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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

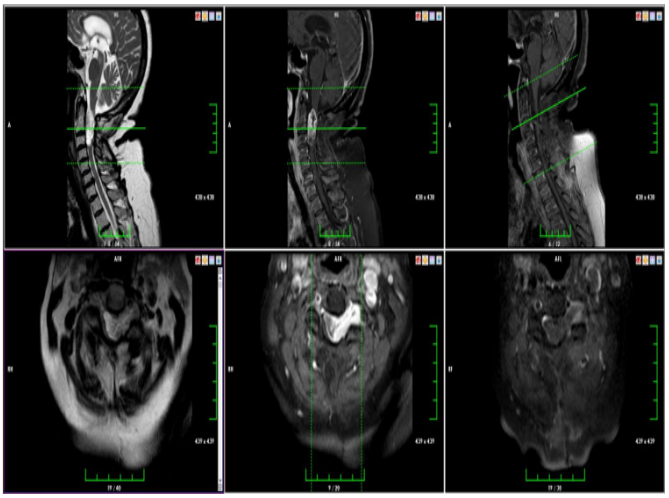

Figure 1. In the cervical MR images taken before surgery, an hourglass-shaped schwannoma extending to the left C2-3 neural foramen at the level of the C2 vertebra is seen. It can also be observed in these images that the tumor was completely removed after surgery

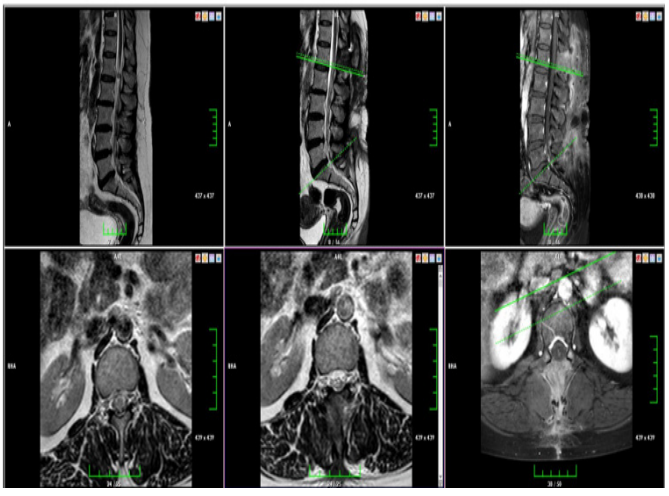

Figure 2. In the lumbar MR images taken before surgery, a schwannoma located in the midline and at the tip of the conus medullaris at the level of the L1 vertebra is seen. It can also be observed in these images that the tumor was completely removed after surgery

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).

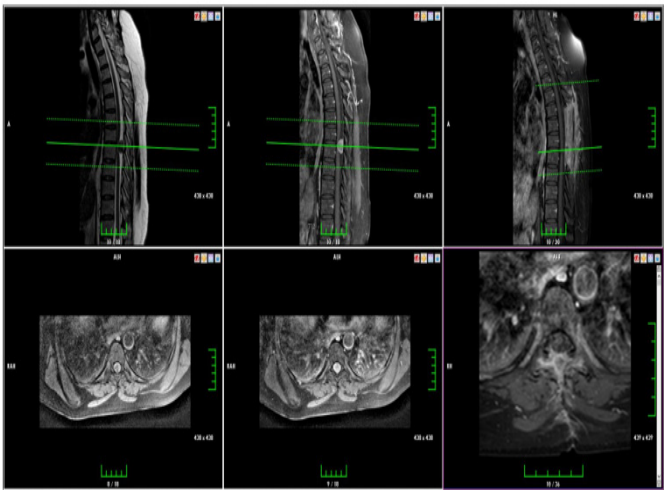

Figure 3. In the thoracic MR images taken before surgery, a meningioma located in the midline at the level of the T8-9 vertebra is seen. It can also be observed in these images that the tumor was completely removed after surgery

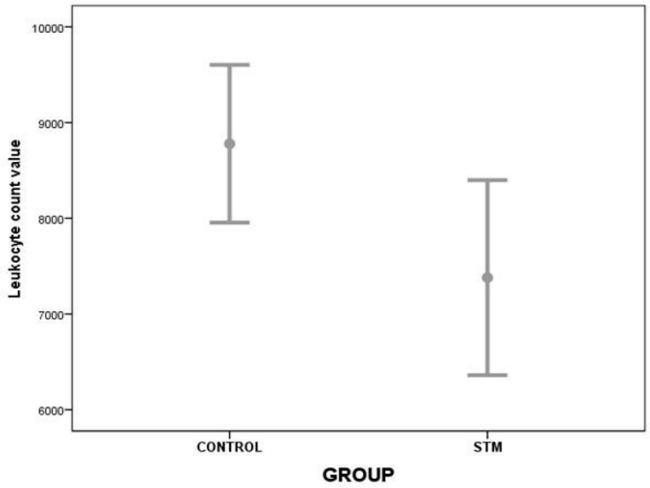

Figure 4. Each error bar shows the lymphocyte count value of the patients and healthy individuals

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).

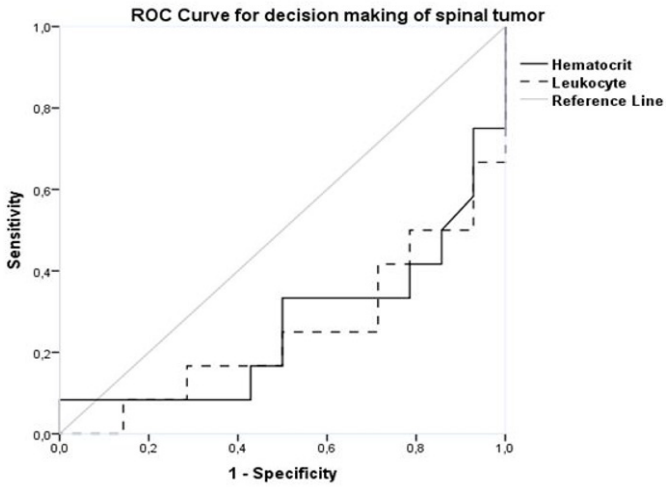

Figure 5. The ROC-curve graph shows the predictive biochemical parameters that may distinguish patients with intradural extramedullary spinal tumors from healthy subjects

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

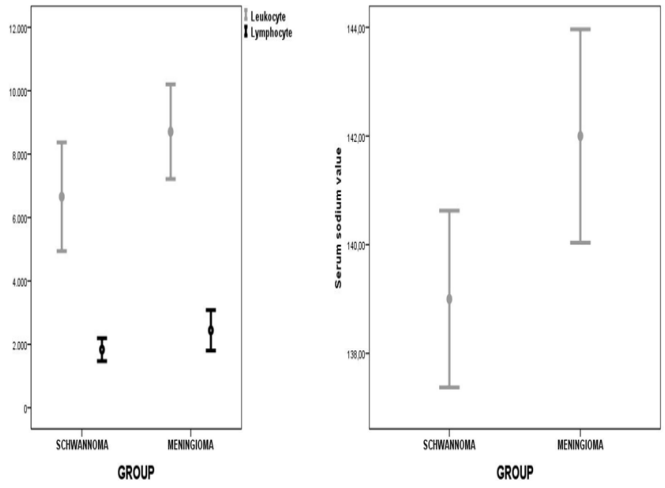

Figure 6. Each error bar shows the leukocyte and lymphocyte count values and serum sodium values in patient groups

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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