studies have reported that cognitive decline in post-acute COVID-19 syndrome may be associated with risk factors such as advanced age, low education level, pre-morbid delirium, male gender, and history of neuropsychiatric disease.[31,32] In our study, consistent with the literature, higher age and lower education level were found in patients with COVID-19 compared to the control group.

Studies have consistently identified attention, memory, and executive functions as the cognitive domains most affected by COVID-19 infection. Many studies have also reported neuroimaging, blood test deterioration, and neurophysiological abnormalities that could potentially reflect pathophysiological aspects of post-COVID cognitive impairment. Although patients with dementia are at high risk of COVID-19 infection, increasing evidence suggests that COVID-19 infection may increase the risk of Alzheimer's disease and that there is a bidirectional relationship between them. Post-COVID cognitive dysfunction is a common and multifaceted problem. Future explanations regarding long-term effects, mechanisms, and treatments will depend on the joint efforts of clinicians, researchers, and patients.

Limitations

There are some limitations to the study. In the study conducted on patients who applied to the outpatient clinic randomly, the difference in age and education level may be coincidental. There may be other factors such as low income level and depression that affect these results. Since there were no baseline cognitive data before the infection, we could not evaluate the cognitive change by comparing it with the previous status.

The effects of longer-term cognitive decline and their clinical significance remain unclear. For these reasons, it can be said that if there are people who complain that their cognitive decline has not returned to its previous level after having COVID, they should be examined in more detail and continued to be followed up clinically.

CONCLUSION

Our study examined cognitive decline in individuals who had contracted COVID-19 within the past 12 weeks, comparing them to a control group. Preliminary findings indicate a noticeable decline in cognitive functions among COVID-19 patients, aligning with previous research on this subject. However, given the multifactorial nature of cognitive impairment and its complex etiology, further studies with larger sample sizes and extended follow-up periods are necessary to confirm these observations and refine our understanding of post-viral cognitive outcomes.

ETHICAL DECLARATIONS

Ethics Committee Approval

Permission to conduct the study was obtained from the Ministry of Health and the Ethics Committee of İstanbul Kanuni Sultan Süleyman Training and Research Hospital, University of Health Sciences (Date: 29.01.2021, Decision No: KAEK/2021.01.29).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

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Relationship between intradural extramedullary spinal tumors and blood biochemical values: a clinical study

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ABSTRACT

Aims: Because the radiological imaging methods may be inadequate in distinguishing intradural extramedullary spinal tumors, histopathological examination methods are still the gold standard. This study was conducted to investigate the relationship between extradural intramedullary spinal tumors and blood count and blood biochemistry parameters, and to present auxiliary parameters that may predict the histopathological diagnosis of these tumors before surgery.

Methods: Patients with intradural extramedullary spinal tumors who underwent surgical intervention and healthy individuals were included in the study. Then they were divided into the control group (healthy individuals; n=14) and the STM group (patients with extradural intramedullary spinal tumors; n=13). In addition, after excluding the control group patients and one patient each with ependymoma and cavernous hemangioma, they were divided into the schwannoma group (patients diagnosed with spinal schwannoma, n=6) and the meningioma group (patients diagnosed with spinal meningioma, n=5). Blood count results and biochemistry findings were analyzed.

Results: Leukocyte count results differed between the control and STM groups (t=2.332, p=0.028). ROC-Curve analysis showed that if the hematocrit level was <40.75% (p=0.042) and if the leukocyte count was <8195 µL, these parameters could differentiate patients with IDEM from healthy individuals (p=0.031). Logistic regression analysis revealed that only leukocyte count was the best predictive marker in distinguishing the IDEM (p=0.041). However, these parameters could not differentiate the patients with intradural extramedullary spinal tumors from healthy subjects because the parameter results were within average laboratory values. In addition, any study parameter could differentiate schwannoma patients from meningioma patients.

Conclusion: At the end of the study, it was concluded that the blood count and blood biochemistry analysis results could not distinguish spinal tumors from healthy individuals in clinical practice. It was also seen that these parameters could not distinguish spinal schwannomas from meningiomas. On the other hand, it was argued that intradural extramedullary spinal tumors did not increase or decrease blood count results and serum CRP levels in patients. As a result, they did not cause an increase in a systemic inflammatory response or immunosuppression and did not have a detrimental effect on the functions of systemic organs.

Keywords: Spinal intradural extramedullary tumors, biochemistry, predictive marker

INTRODUCTION

Spinal tumors are classified as extradural, intradural extramedullary, and intradural intramedullary tumors. Intradural spinal tumors can be diagnostically challenging and often result in significant morbidity.[1] Because the presentation of intradural extramedullary spinal tumors is similar and depends on tumor size and location, clinical features are often not helpful in narrowing the differential diagnosis. The most common symptoms are back or neck pain, radicular pain, weakness, paresthesia, gait disturbance, and bowel and bladder dysfunction.[2,3] Clinical outcomes regarding function preservation are closely linked to the promptness of diagnosis and treatment.[4] Radiologic imaging is significant in determining the cause of clinical findings, and magnetic resonance imaging (MRI) with gadolinium is currently the most sensitive imaging modality.[5] Many clinical studies conducted to diagnose these tumors preoperatively

include radiological imaging methods. However, histopathological examinations are still the gold standard for the histological diagnosis of these tumors, and radiological imaging methods may still be insufficient for the histological diagnosis.[1,6] On the other hand, any study that examined the relationship between these tumors and the blood count values and blood biochemistry values has been found in the literature, and revealed tumor histopathology as a predictive marker through these parameters.

This study was conducted to investigate the relationship between extradural intramedullary spinal tumors and blood count and blood biochemistry parameters, and to present auxiliary parameters that may predict the histopathological diagnosis of these tumors before surgery.

METHODS

Ethics

The study was conducted after the approval of Kırıkkale University Non-interventional Clinical Researches Ethics Committee (Date: 12.03.2025, Decision No: 2025.02.34). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients

Patients with intradural extramedullary spinal tumors detected on radiological imaging between 2015 and 2024 and treated surgically were included in the study. In addition, individuals without any metabolic and rheumatologic disease who presented to the outpatient clinic with low back pain but whose radiologic images did not reveal pathologic findings requiring surgical treatment were also included. The information of these participants was then scanned and recorded in the hospital's digital record system. Subsequently, the participants were divided into two groups as follows:

- Control group (patients without any metabolic or rheumatologic disease; n=14)
- STM group (patients with intradural extramedullary spinal tumors who underwent surgical treatment; n=13)
- After excluding the control group patients and one patient each with myxopapillary ependymoma and cavernous hemangioma, patients with spinal tumors were divided into two groups as follows
- Schwannoma group (patients diagnosed with spinal schwannoma, n=6)
- Meningioma group (patients diagnosed with spinal meningioma, n=5)

Patients who had spinal intradural intramedullary tumors, who had extradural or spinal metastases, who had rheumatologic diseases, who had epidural abscesses, intervertebral discitis, osteomyelitis, or other types of infection, and pediatric patients were excluded from the study.

Methods

Hemoglobin (normal range 12-16 g/dl), hematocrit (normal range 37-47%), leukocytes (normal range 4000-10000 µL), neutrophils (normal range 2000-7000 µL), lymphocytes (normal range 800-4000 /µL), monocytes (normal range 120-1200 µL), basophil (normal range 0-100 µL), eosinophil (normal range 20-500 µL), platelet (normal range 100-420 103µL) counts and erythrocyte sedimentation rate (normal range 0-20 mm/h) were recorded. In addition, serum sodium (normal range 136-145 mmol/L), potassium (normal range 2.5-4.5 mmol/L), creatinine (normal range 0.7-1.2 mg/dl), blood urinary nitrogen (normal range 17-43 mg/dl), aspartate aminotransferase (AST) (normal range 0-40 U/L), alanine aminotransferase (ALT) (normal range 0-41 U/L) and C-reactive protein (CRP) (normal range 0-5 mg/L) levels were recorded. Histopathological examination results of the surgically removed tumor tissues of the patients were also recorded.

Surgery

Each patient was operated on under general anesthesia in the prone position. Regardless of the location or type of tumor, only the posterior approach was used. After laminectomy of the vertebrae at the tumor level, the dura mater was opened through a longitudinal incision, and the tumor was separated from the dura mater and removed. When the tumor was adherent to a nerve root, a neurostimulator was used to determine whether it was a sensory or motor nerve branch. The sensory nerve branch was removed, while the motor nerve branch was carefully separated and preserved. In cases where the tumor was large enough to cause posterior instability, fusion with instrumentation was also performed.

Statistical Analysis

SPSS 20.0v software program was used for statistical analysis. The Kolmogorov-Smirnov test was used to test the normal distribution of the study data. An Independent Samples t-test was used to compare parametric data, and a Mann-Whitney U test was used to compare nonparametric data ($p<0.05$). Spearman's rho correlation test was used to show the correlation between the study parameters ($p<0.05$). The ROC-Curve test was used to determine which study parameters could predict the histopathological diagnosis of spinal tumor, and the sensitivity and specificity of the parameters were determined by obtaining the "cut-off" values ($p<0.05$). Logistic regression test was also used to determine the "best predictive parameter" ($p<0.05$).

RESULTS

After a retrospective review of hospital records, 13 patients (11 females and 1 male) with intradural extramedullary spinal tumors were identified (Table 1). In addition, 14 healthy individuals (10 females and 4 males) were included in the study.

In the STM group, 6 patients were diagnosed with schwannoma (1 cervical, 3 thoracic and 2 lumbar localization) (Figure 1, Figure 2), 5 patients with meningioma (all thoracic localization) (Figure 3), 1 patient with myxopapillary

Table 1. Descriptive table of all patients with intradural extramedullary spinal tumor

Patient	Age	Gender	Symptoms	Level	Histopathology result
MŞ	56	Female	Low back pain	L1	Schwannoma
AT	40	Female	Low back pain	L1-2	Schwannoma
SK	60	Female	Back pain, paraparesis, hypoesthesia in the legs, sphincter disturbance	T3-5	Schwannoma
FA	69	Female	Back pain	C2	Schwannoma
ED	38	Male	Pain in the right arm	T1-2	Schwannoma
YB	47	Female	Back pain	T3	Schwannoma
SC	65	Female	Back pain, paraparesis, and hypoesthesia in the legs	T8-10	Meningioma
NB	65	Female	Back pain, paraparesis, hypoesthesia in the legs, sphincter disturbance	T7-8	Meningioma
HA	65	Female	Back pain, hypoesthesia, and monoparesis in the right arm.	T3	Meningioma
SE	51	Female	Back pain, paraparesis, and hypoesthesia in the legs	T12	Meningioma
İY	62	Female	Back pain, paraparesis, and hypoesthesia in the legs	T10	Meningioma
BD	29	Female	Low back pain, no deficit	L3	Myxopapillary ependymoma
SD	52	Male	Low back pain, paraparesis, and hypoesthesia in the legs, no anal tonus	T6-8	Cavernous hemangioma

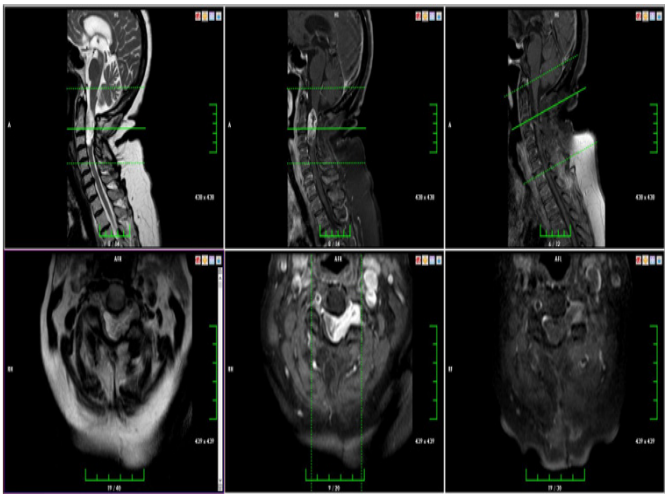

Figure 1. In the cervical MR images taken before surgery, an hourglass-shaped schwannoma extending to the left C2-3 neural foramen at the level of the C2 vertebra is seen. It can also be observed in these images that the tumor was completely removed after surgery

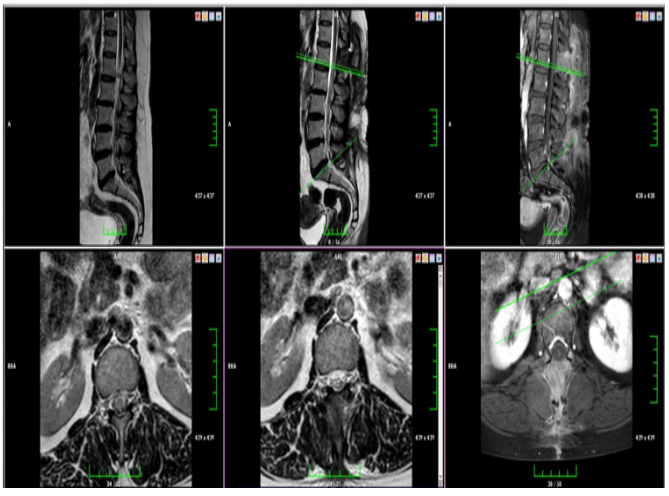

Figure 2. In the lumbar MR images taken before surgery, a schwannoma located in the midline and at the tip of the conus medullaris at the level of the L1 vertebra is seen. It can also be observed in these images that the tumor was completely removed after surgery

ependymoma (lumbar localization) and 1 patient with cavernous hemangioma (thoracic localization). None of the operated patients developed new neurologic deficits and were discharged with persistent preoperative neurologic findings. Statistical analysis showed that the leukocyte count results differed between the control and STM groups (t=2.332, p=0.028). There was no statistical difference between the two groups in terms of other blood count results and biochemical analysis results (Figure 4, Table 2).

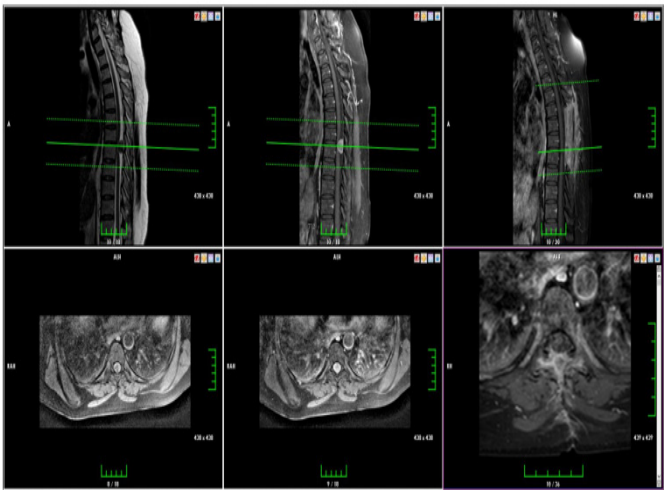

Figure 3. In the thoracic MR images taken before surgery, a meningioma located in the midline at the level of the T8-9 vertebra is seen. It can also be observed in these images that the tumor was completely removed after surgery

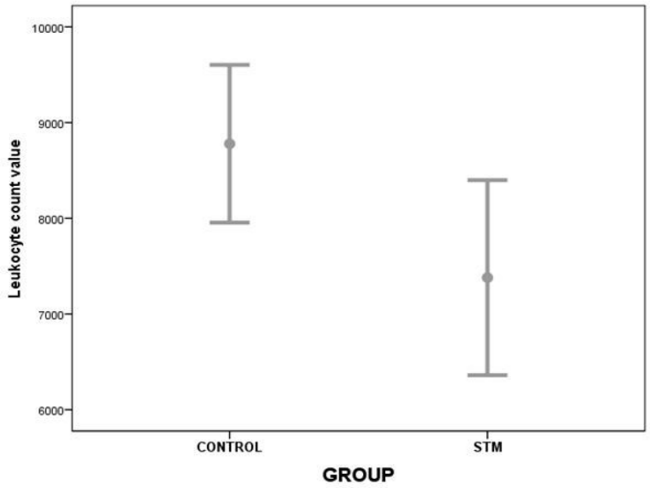

Figure 4. Each error bar shows the lymphocyte count value of the patients and healthy individuals

Table 2. Descriptive table of demographic data, blood count, and blood biochemistry analysis results of the patients and healthy individuals

		Control	STM		
		Mean±SD/median (min-max)/n (%)	Mean±SD/median (min-max)/n (%)	t/Z/X2	p
Age		58.57±19.29	53.77±12.35	0.763*	0.452
Gender	Female	10 (37.0%)	11 (40.7%)	0.678‡	0.410
	Male	4 (14.8%)	2 (7.4%)		
Hemoglobin		14.24±1.59	12.87±2.27	1.834*	0.079
Hematocrit		43.32±3.77	39.64±5.42	2.062*	0.050
Leukocyte		8778.57±1427.32	7380.00±1686.55	2.332*	0.028
Neutrophil		5405.71±1665.98	4766.15±1530.72	1.036*	0.310
Lymphocyte		2425.71±841.08	2011.54±570.41	1.485*	0.150
Monocyte		469.29±102.17	436.15±129.07	0.742*	0.465
Basophil		33.57±18.65	32.31±16.91	0.184*	0.856
Eosinophil		180 (10-510)	100 (40-380)	-0.729†	0.466
Platelet (10^3)		333 (92-428)	244 (186-444)	-1.699†	0.089
Neutrophil to lymphocyte ratio		2.73±2.07	2.56±1.14	0.263*	0.795
Platelet to lymphocyte ratio		139.27±52.32	140.84±41.61	-0.086*	0.932
Lymphocyte-to-monocyte ratio		5.57±2.48	5.1496±2.46	0.445*	0.660
C-reactive protein		1.70 (0.50-13)	2.81 (0.80-32)	-0.850†	0.395
Sodium		139.96±2.21	140.23±2.01	-0.337*	0.739
Potassium		4.53±0.27	4.59±0.42	-0.459*	0.650
Blood urine nitrogen		30.65±10.86	25.15±9.25	1.411*	0.171
Creatinine		0.73±0.12	0.66±0.17	1.198*	0.242
Erythrocyte sedimentation rate		19.07±10.29	21.67±13.31	-0.560*	0.580
Aspartate aminotransferase		19.88±7.18	17.74±5.86	0.844*	0.407
Alanine aminotransferase		24.18±16.16	17.06±7.79	1.439*	0.163

(*) t value: Independent Samples t-test, (†) Z value: Mann-Whitney U test, (‡) X2 value: Pearson Chi-square test, p<0.05, SD: Standard deviation, Min: Minimum, Max: Maximum, n: Number of participants

Correlation analysis showed that as the hematocrit level (r=-0.395, p=0.041) and leukocyte count (r=-0.438, p=0.022) decreased, the probability of spinal tumor diagnosis increased. ROC-curve analysis revealed that if the hematocrit level was <40.75%, 67% sensitivity and 79% specificity (area=0. 265, p=0.042, 95% confidence interval 0.062-0.448) and if the leukocyte count was <8195 µL, 75% sensitivity and 71% specificity (area=0.250, p=0.031, 95% confidence interval 0.056-0.444), these parameters could differentiate patients with intradural extramedullary spinal tumor from healthy individuals. Logistic regression analysis, which was performed to test whether these parameters could best predict the likelihood of spinal tumor, showed that only leukocyte count was found to be the best predictor of intradural extramedullary spinal tumor (B=-0.001, Wald=4.162, p=0.041) (Table 3, Figure 5).

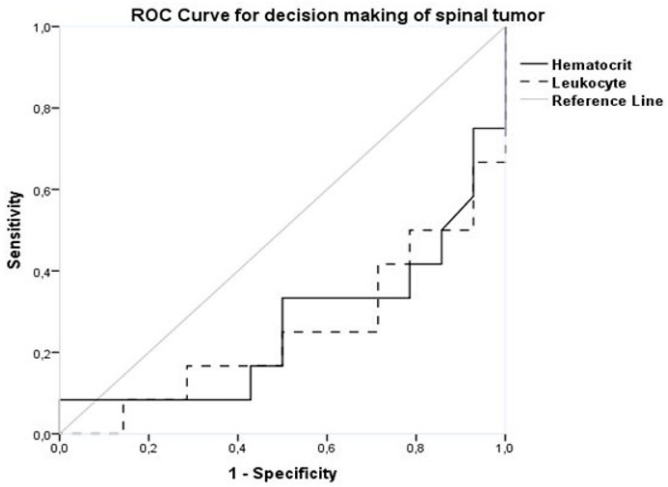

Figure 5. The ROC-curve graph shows the predictive biochemical parameters that may distinguish patients with intradural extramedullary spinal tumors from healthy subjects

Table 3. Table of study parameters that can predict the diagnosis of intradural extramedullary spinal tumor

ROC-curve test for decision-making of spinal tumor					
Variable	**Area**	**Cut-off value**	**p**	**Sensitivity**	**Specificity**
Hematocrit	0.265	<40.75	0.042	67%	79%
Leukocyte	0.250	<8195	0.031	75%	71%
Logistic regression test					
Variable	**B**	**Wald**	**p**		**Odds ratio**
Leukocyte	-0.001	4.162	0.041		0.999

ROC: Receiver operating characteristic

After excluding the control group patients and 1 myxopapillary ependymoma and 1 cavernous hemangioma patient, statistical analysis revealed that leukocyte (t=-2.325, p=0.045) and lymphocyte (t=-2.341, p=0.044) count values and serum sodium level values (t=-3.169, p=0.011) were different between the schwannoma and the meningioma groups (Table 4, Figure 6). As a result of the correlation analysis, it was found that the possibility of the patient's spinal tumor being meningioma may increase when leukocyte count (r=0.635, p=0.036), lymphocyte count (r=0.635, p=0.036),

Table 4. Descriptive table of patients who underwent surgery due to intradural extramedullary schwannoma or meningioma

		Schwannoma	Meningioma		
Variable		**Mean±SD/median (min-max)/n (%)**	**Mean±SD/median (min-max)/n (%)**	**t/Z/X²**	**p**
Age		51.67±12.11	61.60±6.07	-1.658*	0.132
Gender	Female	5 (45.5%)	5 (45.5%)	0.917‡	0.338
	Male	1 (9.1%)	0 (0%)		
Hemoglobin		12.53±2.98	13.18±1.16	-0.454*	0.661
Hematocrit		39.03±7.46	40.32±1.93	-0.372*	0.718
Leukocyte		6655.00±1635.61	8708.00±1200.76	-2.325*	0.045
Neutrophil		4221.67±1460.99	5652.00±1560.31	-1.569*	0.151
Lymphocyte		1833.33±343.49	2440.00±514.25	-2.341*	0.044
Monocyte		421.67±130.60	446.00±126.61	-0.312*	0.762
Basophil		30.00±14.14	42.00±17.89	-1.245*	0.245
Eosinophil		105 (70-380)	90 (40-290)	-0.640†	0.522
Platelet (10^3)		242 (220-444)	266 (209-327)	-0.183†	0.855
Neutrophil to lymphocyte ratio		2.32±0.68	2.47±1.07	-0.295*	0.775
Platelet to lymphocyte ratio		152.09±41.85	111.77±28.92	1.816*	0.103
Lymphocyte-to-monocyte ratio		4.77±2.02	6.02±2.84	-0.854*	0.415
C-reactive protein		4.02±6.15	7.10±7.48	-0.752*	0.472
Sodium		139.00±1.55	142.00±1.58	-3.169*	0.011
Potassium		4.60±0.34	4.72±0.56	-0.442*	0.669
Blood urine nitrogen		22.33±4.50	27.80±9.83	-1.226*	0.251
Creatinine		0.65±0.21	0.62±0.08	0.256*	0.803
Erythrocyte sedimentation rate		20.67±15.10	25.50±13.82	-0.512*	0.623
Aspartate aminotransferase		16.27±3.35	17.60±6.19	-0.456*	0.659
Alanine aminotransferase		14.97±5.94	17.40±5.03	-0.723*	0.488

(*) t value: Independent Samples t-test, (†) Z value: Mann-Whitney U test, (‡) X² value: Pearson Chi-square test, p<0.05, SD: Standard deviation, Min: Minimum, Max: Maximum

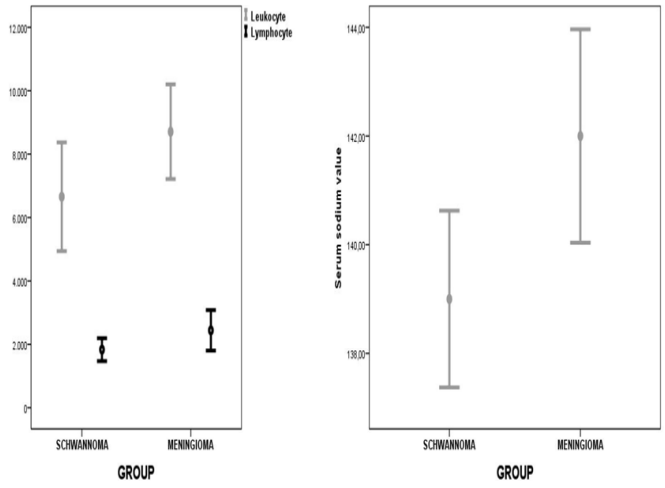

Figure 6. Each error bar shows the leukocyte and lymphocyte count values and serum sodium values in patient groups

and serum sodium level (r=0.732, p=0.010) were high. However, ROC-curve and Logistic Regression analysis, which were performed to determine the study parameters that could differentiate schwannoma patients from meningioma patients, showed that none of the study parameters could be used as predictive markers for the differential diagnosis of intradural extramedullary schwannomas from those of meningiomas.

DISCUSSION

Schwannoma and meningioma are the two most common types of spinal intradural extramedullary tumors, accounting for 55% of cases.[2] Spinal cord tumors exhibit heterogeneity in histologic appearance, clinical symptoms, and prognostic features. If left untreated, these tumors can result in severe neurological deficits and disability. Therefore, an accurate diagnosis is significant for determining the prognosis and the appropriate course of treatment. Meningiomas are typically located in the cervical and upper thoracic segments, and are rare in the lumbosacral region. Although schwannomas and meningiomas exhibit characteristic imaging features, such as calcification and a dura tail in meningiomas and fluid signal with rim enhancement in schwannomas, imaging features like solid, round or oval, well-circumscribed contours of the lesions overlap in critical areas.[7] Some studies suggested that up to 25% of schwannomas cannot be distinguished from meningiomas.[8] Consequently, differentiating spinal meningiomas from schwannomas is not always reliable due to significant overlap in features observed through conventional imaging and clinical assessments. This remains a topic of debate.[9,10]

Meningiomas have a higher recurrence rate than schwannomas. Therefore, a differential diagnosis between the two tumors is essential preoperatively due to the differences in operative approaches and prognoses. Surgical treatment

of schwannomas requires an incision of the dura mater and arachnoid membrane, as these tumors are encountered in the subarachnoid space. To prevent postoperative cerebrospinal fluid (CSF) leakage, the dura mater and arachnoid mater are sutured to form a waterproof dura closure. In contrast, meningiomas are found in the intradural but extra-arachnoid space. The attachment site of the meningioma to the dura mater must be resected along with the tumor to eliminate any remaining tumor cells; thus, preserving the arachnoid membrane aids in preventing postoperative CSF leakage. Preventive measures against tumor recurrence, such as coagulation or complete durotomy of the adhesion site, are crucial for patients with meningioma. Because of these challenges, this study aimed to analyze the predictive values of blood biochemistry parameters that may assist in differential diagnosis between meningioma and schwannoma.[11]

This study revealed that all meningiomas were located in the thoracic region. However, schwannomas could occur at any level of the spinal column. The majority of patients with intradural extramedullary spinal tumors were female. Additionally, patients with meningioma and the majority of patients with schwannoma were also women.

The findings demonstrated that leukocyte and lymphocyte count and serum sodium values in patients with spinal tumors were significantly lower than those in healthy individuals. However, these parameters also remained within normal laboratory ranges. Therefore, it was concluded that these results might not serve as distinguishing parameters between the two groups. In light of these findings, it was suggested that intradural extramedullary spinal tumors do not elevate blood count results, ESR, or serum CRP levels, indicating they do not provoke a systemic inflammatory response. In addition, these tumors do not reduce blood count results. Therefore, they do not compromise systemic immunity. Furthermore, it was asserted that they do not impact blood biochemistry results, thus not causing renal or hepatic insufficiency.

Moreover, correlation analysis conducted on the data of all participants indicated that as hematocrit levels and leukocyte counts decreased, the likelihood of diagnosing intradural extramedullary spinal tumors increased. By these findings, ROC-Curve analysis aimed at differentiating patients with intradural extramedullary spinal tumors from those healthy subjects revealed that a hematocrit level lower than 40.75% could predict these tumors with 67% sensitivity and 79% specificity, and a leukocyte count below 8195 µL could predict them with 75% sensitivity and 71% specificity. Logistic regression analysis, which assessed whether these parameters could effectively predict the presence of intradural extramedullary spinal tumors, showed that only leukocyte count could best serve as a predictor. However, an examination of the numerical data revealed that the threshold values of these study parameters remained within normal laboratory ranges. This suggests that these parameters could not be clinically useful.

Conversely, after excluding data from control group individuals and patients with 1 myxopapillary ependymoma and 1 cavernous hemangioma, it was noted that the blood count and biochemistry analysis results of patients with intradural extramedullary spinal tumors were similar, except for leukocyte counts. Nevertheless, numerical evaluations indicated that leukocyte counts fell within average laboratory range values in this patient group, leading to the inference that these low values may not hold clinical significance. Additionally, correlation analysis on the data of spinal tumor patients revealed that the likelihood of a patient having a meningioma increased when leukocyte count, lymphocyte count, and serum sodium values were elevated. However, ROC-curve analysis and Logistic Regression analysis, which aimed at identifying parameters that could distinguish patients with schwannoma from those with meningioma, showed that none of these study parameters functioned as predictive markers for differential diagnosis of these spinal tumors.

Limitations

This study had several limitations. Firstly, it was retrospective, resulting in a small and non-homogeneous patient group. Consequently, the results obtained may be biased. Nonetheless, since these tumors are rare, a limited number of patients is expected. Secondly, histopathological examination images of the tumors could not be integrated into the study. Finally, the long-term follow-up results of the patients were excluded, as this was beyond the study's scope.

CONCLUSION

At the end of the study, it was concluded that the blood count and blood biochemistry analysis results could not be used to distinguish spinal tumors from healthy individuals in the clinic. It was also seen that these parameters could not be used to distinguish spinal schwannomas from meningiomas. On the other hand, it was argued that intradural extramedullary spinal tumors did not increase or decrease blood count and biochemistry results in patients. As a result, these tumors did not cause immunosuppression or an increase in a systemic inflammatory response, and did not have a detrimental effect on the functions of systemic organs.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was conducted after the approval of Kırıkkale University Non-interventional Clinical Researches Ethics Committee (Date: 12.03.2025, Decision No: 2025.02.34).

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

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Wernicke encephalopathy presenting with rare clinical findings: bilateral VI cranial nerve palsy and pontine lesion

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ABSTRACT

Wernicke encephalopathy (WE) is a serious acute neurological condition that is commonly associated with vitamin B1 (thiamine) deficiency due to alcohol abuse, albeit it can also occur in non-alcoholic settings. In cases with thiamine deficiency, WE is diagnosed by the presence of at least two of the classic clinical findings, including ophthalmoplegia, ataxic gait, and confusion. In this case report, we present a rare clinical manifestation of WE involving bilateral sixth cranial nerve palsy, ataxia, and pontine involvement on magnetic resonance imaging (MRI). A 36-year-old male patient presented with a five-day history of diplopia and a one-month history of hallucinations and insomnia. His medical history revealed chronic alcohol dependence, including recent consumption of homemade alcohol prior to the onset of symptoms. Neurological examination showed restricted lateral gaze in both eyes and an ataxic gait. Brain MRI (T2-weighted axial sections) demonstrated a hyperintense lesion in the midline of the pons. The patient was started on thiamine therapy at a dose of 500 mg/day for five days, followed by maintenance therapy with 200 mg/day for five days and then 100 mg/day for an additional five days. On neurological examination prior to discharge, right eye movements had normalized, while restricted lateral gaze persisted in the left eye. MRI findings in WE include involvement of the ventral thalamus, hypothalamus, mammillary bodies, periaqueductal region, and the floor of the fourth ventricle. Early parenteral thiamine administration remains the cornerstone of treatment. Our patient presented with bilateral sixth cranial nerve palsy and ataxia, along with a hyperintense signal in the midline of the pons on T2-weighted brain MRI. This case has been presented to highlight a rare clinical presentation of WE.

Keywords: Wernicke encephalopathy, diplopia, pontine lesion

INTRODUCTION

Wernicke encephalopathy (WE) is a serious acute neurological condition that is commonly associated with vitamin B1 (thiamine) deficiency due to alcohol abuse, albeit it can also occur in non-alcoholic settings.[1] While the prevalence of WE is estimated at approximately 2% in the general population, it is often underdiagnosed and undertreated. Reports suggest that up to 80% of cases are not identified until postmortem examination.[2,3] In cases with thiamine deficiency, WE is diagnosed by the presence of at least two of the classic clinical findings, including ophthalmoplegia, ataxic gait, and confusion. WE typically develops 4 to 6 weeks following the onset of thiamine deficiency, and the classic triad is observed in only 16–33% of patients during the early phase.[1] Timely recognition and treatment initiation are crucial. Untreated WE may result in irreversible brain damage or death.[3] In this case report, we present a rare clinical manifestation of WE involving bilateral sixth cranial nerve palsy, ataxia, and pontine involvement on magnetic resonance imaging (MRI).

CASE

A 36-year-old male presented with a five-day history of diplopia and a one-month history of hallucinations and insomnia. His medical history revealed no chronic illnesses. He had a history of chronic alcohol dependence and reported regular alcohol consumption on a weekly basis for the past 15 years, including recent intake of homemade alcohol prior to the onset of symptoms. On neurological examination, the patient was alert, cooperative, and oriented. Speech was normal, and there was no nuchal rigidity. Pupils were isocoric with normal light reflexes (+/+), and bilateral restricted lateral gaze was observed. There was no facial asymmetry; muscle strength was preserved; bilateral plantar reflexes were flexor. The patient's gait was ataxic. Cranial computed tomography (CT) and diffusion-weighted magnetic resonance imaging (MRI) revealed no abnormalities. Axial T2-weighted MRI images of the brain showed a hyperintense lesion in the midline of the pons (Figure 1, 2). The patient was admitted to the ward with a prediagnosis of WE. The patient was

started on thiamine therapy at a dose of 500 mg/day for five days, followed by maintenance therapy with 200 mg/day for five days and then 100 mg/day for an additional five days. On neurological examination prior to discharge, right eye movements had normalized, while restricted lateral gaze persisted in the left eye. The patient was referred to the physical therapy and rehabilitation clinic, where balance training was initiated to address ataxic gait. A psychiatric consultation was also obtained, and mirtazapine 15 mg once daily was added to the treatment regimen for insomnia. The patient was discharged on the 11th day with continued maintenance thiamine therapy.

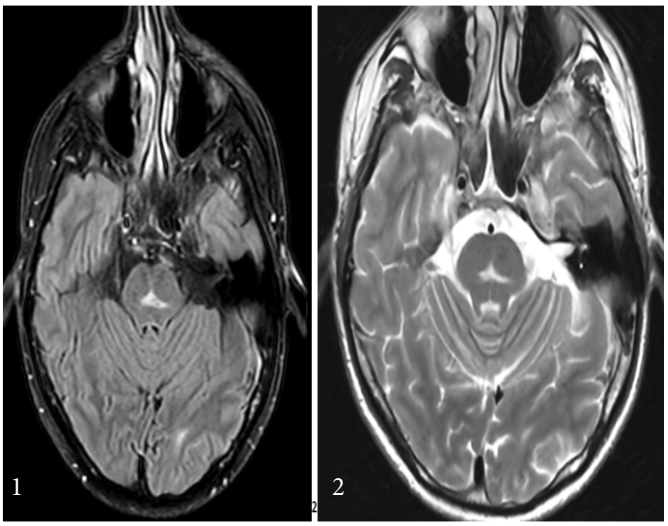

Figure 1, 2: Axial T2-weighted MRI images of the brain showed a hyperintense lesion in the midline of the pons

DISCUSSION

Although alcoholism accounts for approximately half of all cases and is the most common cause of thiamine deficiency in WE, other causes include hyperemesis gravidarum, uremia, starvation, hemodialysis, and a history of gastric surgery.[4] In our case, the patient had a history of chronic alcohol use. During the acute phase of WE, characteristic symptoms include mental status changes, ophthalmoplegia, and ataxia, while the chronic phase may involve Korsakoff syndrome (KS), which is characterized by amnestic disorders and confabulations.[5] Kuzume et al.[6] reported a rare case of WE diagnosed with bilateral sixth cranial nerve palsy, in which neurological symptoms improved following thiamine treatment. Similarly, our patient was diagnosed based on bilateral sixth cranial nerve palsy and ataxia, and symptom improvement was observed with thiamine therapy. MRI has a sensitivity of 53% and a specificity of 93% in the diagnosis of WE and is considered the standard imaging modality for confirming the diagnosis. On T2-weighted MRI, WE is suggested by hyperintense lesions in regions associated with high carbohydrate metabolism, most notably the ventral thalamus, hypothalamus, mammillary bodies, periaqueductal area, and the floor of the fourth ventricle.[7,8] Additional areas of involvement may include the cerebellum, dorsal medulla, pons, cranial nerve nuclei, red nucleus, dentate nucleus, putamen, caudate nucleus, fornix, splenium of the corpus callosum, and pre- and postcentral gyri.[7] In our case, a hyperintense signal change was observed in the midline of the pons on T2-weighted sequences. In a study involving 41 WE patients, MRI was performed on 36, and one-third of them demonstrated T2/FLAIR hyperintensities suggestive of WE. A normal MRI does not exclude the diagnosis of WE.[8] Early parenteral thiamine administration remains the cornerstone of treatment. The literature generally recommends intravenous thiamine at doses ranging from 200 to 500 mg every eight hours for at least several days; however, there is no definitive evidence regarding the optimal dose or duration of treatment.[9]

CONCLUSION

Our patient presented with bilateral sixth cranial nerve palsy and ataxia, along with a hyperintense signal in the midline of the pons on T2-weighted brain MRI. Parenteral thiamine therapy was initiated in accordance with approaches recommended in the literature, and improvement in ophthalmoplegic symptoms was observed. This case has been presented to highlight a rare clinical presentation of WE.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

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Third cranial nerve palsy as an initial presentation of tuberculous meningitis

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ABSTRACT

In this case report, we present a 54-year-old male patient diagnosed with tuberculousmeningitis after presenting with third cranial nerve palsy. Tuberculous meningitis is a rarebut potentially fatal infection in certain clinical conditions, and its diagnosis can bechallenging, especially when patients present with atypical symptoms. Early treatment is crucial,as delayed therapy may lead to a high risk of mortality. This case report highlights the importance of considering tuberculous meningitis in the differential diagnosis after excluding other common and life-threatening causes in the presence of atypical findings, such as third cranial nerve palsy. Prompt initiation of treatment is essential when there is clinical suspicion.

Keywords: Tuberculous, meningitis, abdusens

INTRODUCTION

Tuberculous meningitis (TBM) is a severe form of central nervous systemtuberculosis caused by *Mycobacterium tuberculosis*. It is characterized by a subacuteprogression and often presents with nonspecific symptoms such as fever, headache, andmalaise, which complicates early diagnosis[1,2].

CASE

A 54-year-old male was admitted to an outside facility with complaints of headache anddiplopia that began four days ago. On neurological examination at the outside facility, hisright eye had limited movements upward, downward, and toward the midline. Patient stated severe headache that originates from the right occipital region, radiating toward the right eye. He also reported severe right leg pain, the onset of which was simultaneous with that of the other symptoms. Brain computed tomography (CT), brain diffusion magnetic resonance imaging (MRI), brain and carotid CT angiography, and contrast-enhanced MRI were performed at the same external facility without eliciting pathological findings. After excluding ischemic stroke, cerebral hemorrhage, aneurysm, and cavernous sinus thrombosis, among other differential diagnoses, he was referred to us for further investigation and treatment.

The character of headache at admission to our department remained unchanged—severe pain originating from the right occipital region and radiating to the right eye. Photophobia, phonophobia, nausea, or vomiting did not accompany headache. During the neurological exam, there was a deviation in the right eye during spontaneous gaze. The patient initially presented with limitation of upward, downward, and inward movements of the right eye, accompanied by ptosis on the right side. Unfortunately, as photographs of the patient's initial presentation were not available, they could not be included in this report (Figure). Steroid and mannitol therapy was initiated, and improvement in the patient's right eye began on the 5th day of treatment, with complete resolution observed by the 11th day.The rest of the neurological examination was normal. In the patient's left eye, ptosis and limitation of inward, upward, and downward gaze developed on the 11th day. There was no evidence of meningeal irritation.

He was diagnosed with mantle cell lymphoma four years ago but has been in remission for the last two years without other pathologies. No signs of recurrence were detected in the patient by the department of hematology. Contrast-enhanced brain MRI and MR venography performed at our facility

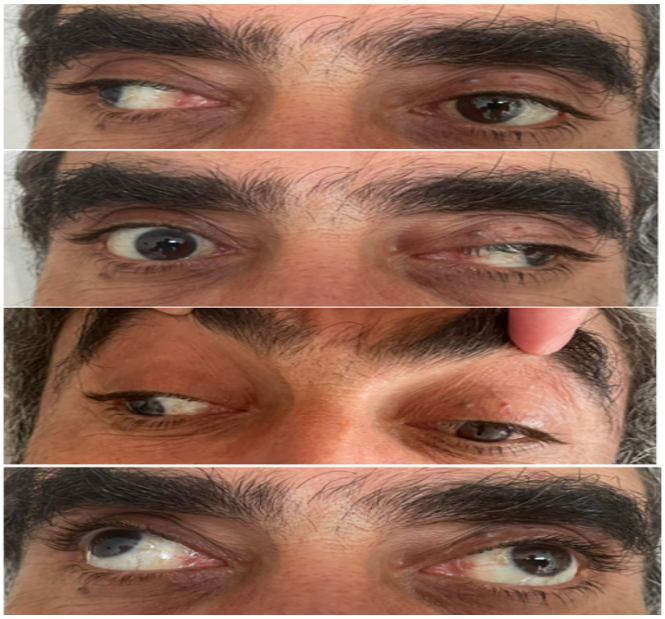

Figure. The right eye deviated outward in spontaneous gaze (1), and there was restriction of movement inward gaze (2), downward gaze (3), and upward gaze (4) in the right eye. Also, inward gaze (1)- downward gaze (3) and upward gaze (4) have been observed in the left eye. (This photo was taken on the 12th day after the first symptom appeared.)

also did not reveal pathological findings for aneurysm, or cavernous sinus thrombosis. The results of routine blood tests were in normal ranges. Fundoscopic examination was normal with no papilledema. A lumbar puncture was carried out which revealed increased cerebrosipinal fluid (CSF) pressure and protein level, with decreased CSF glucose (less than 50% of the simultaneously assayed plasma glucose). Additionally, 920 leukocytes and 70 erythrocytes per mm^3 were detected in the CSF (CSF opening pressure: 28 cmH_2O; CSF glucose: 45 mg/dl; simultaneous plasma glucose: 101 mg/dl; CSF protein: 166 mg/dl). No atypical cells were observed in the CSF pathology; it was reported as a lymphocyte-rich fluid.

The meningitis panel tests (*Cryptococcus gattii/neoformans*, *Listeria monocytogenes*, *Neisseria meningitidis, Streptococcus pneumoniae, Haemophilus influenzae, Streptococcus agalactiae, Escherichia coli* K1, Cytomegalovirus, Enterovirus, Human parechovirus, Varicella zoster virus, Herpes simplex virus 1, Herpes simplex virus 2, Human herpesvirus 7, Human herpesvirus 8, Human herpesvirus 6) performed on the CSF sample were found to be negative. Also, no growth was observed in the culture of the CSF sample and CSF histochemistry analyses showed no atypical cells. TBM was considered in the patient, and a QuantiFERON test was performed. The serum QuantiFERON-TB test resulted positive. The TBM medication was started on 1×300 mg isoniazid, 2×300 mg rifampin, 2×500 mg pyrazinamide, and 2×500 mg ethambutol. Additionally, intravenous steroid therapy was initiated at a dose of 1 mg/kg/day (total 80 mg) and was gradually tapered after 5 days.

The CSF results are presented in Table. In repeated lumbar punctures, a decrease in protein, glucose, opening pressure, and leukocyte count was observed. The patient was started on antiviral therapy (acyclovir 750 mg three times daily for 7 days)and mannitol therapy under the preliminary diagnosis of HSV. Following significant improvement in right eye adduction limitation and ptosis, the patient subsequently developed left eye ptosis and adduction limitation (complete third cranial nerve palsy) one day later. A third lumbar puncture was performed on the patient on the 11th day. Meningitis panel: *Haemophilus influenzae* (meningitis) detected as positive.

DISCUSSION

The diagnosis of TBM heavily depends on clinical presentation, imaging studies, and cerebrospinal fluid (CSF) analysis.[11] Imaging techniques, such as CT and MRI, can show basal meningeal enhancement, hydrocephalus, and tuberculomas, which are indicative of TBM.[3,4] However, in many cases, imaging may not reveal any abnormalities. In our case, no abnormal findings were observed in neuroimaging techniques.[11] On the other hand, the symptoms seen in TBM are not unique to this condition and can also occur in other types of meningitis, such as viral or fungal meningitis. These overlapping symptoms can complicate the diagnostic process.[6]

Cranial nerve involvement is quite common in TBM, and the reported prevalence varies widely depending on the patient population and the stage of the disease. Reported series indicate cranial nerve involvement rates ranging from 17% to 40%.[12-15] Among cranial nerves, the sixth cranial nerve (abducens) is most commonly involved in TBM, with reported involvement rates ranging from 20% to 40%, followed by the oculomotor (10%–30%), facial (5%–15%), and optic nerves (10%–20%).[12,13,15]

The examination of CSF is one of the important steps in diagnosing TBM. CSF analysis typically shows elevated protein levels, low glucose levels, and lymphocytic pleocytosis, which are critical for confirming the diagnosis.[4,5] In our case we also observed elevated protein levels, decreased glucose levels and lymphocytic pleocytosis.

Diagnosing TBM can pose challenges even to experienced clinicians. When patients present with headache and third cranial nerve palsy, as in our case, it is essential to first rule

Table. CSF analysis over time

Day	Opening pressure (n=6-20cmH_2O)	Leukocytes (n=0-5 mm^3)	Protein (mg/dl) (n=15-45 mg/dl)	Glucose (mg/dl) (n=50-80 mg/dl)	Albumin (n=10-30 mg/dl)	Na (n=142-150 mmol/L)	Cl (n=118-132 mmol/L)
Day 1	28	920	166.0	45	53.27	143	118
Day 5	23	250	167.31	32.6	52.57	143	119
Day 11	19	2000	261.16	28.6	44.29	141	120
Day 21	14	None	288.84	19.6	43.58	147	120

n: Normal range of variable, CSF: Cerebrospinal fluid

out other common and potentially fatal conditions such as ischemic stroke, intracranial hemorrhage, and cavernous sinus thrombosis. Once these possibilities are excluded, meningitis should be considered in the differential diagnosis. Neuroimaging should be conducted, and CSF analysis is indispensable for assessment. Besides routine CSF analysis, specific diagnostic tests for Mycobacterium tuberculosis, such as direct smear microscopy and polymerase chain reaction (PCR), should be performed.

In our case, these specific tests yielded negative results; however, other routine CSF analyses aligned with a diagnosis of TBM. Additional diagnostic tests, including the purified protein derivative (PPD) skin test and other evaluations to identify tuberculosis in other organs, can further support the diagnosis. Once TBM is confirmed, or if clinical suspicion is high, treatment should begin immediately without delay.

Treatment for TBM typically involves a prolonged course of antitubercular therapy, often paired with corticosteroids to reduce inflammation and manage complications like hydrocephalus.[4,7] Effective management of TBM is critical, as untreated cases can result in significant morbidity and mortality; studies report case fatality rates ranging from 15% to 68%.[8] Additionally, hydrocephalus, a common complication of TBM, may require surgical intervention to alleviate increased intracranial pressure.[9,10]

CONCLUSION

TBM is a rare but serious condition that may initially present with atypical neurological symptoms such as cranial nerve palsies in the absence of classical meningeal signs. This case emphasizes the vital importance of maintaining a high level of clinical suspicion for TBM in patients presenting with isolated third cranial nerve involvement, especially when neuroimaging does not reveal common vascular or structural pathologies.

In our case, the absence of radiological findings and negative CSF microbiological tests initially complicated the diagnostic process. However, the characteristic CSF findings—lymphocytic pleocytosis, elevated protein, and low glucose—when evaluated together with the clinical course and auxiliary tests such as PPD and QuantiFERON, allowed for a presumptive diagnosis of TBM and timely initiation of antitubercular treatment.

Early diagnosis and prompt treatment of TBM are crucial for reducing long-term neurological sequelae and mortality. This case highlights the necessity of initiating empirical treatment in suspected TBM cases based on clinical judgment supported by laboratory data, without waiting for definitive microbiological confirmation.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

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Arnold-Chiari malformation: a case report

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ABSTRACT

Arnold-Chiari or simply Chiari malformation is the name given to a group of deformities of the posterior fossa and hind brain (cerebellum, pons and medulla oblongata). Chiari I is the least severe and is often found incidentally. It is characterized by one or two pointed (not round) cerebellar tonsil sprotruding 5 mm below the foramen magnum, measured by a line drawn from the basion to the opisthion (McRaeLine). Headache is the most common presenting symptom (60-70%) in CIM cases. It is typically localized to the occipital and/or upper cervical region. The pain is usually paroxysmal and of short duration following Valsalva maneuvers such as coughing, sneezing, laughing, straining. Syringomyelia is observed in 30-70% of CIM patients due to disruption of CSF. Dynamics and progressive scoliosis in some of them. Syringomyelia is most commonly found in the cervical region.

Keywords: Arnold-Chiari malformation, headache, syringomyelia

INTRODUCTION

Arnold-Chiari or simply Chiari malformation is the name given to a group of deformities of the posterior fossa and hind brain (cerebellum, pons and medulla oblongata). Problems range from cerebellar tonsillar herniation through the foramen magnum to absence of the cerebellum with or without other associated intracranial or extracranial defects such as hydrocephalus, syrinx, encephalocele or spinal dysraphism.[1-3]

Chiarimal formations are classified according to the irmorphology and severity of anatomical defects, usually by imaging (orautopsy). Chiari I is the least severe and is often found incidentally. It is characterized by one or two pointed (not round) cerebellar tonsil sprotruding 5 mm below the foramen magnum, measured by a line drawn from the basion to the opisthion (McRaeLine). Chiari II consists of a brain stem herniation and an ascending cerebellum in addition to herniated cerebellar tonsils and vermis due to an open distal spinal dysraphism/ myelomeningocele. Chiari III is a herniation of the hind brain (cerebellum with or without brain stem) into a low occipital or high cervical meningoencephalocele. Chiari IV is now considered obsolete.[4] Before it became an outdated diagnosis, it was a more controversial and rare variant showing severe cerebellar hypoplasia similar to primary cerebellar agenesis. Previously, some have stated that myelomeningocele may be present.[5] While others have argued that the presence of myelomeningocele should be classified as a Chiari II with a vanishing cerebellum.[6] In this case report, we wanted to present a case of Arnold Chiari type 1 who presented with headache and weakness in both upper extremities.

CASE

A 33-year-old patient who has been describing occasional blunt pain in the nape of the neck for about 2 years states that the pain increas esespecially when leaning forward or coughing. He states that the pain has become more frequent in the last 3-4 months and is in the form of a feeling of pressure in the back of the head. He also complained of dizziness, imbalance and occasional ting

Ling and numbness in his hands. In the last 1 month, she has noticed a decrease in fine motor skills (such as difficulty in buttoning buttons). The patient stated that he was sometimes unable to urinate completely and had a feeling of tightness and applied to the urology outpatient clinic with these complaints. No pathology was detected in the urologic evaluation and symptomatic treatment was given but the patient did not benefit.

Neurological Examination

Cranial nevre examination: Normal

Eye movements free in both directions

Direct light reflex/indirect light reflex ++/++

Both upper extremities proximal 4/5, distal 3/5 motor strength

Low erextremity motor examination is normal (5/5)

DTR increased in upper extremities

Bilateral Hoffmann +/+

DTR normal in lower extremities, no pathologic reflexes

Romberg test +

Finger-nose test mildly dysmetric

Segmental decrease in pain and heat sensation (especially in C5-C8 dermatomes)

Mild antalgic gait was observed.

Preoperative cervical MRI image of the patient: Syringomyelia continuing from C2 level to T2 level was observed (Figure 1).

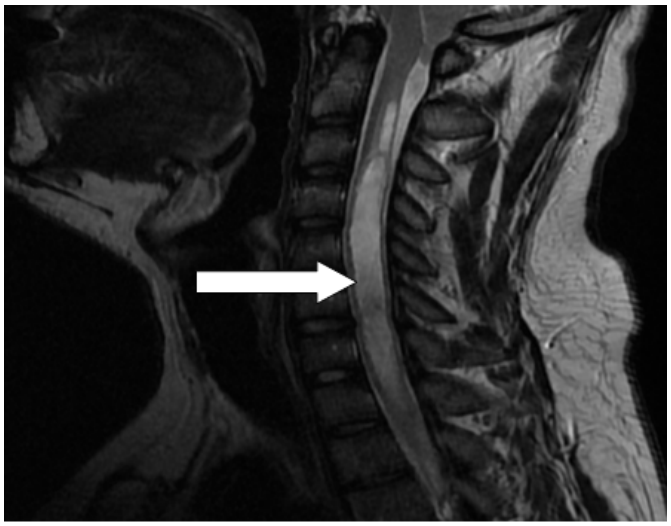

Figure 1. Preop cervical MRI. Sagittal T2 MRI.The patient's cervicothoracally located syrinx is indicated by the whitearrow.
MRI: Magnetic resonance imaging

Postoperative cervical MRI image of the patient: Syringomyelia starting from the C4 level and extending to the C7 level was observed (Figure 2).

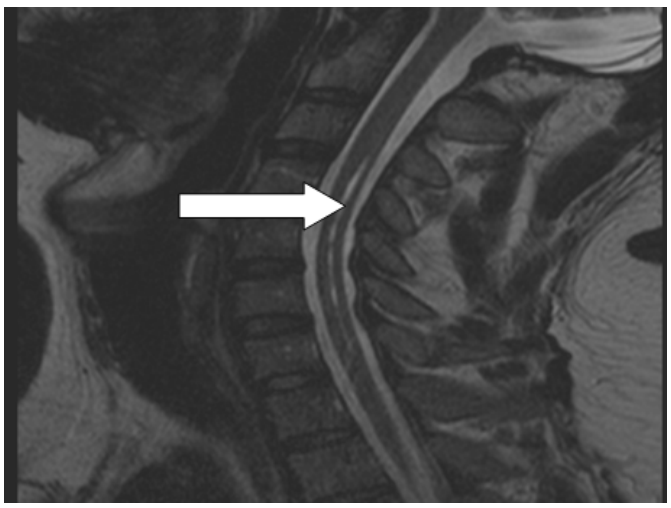

Figure 2. Postoperative cervical MR image Sagittal T2 MR image of the patient's cervicothoracic region with markedly decreased syrinx
MRI: Magnetic resonance imaging

DISCUSSION

Arnold-Chiari or simply Chiari malformation is the name given to a group of deformities of the posterior fossa and hind brain (cerebellum, pons and medulla oblongata). Chiari I is the least severe and is often found incidentally. It is characterized by one or two pointed (not round) cerebellar tonsil sprotruding 5 mm below the foramen magnum, measured by a line drawn from the basion to the opisthion (McRaeLine).[9]

In most cases, the volume of the posterior fossa is small. Syringomyelia in CM1 results from the cerebellar tonsils blocking normal CSF flow through the foramen magnum during the cardiac cycle. Surgical removal of the obstruction to CSF flow results in resolution of the syrinx.[10]

Early observations by Chiari and others suggested a common mechanism of cerebellar ectopia and cerebrospinal fluid disorders (e.g., hydrocephalus and syringomyelia). Critical animal studies by Dorcus Padget advanced our understanding of the embryologic basis of CMI-IV and its relations hiptodysraphism, as in the more severe Chiari malformations and Dandy-Walker malformation.[10] Further studies by Miguel Marín-Padilla supported that these malformations (CMI-IV, Dandy-Walker malformations and various forms of dysraphism) result from various disorders of neuraxial induction.[11]

The most common presentation in Chiari I malformation is suboccipital headaches and/or neck pain (80%). Symptoms are exacerbated when asked to perform the Valsalva maneuver. Other common presentations include eye disorders, auto neurologic symptoms (dizziness, hearing loss, vertigo), gait ataxia and generalized fatigue. Although much less common, the literature reports numerous case studies where patients present with isolated limb pain or weakness, one such report involves the presentation of unilateral shoulder pain with isolated muscle weaknessto a sports medicine clinic.[12]

Myelopathy classically presents with “discrete sensory loss” (loss of pain and temperature sensation, preserved fine touch and proprioception) and motor weakness.[13,14]

Cerebellar findings such as ataxia, dysmetria and nystagmus and lower cranial nevre deficits (IX, X, XI, XII CN) are caused either by direct compression of the cerebellum or medulla in the foramen magnum or by syringomyelia or syringobulnia.

Sleep apnea may occur in a patient with Chiari malformation due to weakness in the pharyngeal muscles caused by compression of the brainstem, upper spinal cordor lower cranial nerve.[15]

CONLUSION

We need to exclude some conditions that come with a clinical presentation similar to Arnold Chiari-like. Intracranial hypotension –may mimic midbrain prolapse, cerebellar tonsilor posterior brain herniation. Normal variant cerebellar tonsil ectopia -does not meet the criteria for Chiari malformation and is an incidental finding in an asymptomatic patient. Cerebellar tonsillar herniation caused

by increased intracranial pressure (ICP)-ICP causes such as neoplasm, hydrocephalus, mass effect from trauma or hemorrhage should be evaluated.

With early diagnosis and close follow-up in Arnold chiari malformation, we can make the correct diagnosis and maximize the patient's life standard with surgical operation at the most appropriate time.

ETHICAL DECLARATIONS

InformedConsent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Letter to the Editor

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Neurobiobanking in Africa: Accelerating stroke care equity, curation and research—a functional approach

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ABSTRACT

Neurobiobanking—the systematic collection, processing, and storage of central nervous system (CNS) tissues and associated data—holds immense promise for elucidating the genetic, molecular, and environmental determinants of stroke. In Africa, where stroke incidence is rising, age of onset is younger, and outcomes are poorer than in high-income settings, region-specific neurobiologic repositories can drive equitable research and tailored interventions. Despite significant advances through precision healthcare initiatives like H3Africa and the National Health Laboratory Service (NHLS) National Biobank, most countries still grapple with funding shortfalls, infrastructure gaps, trained personnel inadequacy and schismic regulatory frameworks. This focused communication outlines the current visage of neurobiobanking in Africa, showcases its critical role in addressing the continent's huge stroke burden, and proposes actionable strategies to establish inclusive, ethically governed, and sustainable neurobiobank networks.

Keywords: Neurobiobanking, Africa, stroke care

Dear editor,

We bring to your attention a topic of prospective and active significance.

INTRODUCTION

Biobanking, defined as the organized collection, assessment, storage, and sampling of biological specimens linked to rich clinical and demographic data, is pivotal for biomedical research.[1] Neurobiobanks extend this paradigm to CNS tissues—whole brains, sections, neural fluids—and integrate imaging and clinical datasets, enabling insights into neurological disorders, including stroke.[2] Globally, stroke remains a leading cause of mortality and disability; sub-Saharan Africa exhibits some of the world's highest age-adjusted prevalence rates, with hemorrhagic strokes accounting for 29–57% of cases and a notably younger age of onset compared to other populations.[3] These disparities underscore the urgent need for African-centric neurobiobank resources to inform equitable stroke care.

Current State of Biobanking in Africa

Pan-African genomic initiatives: The Human Heredity and Health in Africa (H3Africa) consortium, launched in 2012 by the NIH and Wellcome Trust, has established genomic research hubs and bioinformatics networks across 30 countries, training hundreds of African scientists and generating continent-specific genomic data.[4]

National biobank leadership: South Africa's National Health Laboratory Service (NHLS) houses a premier National Biobank—ISO-certified in 2019—which archives serum, plasma, DNA, histological slides, and more under robust quality-management and ethical governance frameworks.[5]

Persistent Challenges

Yet, most African nations face constrained budgets, intermittent power and cold-chain infrastructure, and a dearth of trained biobank personnel.[6] Fragmented or outdated ethical and regulatory guidelines further hinder harmonized governance, risking exploitative "parachute research" and undermining local trust.[7] Simultaneously, awareness of

biobanks' translational value is growing, as evidenced by increased stakeholder engagement through networks like MBirSA.[8] Furthermore, there is the place of policymaking and public apathy towards credible interventions - which is most likely fueled by ethico-moral inclinations and biases.

Importance of Neurobiobanking for Stroke Treatment

With sub-Saharan Africa's stroke incidence climbing, and case fatality and disability rates exceeding those in high-income settings, robust neurobiobanking can reveal genetic and environmental risk factors unique to African populations.[9] Most stroke genomics research to date has centered on European ancestry cohorts, leaving vast knowledge gaps for continental Africans.[10] Neurobiobank-driven discovery of novel biomarkers—such as plasma VEGF levels—and population-specific risk loci promises precision prevention and targeted therapeutics.[11] Beyond science, these repositories foster equitable collaborations, retain local expertise, and ensure that African patients benefit directly from research conducted on their samples.[11,12] A typical example of this is the McGill's university Neuro Research Open Biobank Repository, depicted below-Figure.[13]

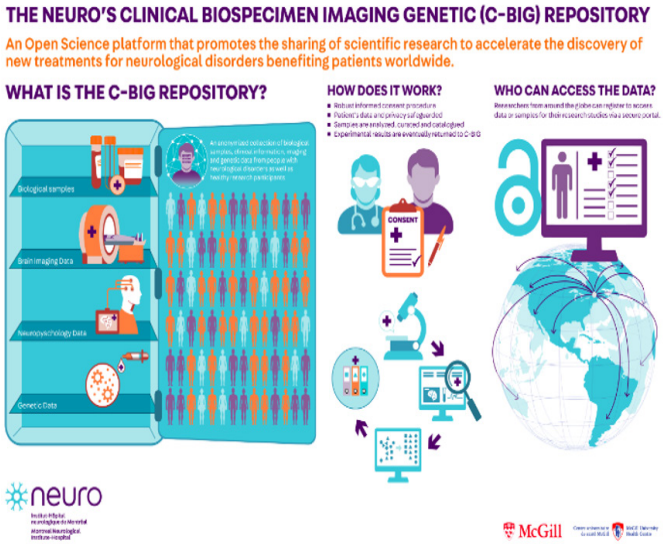

Figure: The schematic illustration of the Neuro C-BIG repository, McGill University, Canada[13] Open Biobank (research). The Neuro. Available from: https://www.mcgill.ca/neuro/research/open-biobank/research © 2025 by McGill University is licensed under CC BY-NC 4.0

Recommendations for Equity-Driven Neurobiobanking

1. Regional Neurobiobank Hubs: Governments, the African Union, and WHO-AFRO should mandate neurobiobanking as a health priority, establishing multi-country hubs modeled on H3Africa, with seed funding from NIH, Wellcome, and African development banks.

2. Sustainable funding streams: Global funders must earmark non-communicable disease grants to include neurobiobanking components. Intra-continental partnerships (e.g., Africa-India) can pool resources and reduce costs.

3. Capacity building: Leverage institutions such as the African Academy of Neurology for specialized training in biobank management, genomic analysis, and neuroethics. Deploy mobile laboratories and drone logistics to bridge rural infrastructure gaps.

4. Community engagement and governance: Co-develop consent models and benefit-sharing plans with local leaders to build trust and ensure reciprocal benefits, avoiding extractive research practices.

5. Technology and innovation: Integrate AI for data management, blockchain for secure sharing, and renewable-energy-powered freezers to ensure sustainable storage in low-resource settings.

6. Inclusive global collaboration: Journals and consortia should require representation of African neurobiobank data and authorship, with data-sharing policies that protect local ownership while facilitating open science.

CONCLUSION

Neurobiobanking represents a transformative strategy to confront Africa's disproportionate stroke burden. By bolstering infrastructure, harmonizing governance, and fostering equitable partnerships, Africa can generate critical insights into stroke pathophysiology, tailor interventions to its populations, and advance global precision medicine. The neurology and public health communities must unite to ensure that African voices, samples, and researchers are integral to the future of stroke research and care.

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Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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