



Comprehensive Evaluation of Acute Transverse Myelitis Spectrum Disorders: A Retrospective Analysis of 52 Patients

Akut Transvers Miyelit Spektrum Hastalıklarının Kapsamlı Bir Değerlendirmesi: 52 Hastanın Retrospektif Analizi

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Abstract

Objective: Acute transverse myelitis (ATM) is defined as focal inflammation of the spinal cord, which may be idiopathic or secondary to an infection or systemic disease without cord compression. In this study, we aimed to evaluate the clinical, radiological, and etiological findings of patients who were diagnosed with ATM. **Materials and Methods:** Fifty-two patients who were diagnosed with ATM in our clinic between January 2015 and June 2022 and continued regular follow-up were included in the study. Demographic data, results of the serum and cerebrospinal fluid (CSF) analyses, and spinal imaging features of the patients were retrospectively recorded. Patients were divided into two groups according to their etiology: idiopathic ATM (iATM) and secondary ATM (sATM).

Results: A total of 52 patients, of whom 36 (69.2%) were women and 16 (30.8%) were men, were included in the study. The mean age of the patients was 40.27 \pm 14.44 years, and the mean follow-up period was 2.68 \pm 1.93 years. Of the 52 patients, 37 (71.1%) were evaluated as sATM and 15(28.9%) as iATM. A total of 24 (46.4%) patients were diagnosed with multiple sclerosis, and one patient (1.9%) was diagnosed with ATM due to infection. There was no statistically significant difference in clinical findings between the iATM and sATM groups. There was also no significant difference between the groups in the CSF analysis. Although three patients had aquaporin-4 antibody positivity, oligodendrocyte glycoprotein antibody was positive in only one patient. Cervical region involvement (most commonly between C4 and C6) was observed in 41 (78%) patients. Longitudinal extensive myelitis was seen in 43.2% of the sATM group and 26.7% of the iATM group, but there was no significant statistical difference between them. Six (11.5%) patients required admittance to the intensive care unit and one (1.9%) required mechanical ventilation. One patient died from pneumonia 6 months after being discharged from the hospital.

Conclusion: ATM is a rare neurological disorder that has a high risk of morbidity. Therefore, differential diagnosis and rapid treatment, arranged according to the underlying process, play important roles in the recovery period.

Keywords: Transverse myelitis, spinal cord diseases, multiple sclerosis, neuromyelitis optica spectrum diseases

Öz

Amaç: Akut transvers miyelit (ATM), spinal korda kompresyon olmaksızın gelişen, idiopatik, enfeksiyöz veya sistemik hastalığa ikincil olarak ortaya çıkabilen, omuriliğin fokal enflamasyonu olarak tanımlanır. Bu çalışmamızdaki amacımız ATM tanısı ile izlediğimiz olguların klinik, radyolojik ve etiyolojik bulgularını değerlendirmektir.

Gereç ve Yöntem: Çalışmaya Ocak 2015-Haziran 2022 tarihleri arasında ATM ön tanısı ile kliniğimizde izlenen ve düzenli takipleri devem edilen 52 hasta alındı. Hastaların demografik verileri, serum ve beyin omurilik sıvısı (BOS) analizleri, spinal görüntülemeleri retrospektif olarak kayıt edildi. Hastalar etiyolojilerine göre idiyopatik ATM (iATM) ve sekonder ATM (sATM) şeklinde iki gruba ayrılarak karşılaştırıldı.

Bulgular: Çalışmaya 36'sı kadın (%69,2), 16'sı erkek (%30,8) toplam 52 hasta dahil edildi. Yaş ortalamaları 40,27 \pm 14,44, ortalama takip süreleri 2,68 \pm 1,93 yıl idi. Elli iki hastanın 37'si (%71,1) sATM, 15'i (%28,9) iATM olarak değerlendirildi. Yirmi dört (%46,4) hasta multipl skleroz, bir (%1,9) hasta enfeksiyona ikincil ATM tanısı aldı. iATM ve sATM grupları arasında klinik bulgular açısından anlamlı istatistiksel farklılık saptanmadı. BOS incelemesinde gruplar arasında anlamlı farklılık bulunmadı. Üç hastada akuaporin-4, bir hastada miyelin oligodendrosit glikoprotein antikoru pozitif bulundu. Kırk bir (%78) hastada servikal

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[©]Copyright 2023 by the Turkish Neurological Society / Turkish Journal of Neurology published by Galenos Publishing House. Licensed by Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 (CC BY-NC-ND) International License. bölge tutulumu (en sık C4–C6 arası) gözlendi. Uzun segment miyelit, sATM grubunda %43,2 oranında iATM grubunda ise %26,7 oranında görüldü, ancak gruplar arasında anlamlı istatistiksel farklılık saptanmadı. İzlemde altı (%11,5) hastanın yoğun bakım, bir (%1,9) hastanın da mekanik ventilatör ihtiyacı gelişti. Bir hasta taburculuk sonrası izleminin altıncı ayında pnömoni nedeniyle eksitus oldu.

Sonuç: ATM nadir görülen, morbidite olasılığı yüksek olan bir nörolojik hastalıktır. Bu nedenle, ayırıcı tanı ve altta yatan sürece göre düzenlenmiş hızlı tedavi iyileşme sürecinde önemli rol oynamaktadır.

Anahtar Kelimeler: Transvers miyelit, omurilik hastalıkları, multipl skleroz, nöromiyelit optika spektrum hastalıkları

Introduction

Acute transverse myelitis (ATM) is a syndrome characterized by acute or subacute spinal cord dysfunction (1,2,3,4,5). Clinical symptoms may vary depending on the level of damage to the spinal cord and often include severe back pain, weakness, numbness, difficulty controlling the bowel or bladder, muscle spasms, and breathing problems. It may present with conditions characterized by motor, sensory, and autonomic dysfunctions secondary to spinal cord injury (3). Etiologically, ATM may develop due to idiopathic or secondary causes, including infectious, paraneoplastic, vascular, toxic, systemic autoimmune disorders, and acquired demyelinating diseases. It may also occur as a part of central nervous system diseases, such as neuromyelitis optica spectrum diseases (NMOSDs), anti-myelin oligodendrocyte glycoprotein (MOG)-associated diseases (MOGAD) or typical multiple sclerosis (MS) (1,2,3). All subtypes of ATM are rare neurological diseases. Although the general prevalence of idiopathic ATM (iATM) is not exactly known, it has been reported as 7.9 per 100,000 in a recent epidemiological study (4). iATM is responsible for approximately 50% of transverse myelitis cases; however, this rate may vary ethnically and geographically (1).

Definitive diagnosis of myelitis is based on clinical findings and confirmation of inflammation through laboratory and imaging studies. ATM is an intensively researched disease because it is highly idiopathic. Research on ATM aims to provide more information about the etiology, prognosis, treatment, and prevention of the disease. Our aim in this study was to evaluate the clinical, radiological, and etiological findings of patients diagnosed with ATM in the light of the literature.

Materials and Methods

Patients aged >18 years who were admitted to the University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital, Neurology Clinic with first-episode myelitis between January 2015 and June 2022 and were followed up with a diagnosis of ATM were included in the study. Patients with degenerative spinal cord disease, myelopathy, or intramedullary neoplasia, and patients with NMOSD, MOGAD, or MS who presented with a myelitis attack were excluded from the study. Demographic data, such as age, gender, clinical findings at admission to the hospital, and the time between the onset of symptoms and admission to the hospital, were recorded retrospectively. Patients with ATM that developed within 4 hours were considered to have acute onset ATM and patients with ATM that developed between 4 hours and 21 days were considered to have subacute onset ATM. Neurological disorders resulting from ATM were examined under the headings of sensory, motor, and sphincter dysfunction. A loss of function in all three areas was considered complete ATM, and a loss of function in any or both of these areas was considered incomplete ATM.

Protein level, cell count, oligoclonal band (OCB) positivity, immunoglobulin G (IgG) index, and viral serology {human immunodeficiency virus (HIV), cytomegalovirus (CMV), hepatitis A, B, C, herpes simplex virus (HSV) 1/2, varicella zoster virus (VZV)] findings of the patients who underwent cerebrospinal fluid (CSF) examination were analyzed. The formation of immunoglobulin M (IgM) in serum and/or CSF was considered a positive viral serology. The vasculitis markers aquaporin 4 IgG (AQP-4) and MOG antibody test results were recorded.

Patients with spinal magnetic resonance imaging (MRI) were included in the study. The MRI images were examined retrospectively by two neurologists. The involvement of three or more vertebral segments in MRI on sagittal spinal T2 sequences was considered to be long extensive transverse myelitis (LETM). The location of the lesions in the longitudinal and transverse planes and their location in the spinal cord and affected region of the medulla spinalis were evaluated. The number of lesions and their distribution within the spinal cord were examined. Lesion localizations in the cervical (C), thoracic (T), and lumbar (L) regions were recorded. Patients whose etiological cause was not detected during follow-up were classified as having iATM; patients with infectious, vascular, inflammatory, or autoimmune pathology were classified as having secondary ATM (sATM), and clinical and imaging features were compared between the groups.

The study was conducted in accordance with the ethical standards of the Declaration of Helsinki, and the study was approved by the University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital, Non-Interventional Research Ethics Committee (number: 2022/12-33, date: November 1, 2023).

Statistical Analysis

Statistical analyses were performed using the IBM-SPSS 25.0 statistical package program. The suitability of the data for normal distribution was examined using the Shapiro–Wilk test. Descriptive summary statistics were expressed as mean \pm standard deviation and/or median (minimum–maximum) for continuous variables and frequency and percentage for categorical variables. The relationship between categorical data was evaluated using the chi-squared test. The Mann–Whitney U test was used to compare the means of two groups in data that did not comply with normal distribution. The statistical significance level was accepted as P < 0.05.

Results

A total of 52 patients, of whom 36 (69.2%) were women and 16 (30.8%) were men, were included in the study. The average age of the patients was 40.27 ± 14.44 years, and the average followup period after the first clinical finding was 2.68 ± 1.93 years. Although an etiological diagnosis was reached in 71.1% of the patients, no known cause was detected in 28.9%. During their follow-up, 24 (46.4%) of the patients who presented with their first myelitis attack were diagnosed as having MS, and three (9.6%) were diagnosed as having NMOSD. ATM due to infection was detected in one (1.9%) patient, and the causative agent was found to be VZV. Nine (17.3%) patients had isolated motor findings, and 16 (30.8%) patients had sensory and motor findings. Sphincter dysfunction was found in 17.3% of the patients. There was no significant difference between the groups in terms of clinical findings (P > 0.05). The etiological distribution during the follow-up of the patients is shown in Figure 1.

Of the patients diagnosed as having iATM, 10 (66.7%) were female and five (33.3%) were male. The mean age in patients with iATM was 34.13 ± 11.71 years and was statistically lower than in the sATM group (P = 0.034). There was no significant difference between the two groups in terms of the time between the onset of symptoms and admission to the hospital (P = 0.509). In patients with iATM, 66.7% had acute and 33.3% had subacute clinical onset. Sphincter dysfunction was detected in 13.3% of the patients. Regarding spinal cord involvement, six (40%) of the patients with iATM had complete involvement and nine (60%) had incomplete involvement.

The average age of the 37 patients diagnosed as having sATM, of whom 26 (70.3%) were female and 11 (29.7%) were male, was 42.76 \pm 14.82 years. There was no significant difference between the groups in terms of gender distribution (P = 0.799). Incomplete involvement was observed in 48.6% of the patients in this group. Isolated motor symptoms were detected in seven (18.9%) patients, and combined sensory and motor symptoms were detected in 12 (32.4%) patients. Sphincter dysfunction was detected in 18.9% of the patients. Demographic and clinical data of the patients are presented in Table 1.

Lumbar puncture was performed in 48 (92.3%) of the patients. The CSF protein level was 42.7 \pm 18.7 g/dl in the sATM group and 47.4 \pm 24.4 g/dL in the iATM group. There was no statistically significant difference between the two groups (*P* = 0.552). OCB positivity was observed in 65% of patients with



ATM ETIOLOGICAL CAUSES

• MS • NMOSD • Sarcoidosis • MOGAD • VZV myelitis • iATM

Figure 1. Etiological distribution of all patients with acute transverse myelitis

ATM: Acute transverse myelitis, MS: Multiple sclerosis, NMOSD: Neuromyelitis optica spectrum diseases, VZV: Varicella zoster virus, iATM: Idiopathic acute transverse myelitis sATM. Considering the OCB types of these patients, 18 (85.7%) were compatible with type II, two (9.5%) were with type III, and one (4.8%) was compatible with type IV. While AQP-4 antibody positivity was detected in three (5.8%) patients, MOG antibody positivity was found in one (1.9%) patient. The laboratory and imaging findings of the patients are presented in Table 2.

LETM was found in 44.7% of the patients with iATM and 26.7% of the patients with sATM. Lesion localization was observed in the C4–C6 spinal segments in the cervical region and T4–T7 spinal segments in the thoracic region. The most common site of ATM involvement was the cervical region (78%). No statistically significant difference was detected between the groups in terms of lesion location and length (P = 0.266) (Table 2). Lesion localizations are shown in Figure 2.

The initial treatment in all patients was 1000 mg/day of intravenous methylprednisolone (7-10 days). After corticosteroid (CS) treatment, eight (13.5%) patients received plasmapheresis (PE) and three (5.8%) patients received intravenous immunoglobulin (IVIg) treatment. During follow-up, six (11.5%) patients required hospitalization in the intensive care unit (ICU) and one (1.9%) patient required mechanical ventilator support due to pneumonia (Figure 3). Of the six patients who were monitored in the ICU and underwent PE, five (83.3%) were female and one (16.7%) was male, and their average age was 47.0 ± 25.75 years. Four of the patients were monitored in the ICU because of severe hypotension that occurred during PE, one due to bradycardia and one due to hospital-acquired pneumonia (Figure 4). Two patients were diagnosed as having AQP-4 antibody-positive NMOSD, and one patient was diagnosed as having MS during follow-up. Although no death was observed in any of our patients during hospital follow-up, one patient died due to pneumonia in the third month after discharge.

Table 1. Demographic and clinical data of the patients				
	iATM	sATM	P *	
Age (years)	34.13 ± 11.71	42.76 ± 14.82	0.034	
Gender (F/M)	10/5	26/11	0.799	
Average follow up time (years)	2.34 ± 1.84	2.81 ± 1.97	0.430	
Type of initiation n, (%)				
Acute	10 (66.7)	21 (56.8)	0.509	
Subacute	5 (33.3)	16 (43.2)		
Clinical findings (%)				
Incomplete involvement	9 (60)	18 (48.6)	0.226	
Complete involvement	6 (40)	19 (51.4)		
Motor findings	2 (13.3)	7 (18.9)		
Sensory findings	9 (60)	18 (48.6)	0.993	
Sensory + motor	4 (26.7)	12 (32.4)		
Sphincter involvement (%)				
Yes	2 (13.3)	7 (18.9)	0.485	
No	13 (86.7)	30 (81.1)		

*Mann-Whitney U test; chi-squared (χ^2) test, F: Female, M: Male, iATM: Idiopathic acute transverse myelitis, sATM: Secondary acute transverse myelitis



Figure 2. Localization of lesions identified through magnetic resonance imaging in all patients with acute transverse myelitis

Table 2. Laboratory and imaging findings of the patients				
	iATM	sATM	p *	
LP (%)				
Performed	12 (80)	36 (97.3)	0.067	
Not performed	3 (20)	1 (2.7)		
CSF (%)				
OCB (+)	0	21 (65.6)	0.001	
OCB (-)	11	11 (34.4)		
Protein	42.7 ± 18.7	47.4 ± 24.4	0.552	
IgG index	0.69 ± 0.69	0.99 ± 0.59	0.194	
Anti-NMO (%)		3 (5.8)		
Anti-MOG (%)		1 (1.9)		
Localization in MRI				
Cervical	11 (73.3)	20 (52.7)	0.608	
Thoracic	4 (26.7)	17 (44.7)	0.199	
Lumbar	0	1 (2.6)	0.520	
Leison length				
<3 segments	11 (73.3)	21 (56.8)	0.266	
≥3 segments	4 (26.7)	16 (43.2)		

*Mann-Whitney U test; chi-square (χ^2) test, iATM: Idiopathic acute transverse myelitis, sATM: Secondary acute transverse myelitis, CSF: Cerebrospinal fluid, OCB: Oligoclonal band, IgG: Immunoglobulin G, NMO: Neuromyelitis optica spectrum, MOG: Myelin oligodendrocyte glycoprotein, MRI: Magnetic resonance imaging, LP: Lumbar puncture

Discussion

Accurate diagnosis and effective treatment of ATM in the early stages are critical for preventing mortality and morbidity. The diagnosis of iATM can be made based on the clinical, laboratory, and imaging findings, and other causes are excluded. In large literature series, the frequency of iATM has been reported to be 15%-50% (1,4,5,6,7,8). In our study, similar to the literature, an etiological cause was detected in 71.1% of the patients, and 28.9% were evaluated as iATM.

The relationship between ATM and age is not yet clear. Some studies have reported that it has two peaks, at ages of 10–20 years

and 30–40 years (3). However, Berman et al. (9) noted in their epidemiological study that the frequency of ATM increased over the age of 40 years. If encountered at an advanced age, vascular diseases, such as dural arteriovenous fistula and paraneoplastic processes, should be considered (1,10). Paraneoplastic processes can occur before primary neoplasia occurs; therefore, patients with iATM should be scanned intermittently for neoplasia. In this study, the average age of patients with iATM was lower. No paraneoplastic condition or vascular event was found in the followup of any of the patients after the acute period.

A CSF examination is extremely important to determine the etiology of ATM. OCB analysis shows a narrow range of electrophoretic dissociation of certain Igs in the CSF. The presence of OCB indicates that there is an inflammatory process in the brain and spinal cord. OCBs can be detected in the CSF of most patients with ATM. For this reason, OCB, although not specific, can be used in the diagnosis of ATM. One study reported that OCB was found in the CSF of 85% of the patients with ATM (11). In another study, the frequency of OCB in CSF was reported to be 60%-80% (12). However, Keegan et al. (13) reported that the presence of OCB in CSF was found in only 40%-50% of the patients with ATM (13). Bourre et al. (14) showed that although 92% of the patients diagnosed as having clinically definite MS were found to have OCB, this rate was only 38% in iATMs among 82 patients with ATM. In this study, OCB positivity was found in 65% of patients with sATM. However, OCB positivity was detected in 87.5% of the patients diagnosed as having MS. No significant difference was detected between the groups in terms of CSF protein levels or IgG index, which were indirect indicators of inflammation.

Infectious pathogens are an important etiological cause and can cause acute myelitis through direct pathogenic effects or parainfectious pathways. Infections that cause ATM may include viruses and bacteria. In particular, infections such as mycoplasma pneumonia, HSV, VZV, Epstein–Barr virus, HIV, enteroviruses, and CMV have been associated with ATM (8). In some studies, HSV and VZV infections have been reported as the etiological cause in 10%–20% of the patients with ATM (1,2,8). ATM due to VZV usually occurs with the reactivation of latent virus or direct invasion of the virus into the spinal cord after acute infection. Moreover, since it may cause vasculopathy in patients, it may also



Figure 3. A 73-year-old woman with AQP-4 immunoglobulin G antibody-positive NMOSD and complete ATM. In spinal MRI, a lesion is seen as hyperintense in T2-weighted sections extending longitudinally in all cervical and upper thoracic segments in cervical and thoracic MRI and with significant contrast enhancement in the posterior part of the spinal cord in axial sections (shown with yellow arrows)

AQP-4: Aquaporin-4, NMOSD: Neuromyelitis optica spectrum disease, ATM: Acute transverse myelitis MRI: Magnetic resonance imaging



Figure 4. A 19-year-old woman with complete idiopathic acute transverse myelitis. In thoracic magnetic resonance imaging, a hyperintense lesion is seen in T2-weighted sections extending from the T9 vertebra level to the T12 vertebra level, and a diffuse lesion without significant contrast enhancement is seen in the central part of the medulla spinalis in axial sections (shown with yellow arrows)

present with serious clinical conditions, such as the sudden onset of spinal shock (15). A definitive diagnosis is usually made by demonstrating VZV IgM, IgG, and DNA in serum and/or CSF (15). In our case series, the diagnosis of VZV-related myelitis was confirmed in one patient by showing both VZV IgM positivity in serum and VZV DNA in CSF.

In radiological imaging, the spinal cord lesion in ATM is usually more than two segments long, and involvement of the cervical and thoracic regions is usually observed (1,16). However, in patients with iATM and partial myelitis, short-segment involvement in the cervical region is more common (16). In particular, 42%–62% of patients with partial ATM turn into clinically definite MS in their long-term follow-up (17). Typical spinal lesions of MS are less than two vertebral segments long and are located in the upper-middle cervical region (1,16,17). Nowak et al. (18) claimed in their case series that the main cause of ATM was MS. In our study, there were many patients diagnosed as having MS after having incomplete myelitis among the patients with sATM, and lesions were observed in the cervical region, similar to the literature. Additionally, the middle-lower segment in the cervical region and the middle segment in the thoracic region were more frequently involved. No statistically significant difference was detected between the iATM and sATM groups in terms of lesion localization.

In recent years, the number of patients with ATM associated with NMOSD and MOGAD, defined by pathogenesis and clinical presentations different from MS, has been increasing. Typical MRI features of NMOSD's spinal cord involvement include the lesions being expansive, affecting the cord diffusely longer than three vertebral segments, having necrotic features, and being centrally located. NMOSDs can be diagnosed in 60%-80% of patients with LETM (19). Although craniocervical and upper thoracic segments are mostly involved in NMOSD, lower thoracic segment and conus medullaris involvements are more common in MOGAD (20). In our study, LETM was observed at the cervicothoracic level in all AOP-4 antibody-positive patients with NMOSD, similar to the literature. In the patient with positive MOG antibody, spinal cord involvement was observed between the T8 and L1 segments. Additionally, this patient's first clinical complaint was urinary incontinence and paraparesis due to conus medullaris involvement.

Early diagnosis and treatment are very effective in the prognosis of ATM. Intravenous CSs, PE, IVIg, and other immune modulators are drugs commonly used to treat ATM. Treatment is started by administering methylprednisolone (1000 mg/day) intravenously for 5-10 days (1). Another effective treatment, particularly in childhood, is IVIg; however, there is conflicting information in the literature about its effectiveness. Some studies have shown that IVIg treatment contributes to the rapid improvement of symptoms and reduced relapses in patients with ATM (21); however, other studies report that the role of IVIg in ATM treatment is unclear (22). PE is considered to be another effective method in the treatment of ATM. Various studies have shown that PE rapidly improves patients' symptoms and is effective in regaining their physical functions (23,24). Bonnan et al. (24) applied five cycles of PE every other day in addition to CS treatment for 29 of 96 spinal attacks in 43 patients with NMOSD. During the follow-up of the patients, clinical improvement was found to be faster and permanent disability was less in the group in which PE treatment was added to CSs, compared with the group in which only CSs were applied (24). Moreover, although hypotension and fluid-electrolyte imbalance may occur during or after the PE procedure, most of these problems can be

identified and resolved quickly and are rarely serious. However, therapeutic PE is an invasive procedure, and complications such as catheter and/or set blockage, allergic reaction, rash, hypotension, bradycardia, nausea, vomiting, and headache may occur (25). In our study, high-dose CS treatment was started in all our patients, PE was applied in eight patients, and IVIg was applied in three patients with insufficient improvement in the clinical condition. Severe hypotension was observed during the PE procedure in four of our patients, and bradycardia was observed in one patient, and the therapeutic PE procedure was continued with monitoring in the ICU.

Study Limitations

Although our hospital is a key center to which patients diagnosed as having ATM are referred from many provinces, the fact that it is the only center with a limited number of patients is one of the limitations of our study and may constrain the generalization of the data. However, it is vital to describe the clinical course and disease characteristics of a group of patients who have been followed and investigated for a long time in a single center. Additionally, since it is a retrospective study, a definitive causal relationship cannot be established regarding the results of our study. However, evaluating our patients' long-term treatment responses and follow-up results is important for us to evaluate the accuracy of diagnoses and the effectiveness of treatment plans.

Conclusion

ATM is a neurological condition that develops as a result of damage to the spinal cord due to different etiological reasons and can lead to serious morbidity. It is crucial to investigate the etiological causes in detail and initiate appropriate treatment quickly. Treatment varies depending on the determination of the underlying cause and severity of the disease. In the follow-up of patients with ATM whose cause cannot be determined, patients should be closely monitored for the development of autoimmune diseases, such as MS, NMOAD, and MOGAD, and, if necessary, auxiliary diagnostic tests should be repeated at regular intervals.

Ethics

Ethics Committee Approval: University of Health Sciences Türkiye, İzmir Tepecik Training and Research Hospital, Non-Interventional Research Ethics Committee (number: 2022/12-33, date: November 1, 2023).

Informed Consent: Retrospective study. Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: L.Ö., T.D.Ö., T.G., A.S., Concept: L.Ö., T.D.Ö., T.G., U.Ş., Design: L.Ö., T.D.Ö, T.G., A.S., U.Ş., Data Collection or Processing: T.D.Ö., T.G., Analysis or Interpretation: L.Ö., Literature Search: L.Ö., T.G., Writing: L.Ö.

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