Olgu Sunumu
Case Report

A rare disease in the differential diagnosis of Multiple Sclerosis (MS): Granulomatosis with Polyangiitis- (GPA) (Wegener Granulomatosis)

MS AYIRICI TANISINDA NADİR GÖRÜLEN BİR HASTALIK: WEGENER GRANÜLOMATOZU POLİANJİTİS İLİŞKİLİ GRANÜLOMATOSİS)

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ABSTRACT

Granulomatosis with polyangiitis (GPA), Wegener's Granulomatosis (WG), is a systemic inflammatory disease of unknown etiology, with small and medium arteries involvement, characterized by necrotizing granulomatosis. In this article, we present a patient who was referred to our Multiple Sclerosis (MS) outpatient clinic due to the results of MRI scans suspicion of MS, however was diagnosed as GPA with the peripheral and central nervous systems involvement as a result of the examination. 39-year-old female had visual impairment, hearing loss, and weakness in her right arm and leg. In her history, she had shortness of breath and complaints of painful urination and bloody urine. Her visual acutiy was both 0.4. In the muscle strength examination, right upper extremity was 3/5 and right lower extremity was 2/5. There was hypoesthesia in the right extremity. Biochemistry values were normal. She had diffuse purpuritic lesions of the lower extremity. On cranial MRI, in non-specific T2-FLAIR hyperintense foci settled in white matter and the right optic nerve was evaluated to have a slight kink. Multiple Sclerosis (MS) is an autoimmune central nervous system (CNS) disease characterized with inflammation, demyelination and axon damage. MS is diagnosed according to McDonald's Criteria that revised in 2017. A lot of disase-disease-are in the differential diagnosis of MS. GPA may affect peripheral and central nervous systems in varying proportions (10%-45%). Although GPA is with atypical onset especially involvement of central nervous system is rarely seen, it takes part in the differential diagnosis of MS.

Keywords: A Rare Disease, Differential Diagnosis of Multiple Sclerosis, Granulomatosis with Polyangiitis, Rheumatological Diseases with Atypical Course

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ÖZ

Polianjitis ilişkili Granülomatosis (GPA), Wegener Granülomatosis (WG), küçük ve orta boy arterleri etkileyen, nekrotizan granulomlar ile karekterize, etolojisi bilinmeyen, sistemik inflamatuar bir hastalıktır. Biz bu olgumuzda, MRI görüntülemeleri ve klinik olarak Multipl Skleroz (MS)'ten- şüphelenildiği için MS polikliniğimize- yönlendirilen, incelemeler neticesinde periferal ve santral sinir sistemi tutulumlu GPA tanısı konulan bir hastamızı sunuyoruz.

39 yaşında kadın hasta, görme ve işitme kaybı, sağ bacağında ve kolunda güç kaybı şikayetleriyle başvurdu. Öyküsünde nefes darlığı, idrar yaparken yanma ve kanlı işeme bulunmaktaydı. Muayenesinde görme düzeyi bilateral 0,4 düzeyinde, sağ üst ekstremite kas gücü 3/5, sağ alt ekstremite kas gücü 2/5 idi. Sağ ekstremitede hipoestezi mevcuttu. Biyokimya değerleri normaldi. Takiplerinde alt ekstremitede diffüz purpiritik lezyon geliştiği görüldü. Kranial MR' ında, T2- FLAIR sekanslarında izlenen beyaz cevherde nonspesifik hiperintensiteler ve sağ optik sinirde "kink" görünümü izlendi.

Multipl Skleroz (MS), santral sinir sistemini etkileyen, inflamasyon, demyelinizasyon ve akson hasarı ile uyumlu otoimmün bir hastalıktır. MS tanısı 2017 yılında revize edilen McDonald kriterlerine göre konur. Pek çok hastalık MS' in ayırıcı tanısına girmektedir. GPA santral ve periferik sinir sistemini değişik oranlarda etkilemektedir (%10-45). Özellikle santral sinir sisteminin de etkilendiği atipik seyirli GPA nadir görülmesine rağmen MS in ayırıcı tanısında akılda tutulmalıdır.

Anahtar Kelimeler: Multipl Skleroz ayırıcı tanısı, Wegener Granülomatozu, Polianjitis ilişkili Granülomatosis, Atipik Seyirli Romatolojik Hastalıklar,

Granulomatosis with polyangiitis (GPA), Wegener's Granulomatosis (WG), is a systemic inflammatory disease of unknown etiology which is with small and medium arteries involvement and characterized by necrotizing granulomatosis. It is frequently associated with ANCA, affects the upper and lower respiratory tracts and kidneys. It may affect the peripheral and central nervous systems at varying rates (10%-45%). Central nervous system involvement may show clinical and radiological findings similar to Multiple Sclerosis (MS), and therefore it is included in the differential diagnosis of demyelinating diseases. In this report, we present a patient who was referred to our MS outpatient clinic with suspicion of MS due to the results of MRI scans. However, the patient was diagnosed as GPA with the peripheral and central nervous systems involvement in our clinic.

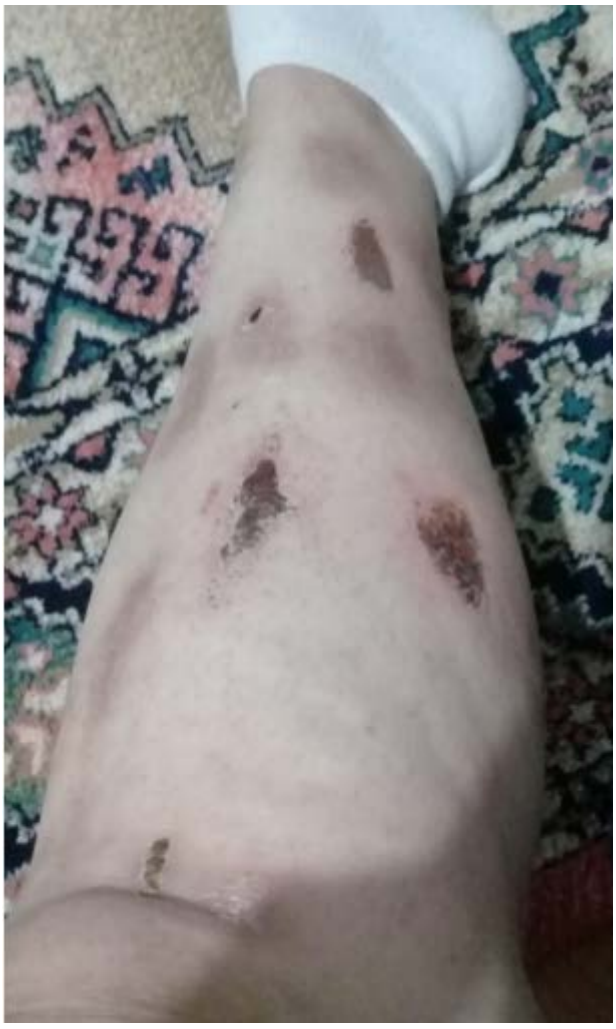
CASE

Thirty nine year old female patient was referred to our outpatient clinic with pre-diagnosis of MS. The patient had ongoing complaints for several years such as visual impairment, hearing loss, and weakness in her right arm and leg. She had no known disease other than treatment-persistant urinary tract infection and asthma. In her medical history, there were peripheral facial nerve paralysis that healed without sequelae, sudden and non-healing hearing loss in her right ear and operation for maxillary sinus hemangioma. The patient had been suffering from a wandering joint pain for the past ten years, with swelling of the joints and morning stiffness. Once in a while she had oral aphthae-like mouth sores but never genital ulcers. She had 3 miscarriages in her pregnancies. She had lost 10 kilos in the last 2 months and had night sweats without a fever. In the physical examination of the patient; she was conscious, cooperative and oriented. Visual acuity without glass was both 0.4 in the right and the left. Anterior and posterior segments, optic disc and macula were normal. Eye movements were correlated in all directions. There was no facial asymmetry. There were total hearing loss in the right and partial hearing loss in the left. In the muscle strength examination, right upper extremity was 3/5 and right lower extremity was 2/5. There was

hypoesthesia on the right extremity. Romberg test was positive. The plantar response was flexor bilaterally. She could walk with support.

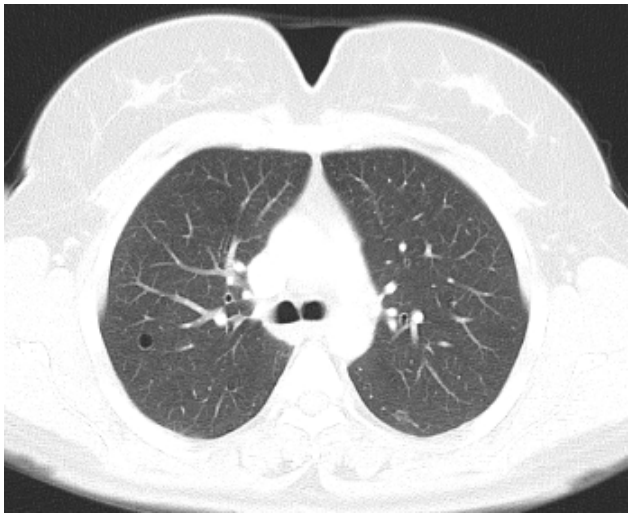
During the follow-up, diffuse purpuritic lesions of the lower extremity developed (Figure 1). The other examination findings were normal.

Figure 1. Diffuse purpuritic lesions of the lower extremity



There was a slight TSH increase with normal fT3 and fT4 in blood biochemistry. There were leukocyte clusters and erythrocytes in complete urine analysis. Among the vascular markers, ANA was + (fine-spotted +, nucleolar ++), Anti-Sm was low titer positive and the others including C ANCA, P ANCA, Anti ds DNA were negative. There were minimal centriaciner emphysematous changes in the upper lobes and superior segments of the lower lobes of both lungs. And one each thin-walled air cyst less than 1 cm was observed in the right upper lobe posterior segment and left lower lobe anterior segment in chest CT (Figure 2).

Figure 2. Minimal centriaciner emphysematous changes and air cyst less than 1 cm was observed in the right upper lobe



On Cranial MRI, in non-specific T2-FLAIR sequences there was a hyperintense foci settled in white matter and there was an increase in CSF signal intensity at paraoptic distances. The right optic nerve was evaluated to have a slight kink. (Figure. 3a, 3b, 3c)

Figure 3-a. On Cranial MRI, non-specific T2-FLAIR sequences hyperintense in white matter and there was an increase in CSF signal intensity at paraoptic distances.

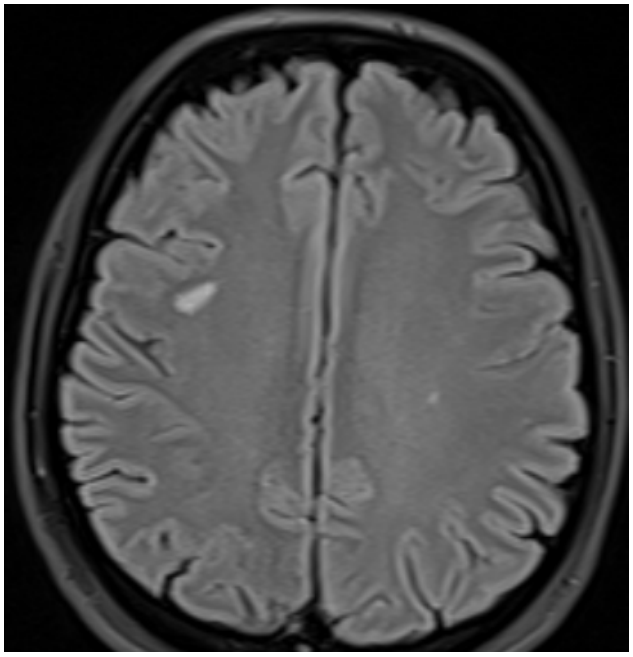


Figure 3-b. On Cranial MRI, non-specific T2-FLAIR sequences hyperintense in white matter and there was an increase in CSF signal intensity at paraoptic distances.

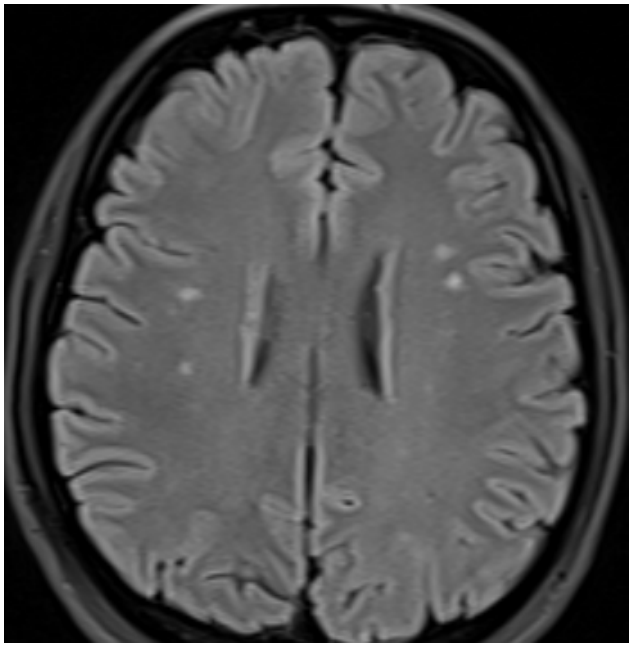
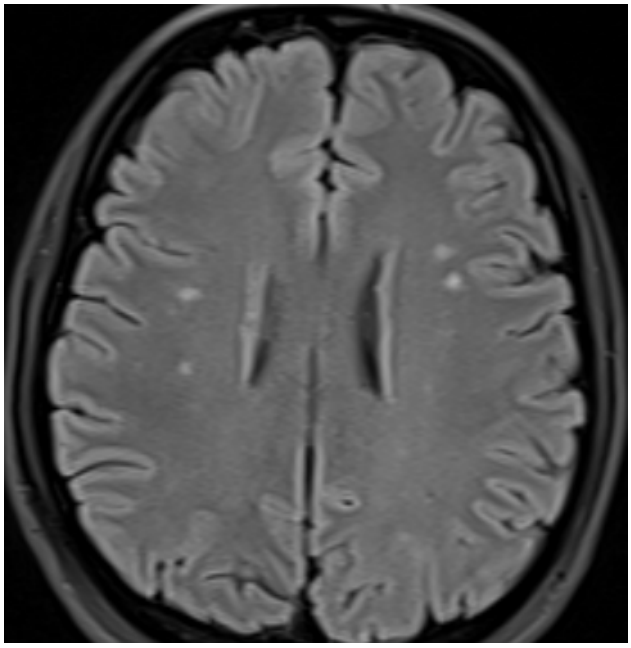


Figure 3-c. On Cranial MRI, non-specific T2-FLAIR sequences hyperintense in white matter and there was an increase in CSF signal intensity at paraoptic distances.



Cervical, thoracic and lumbar vertebral MRIs showed hemangioma on multiple vertebra corpuses (Figure 4).

Figure 4. Vertebral MRIs showed hemangioma on multiple vertebra corpuse

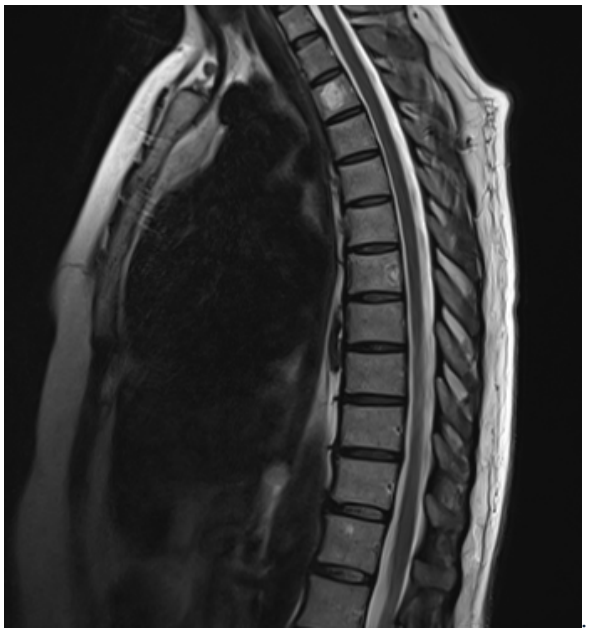


Figure 5. EMG was evaluated as compatible with dominant motor axonal neuropathy in lower extremity

Motor Nerve Conduction Studies

MNCS			
Nerve	Lat ms	Amp mV	CV m/s
Medianus Motor Right			
Wrist - APB	2.63	**8.3**	
Elbow-Wrist	6.52	**7.3**	61.7
Peroneus Motor Left			
Ankle - EDB	4.29	**2.4**	
Fib. head-Ankle	11.0	**3.1**	46.2
Peroneus Motor Right			
Ankle - EDB	**5.70**	**2.6**	
Fib. head-Ankle	12.7	**2.8**	45.0
Tibialis Motor Left			
Ankle - Abd hal	5.00	6.4	
Knee-Ankle	11.5	**5.1**	59.2
Tibialis Motor Right			
Ankle - Abd hal	3.91	8.6	
Knee-Ankle	12.6	**6.0**	44.9
Ulnaris Motor Right			
Wrist - ADM	2.27	19.9	
Bl. elbow-Wrist	6.33	13.0	62.8

Sensory Nerve Conduction Studies

SNCS			
Nerve	S.Lat ms	Amp uV	CV m/s
Medianus Sensory Right			
Dig III - Wrist	2.47	17.1	50.6
Suralis Sensory Right			
Mid. lower leg - Lat. Malleolus	2.08	6.8	43.3
Ulnaris Sensory Right			
Dig V - Wrist	1.95	10.1	51.3

Brain MR angiography and paranasal sinus CT examinations were reported as normal. Fundus Fluorescein Angiography (FFA) showed findings of inactive vasculitis. Optic Coherans Tomograpy (OCT) was normal. In the audiometry test for hearing examination, there was no response from the right side and moderate SN hearing loss with 65 dB on the left. EMG was evaluated as compatible with dominant motor axonal neuropathy in lower extremity (Figure 5).

While the examination of the patient was in progress, pulse steroid treatment was initiated considering the patient had advanced systemic vasculitis and this treatment was continued at weekly doses. Azatiopurine 2X50 mg was started simultaneously. The patient was reffered to rheumatology clinic in line with her medical history and findings. Finally the patient was diagnosed as granulomatosis with polyangitis by Rheumatology and her follow-up and treatment continues in that department.

DISCUSSION

Multiple Sclerosis (MS) is an autoimmune central nervous system (CNS) disease characterized with inflammation, demyelination and axon damage. The disease often occurs in young adults. Some types go on with attacks while some other types are progressive. Although all the signs and symptoms related to CNS damage may occur in MS patients, some of them are seen very often and some are seen so rarely to be considered as dangerous (1). In the differential diagnosis of MS; idiopathic inflammatory demyelinating diseases and variants of MS, primary and secondary inflammatory vascular diseases, systemic collagen/vascular diseases (SLE, Antiphospholipid Antibody Syndrome, Primary Sjögren Syndrome, Susac Syndrome, Granulomatosis-related Angiitis-Wegener), granulomatous diseases, neoplastic/lymphoproliferative diseases, paraneoplastic diseases, mitochondrial diseases and nutritional diseases take part (1-2). The patient was referred with suspicion of MS. MS is diagnosed according to McDonald's Criteria that revised in 2017 (3). She did not meet McDonald's criteria. Besides, she has atypical MRI findings, peripheral nerve involvement and systemic symptoms. Then the MS was

ruled out. Behçet's disease, Susac syndrome, collagen tissue diseases, systemic vasculitis such as GPA were considered in the differential diagnosis of the patient.

Behçet's disease is an idiopathic, chronic, multisystemic, vascular and inflammatory disease. It usually presents with urogenital ulcer and uveitis. The form in which primary neurological findings are seen is called "Neuro Behçet". Brain MRI usually shows brain stem involvement as parenchyma, and dural sinus occlusions as extraparenchyma. The patient did not suffer from genital ulcers, iritis, uveitis, skin findings that is why Behçet's disease is unlikely (4-5).

Susac's syndrome which is characterized with encephalopathy, retinal involvement and sensory-neural deafness due to micro-angiopathic changes in brain, retina and cochlea usually occurs among young women (6). Therefore it was ruled out from differential diagnosis. Because Susac's syndrome is generally monophasic and no systemic symptoms observed. Besides, the patient's OCT and FFA were normal. Primary central nervous system vasculitis was excluded because the patient had symptoms of systemic vasculitis. One of the diseases in the differential diagnosis of MS is rarely associated with GPA. GPA, is a systemic inflammatory disease of unknown etiology, with small and medium arteries involvement, characterized by necrotizing granulomatosis. Considering that survival without any treatment is with a 1-year survival rate of less than 30% but more than 80% of patients who are treated are alive at least for eight years early diagnosis and treatment are of great importance (7). GPA is often associated with ANCA and affects the upper and lower respiratory tracts and kidneys. The diagnosis and classification are also made according to whether these two systems are affected or not. As seen in our case, skin lesions such as purpura, nodule, hemorrhagic blister and systemic complaints such as fever, fatigue and weight loss can be seen (7). In MS, there is no systemic effect. Wegener's Granulomatosis may affect peripheral and central nervous systems in varying proportions (%10-45). It affects central nervous system with extracranial granuloma invasion, intracranial granuloma formation and vasculitis effects. As a central nervous system vasculitis, the disease manifests itself with intracranial hemorrhage, transient ischemic attack, ischemic infarction, central venous infarction and spinal cord arterial and venous thrombosis symptoms. MRI shows nonspecific findings in white matter (8). These findings may be confused with MS. In our case, there were white matter lesions on MRI and paresis in the right extremity on examination.

Cranial nerve involvement can be seen in Wegener's Granulomatosis. Visual problems due to orbital granulomatous mass effect and ischemic optic neuropathy are the result of the second cranial damage. Facial paralysis is seen more commonly than other cranial nerves involvement (9). Sensory-neural hearing loss may occur (8). These symptoms may be confused with MS if not well questioned. It is seen that these findings appear in different times in our patient. In 67% of patients with GPA, peripheral nerve involvement is seen as sensory-motor polyneuropathy or mono-neuritis multiplex due to vasculitis of vaso nervosums (9). Peripheral nerve involvement is not seen in MS. EMG detected a dominant motor axonal neuropathy in the lower extremity in our case.

Although GPA with atypical onset is very rare and especially involvement of central nervous system is rarely seen, it takes part in the differential diagnosis of MS. Central nervous system involvement of the GPA is very rare that our case was confused having MS instead. It would be worthy to keep in mind GPA as a differential diagnosis of MS.

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