Euras J Fam Med 2019;8(1):45-50. doi:10.33880/ejfm.2019080105

A Wegener Granulomatosis Case Presented with Arthralgia

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https://doi.org/10.33880/ejfm.2019080106

Case Report / Olgu Sunumu

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Date of submission
29.10.2018

Date of acceptance
12.02.2019

ÖZ

Wegener Granülomatozu özellikle üst solunum yolları, akciğer ve böbrekler olmak üzere, tüm organları tutabilen nekrotizan granülomatöz vaskülitik bir hastalıktır. Ortalama görülme yaşı 40-55 tir. Kadın ve erkek eşit etkilenir. Akciğer tutulumu Wegener granülomatozisli hastaların %90'ında mevcuttur. Wegener Granülomatozu, tanı ve tedavisi geciktiğinde, mortalitesi yüksek olan bir hastalıktır. WG'nin hemoptizi ve hematüri gibi semptomları olabileceği gibi; birçok konnektif doku hastalığı ve vaskülitte olabilen şiddetli artralji ve artritle de prezente olabilir. 52 yaşında erkek hasta. 2 ay önce başlayan eklemlerde ağrı şikayetiyle başvurduğu merkezde analjezik tedavisi uygulanmış ancak fayda görmemesi nedeniyle sol diz ve her iki omuzuna intraartiküler enjeksiyon tedavisi yapılmış. Şikayetleri gerilemeyen hastanın son 2 ayda 20kg kaybı olmuş. Tam idrar tahlilinde: her sahada 14-15 eritrosit ve 10-12 lökosit, protein; 1 pozitif saptandı. Hastanın 3 gün sonraki poliklinik kontrolünde CRP'si:61 mg/L, sedimantasyonu: 82 mm saptanması üzerine ileri tetkik amacıyla hospitalize edildi. Böbrek biyopsisi raporunda, ön planda "pauci-immun glomerulonefrit" düşünüldü. İlk 3 gün 1 gr pulse, 4. günden itibaren 1 mg/kg metilprednizolon tedavisi ve siklofosfamid tedavisi uygulandı.

Anahtar kelimeler: Wegener granülamotozu, vaskülit, hemoptizi, artralji

Artralji ile Başvuran Bir Wegener Granülamatozu Olgusu

ABSTRACT

Granulomatosis with polyangitis (GPA/WG) (previously known as Wegener granulomatosis) is a multisystem systemic necrotizing non-caeseating granulomatous vasculitis affecting small to medium sized arteries, capillaries and veins, with a predilection for the respiratory system and kidneys. The average incidence of this disease is 40-55. 90% of the WG patients have pulmonary involvement. Wegener Granulomatosis is a disease with high mortality when its diagnosis and treatment is delayed. Although WG may have symptoms such as hemoptysis and hematuria, it should be noted that it may present with severe arthralgia and arthritis which may be in many connective tissue diseases and vasculitis. Male patient, 52 years old. Analgesic treatment was applied when he came to the center due to arthralgia two months ago, however, there was no change in his complaints and intra-articular injection treatment was applied on left knee and both shoulders. The symptoms did not regress and the patient lost 20 kg within the last two months. In urine analysis, 14-15 erythrocyte and 10-15 leucocyte detected in every field; 1 positive detected. The patient was hospitalized in order to make further examination upon the determination of CRP: 61 mg/L and ESR: 82 mm/hr in the next polyclinic control after three days. In the kidney biopsy report, "Pauci-immun glomerulonephritis" was primarily considered in the phenomenon. For the first three days 1 gr pulse and by the fourth day 1 mg/kg methylprednisolone and cyclophosphamide treatment was applied.

Keywords: Wegener's granulomatosis, vasculitis, hemoptysis, arthralgia

How to cite / Atıf için: Yılmaz D, Toprak D, Karatemiz G, Borlu F. A Wegener Granulomatosis Case Presented with Arthralgia. Euras J Fam Med 2019;8(1):45-50. doi:10.33880/ejfm.2019080106

Conflict of interest: No conflict of interest was declared by the authors.
Financial disclosure: No financial disclosure was declared by the authors.

Introduction

Granulomatosis with polyangitis, previously known as Wegener granulomatosis is a multisystem systemic necrotizing non-caseating granulomatous vasculitis affecting small to medium sized arteries, capillaries and veins, with a predilection for the respiratory system and kidneys. The average incidence of this disease is 40-55. 90% of the Wegener granulomatosis patients have pulmonary involvement. Wegener's granulomatosis is a form of vasculitis with prevalence of approximately 3/100000. In this case report a Wegener granulomatosis presented with hemoptysis and arthralgia is presented and evaluated. Although the exact involvement is confirmed by renal biopsy, generally non-invasive urine analysis is adequate for the diagnosis and treatment selection when combined with other findings.

Case

Male patient, 52 years old. Analgesic treatment was applied when he came to the hospital due to arthralgia two months ago. However, there was no change in his complaints and intra-articular injection treatment was applied on left knee and both shoulders. The symptoms did not regress and the patient lost 20 kg within the last two months. The patient applied to the Lung Disease Department due to hemoptysis which occurred and last for 1 week within this period; and he was directed to Internal Medicine Policlinics after the evaluation of his test results. With these current complaints, the patient applied to our emergency department. The test results were as follows: Hb: 12.4 g/dl, Hct: 37.2%, WBC: 12.74x 10^3/uL, Plt: 372x10^3/uL.

In urine analysis, 14-15 erythrocyte and 10-15 leucocyte detected in every field. The patient was hospitalized in order to make further examination upon the determination of CRP: 61 mg/L and ESR: 82 mm/hr in the next polyclinic control after three days.

On the physical examination, arthritis was detected on the left and right shoulder joints and left knee joint; and oligo-articular ambulant arthralgia was detected on major joints. There were no rheumatoid nodules, alopecia, oropharyngeal-genital aft, eye dryness or active petechia-purpura. There were hyperpigmented marks of the previous petechial attack in both pretibial areas (Figure 1).

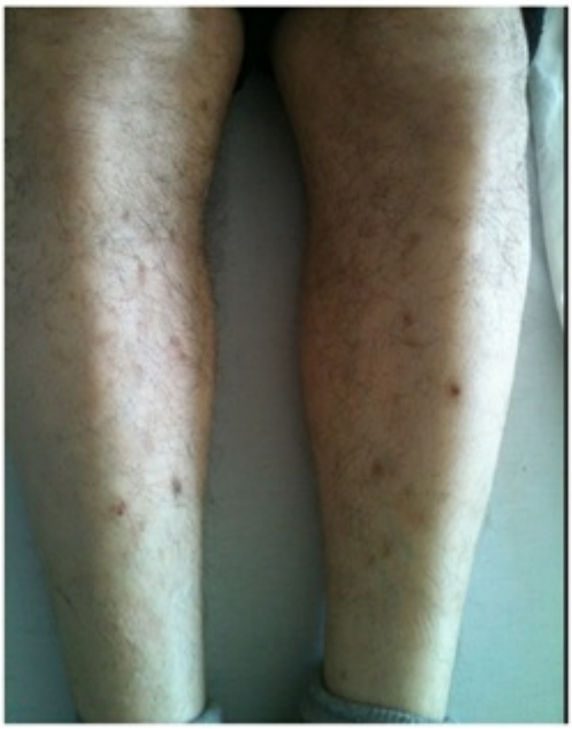

Figure 1: Hyperpigmented marks of the previous petechial attack in both pretibial areas

In fundus examination, skelf and dot hemorrhage were detected on bilateral soft water joint. Moreover, it is detected that the patient had non-proliferative diabetic retinopathy. There was no eruption observed during the patient follow-up; he had one conjunctivitis attack. Sinusitis was found in his otorhinolaryngology examination. The ECO values were normal and the results of tests made after the patient was interned to service are given in Table 1 and 2.

Table 1: The bio-chemical and hormonal test results of the patient after hospitalization

Test	Result	Test	Result
Glucose	**287** mg/dL	HbA1c	%**13.1**
Urea	38 mg/dL	C-peptide	**1.05** ng/mL
Creatinine	0.94 mg/dL	fT4	1.29 ng/dL (0.80-1.67)
Albumin	**3.4** g/dL	TSH	0.57 uIU/mL (0.27-4.20)
Globulin	**3.90** g/dL	B12	358.8 pg/mL
Hgb	**11.1** g/dL	Cortisol	16.94 ug/dL
Hct	%**34.2**	INR	1.15
Iron	**28** ug/dL	Fibrinogen	**719** mg/dL
Ferritin	**456.3** ng/mL	CK	26 U/L
RBC	**3.87** x10^6/uL	CRP	**208.5** mg/L
WBC	**10.20** x10^3/uL	Sedimentation	**95** mm

Table 2: The results of the urine and antibody scan tests after hospitalization

TEST	RESULT
TİT	Protein (++) mg/dL, glucose(+++) mg/dL, erythrocyte: Negative, leucocyte: Negative; albumin/creatinin:**1203** mg/g
24 hour urine test	albumin: **7410** mg/day, creatinine: **5980** mg/day, protein: **9360** mg/day
ANTIBODY SCAN	
ANTI-ds DNA	Negative,
Sm Antibody	**2 positive** IU/mL,
MPO ANCA (pANCA)	Negative,
PR3 ANCA (cANCA)	**>200 highly positive** AU/mL
Anti-nuclear antibody (ANA)	1/100 titer **(+) weak positive**
Anti-Cardiolipin Antibody Ig M and Anti-Cardiolipin Antibody Ig G	Negative
Anti-CCP IgG	Negative
Complement 3 and complement 4	Normal.
HbsAg	Negative
Anti HBs	**157** mLU/mL
HIV Ag/Ab	Negative
Anti HCV	Negative
Anti HBc IgM	Negative
Anti HAV IgM	Negative
Anti HBe	Negative

Left shoulder MRI: Bursitis, contusion/ hemorrhage on deltoid muscle, focal and full-thickness rupture on supraspinatus tendon (no trauma history).

Right shoulder MRI: Biceps tenosynovitis, tendonitis on supraspinatus tendon, partial rupture, effusion displaying lobulation.

Neck-Thorax-Abdominal CT: Right apical fibrotic specific infection sequels on lung parenchyma, peripheral nonspecific micro-nodules locally, central peribronchial thickness, nodular pattern (beginning of granulomatosis) image through bronchial trachea, yet it was regarded as non-infectious (Figure 2).

In the preliminary results of the kidney biopsy; it was found global sclerosis, cellular crescent and necrosis on one of the crescents. For the first three days 1 gr pulse and by the fourth day 1 mg/kg methyl-prednisolone and cyclophosphamide treatment was applied.

In the kidney biopsy report, “Focal extracapil proliferation on glomerulus, focal tubular atrophy, focal interstitial fibrosis” were detected. No symptom of immune complex nephritides was monitored in immunofluorescence studies. “Pauci-immun glomerulonephritis” was primarily considered in the phenomenon.

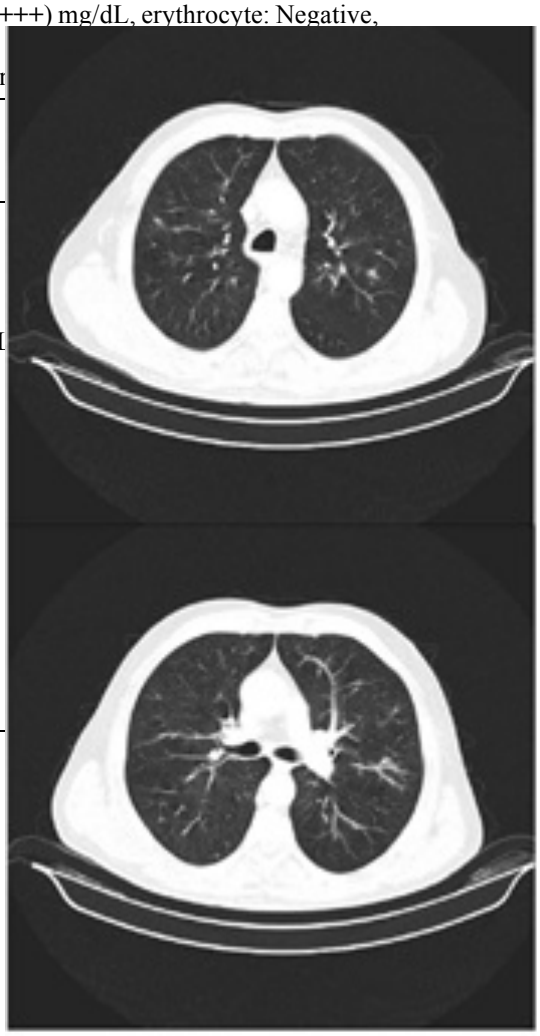

Figure 2: Neck-thorax-abdominal CT

After we started the treatment, the patient’s main complaint (arthralgia) regressed. His general condition got better and he began actively moving his shoulder and elbow joints which he could not during the treatment, the hemoptysis did not relapse. Hematuria and proteinuria in spot urine regressed and he was discharged from the hospital after being suggested about regular polyclinic checks.

Discussion

Wegener's Granulomatosis (WG, Granulomatosis polyangitis) is a necrotizing granulomatous vasculitic disease, which mainly affects upper and lower respiratory tract, lungs and kidneys, but may also affect all other organs. WG was first described by Heinz Klinger in 1931. But later, the upper and lower respiratory tract, skin involvement and focal

glomerulonephritis, necrotizing granuloma feature were characterized histologically by Frederich Wegener in 1938 (1).

American Rheumatology Association sets these four diagnosis criteria for WG (2):

1) Abnormal urine sediment

2) Abnormal chest radiograph

3) Existence of oral or nasal inflammation

4) Granulomata inflammation display in biopsy

The existence of two or more of these criteria is 88% susceptible and 99% specific (3). Our case meets all of these 4 criteria.

Wegener's granulomatosis is a form of vasculitis with prevalence of approximately 1/420000 (4). WG is usually diagnosed between the ages of 40 and 55 (2). The etiology of WG is unknown, and it is considered to be an autoimmune disease (5). Elevated antineutrophil cytoplasmic antibodies (c-ANCAs), which are a type of autoantibody in IgG structure, and occur against PR3 in neutrophil cytoplasm, play an important role in etiopathogenesis of WG (6). In our case, c-ANCA (>200) is determined to be highly positive. Pulmonary involvement is present in 90% of Wegener's granulomatosis patients (7). Renal involvement is seen in 80% of patients and usually indicates a non-specific glomerulonephritis in renal biopsy samples (8). Lung biopsy usually shows granulomatous small vessel necrotizing vasculitis (7).

The upper respiratory tract involvement includes chronic sinusitis, otitis media and hearing loss (9). The lower respiratory tract involvement can appear with hoarseness, difficulty in breathing, cough, hemoptysis, wheezing or stridor (10). In our case, the presentation of the disease appears with both lower and upper respiratory tract involvement; the symptoms like hemoptysis, sinusitis and cough appear.

The most commonly seen radiological finding in WG patients is pulmonary nodules which are generally bilateral (11). In our phenomenon, bilateral epidemic nodular pattern is observed in lung. Nearly 40% of bronchial and peri-bronchial thickness is reported in small airways (12). In the Thorax CT scan of our patient, early stage fusiform bronchiectasis changes and central peribronchial thickness are monitored.

Icy glass appearance is the second most common radiological finding (13). In our patient's control thoracic CT, ground-glass opacity was observed around the nodular opacities in the apicoposterior location of the left lung upper lobe. Although lungs are the most commonly affected organ system in WG, estimated incidence rate of alveolar hemorrhage, which is caused by capillaritis, is 7-45% (14). Our patient also had a history of hemoptysis of one week duration. Skin lesions are especially important in order to obtain pathological material and in terms of clinical signs, and seen at a rate of 13-14% at the beginning of the disease (15,16). Our patient had hyperpigmented scars of petechiae at the bilateral pretibial localization, that were previously obtained in the form of attacks. The skin lesions did not help us for the pathological diagnosis since they were not in the active period.

Neurological examination revealed motor weakness in the left upper extremity, hypoesthesia, hypoalgesia and elevated deep tendon reflexes. Our peripheral polyneuropathy findings were consistent with the literature. Renal involvement is seen in 20% of cases as the first signs of the disease, and characterized with focal segmental glomerulonephritis (16,17). It is the most important factor that is negatively affecting prognosis (18). Renal involvement arises in 57% of patients with proteinuria, urinary erythrocytes and erythrocyte cylender, and elevated urea and creatinine levels in the severe cases (19). Although the exact involvement is confirmed by renal biopsy, generally non-invasive urine analysis is adequate for the diagnosis and treatment selection when combined with other findings (18).

Laboratory studies revealed >9 g/day proteinuria, hematuria and also epithelial cell cylinders, granular cylinders, cellular cylinders, which are considered as tubular degradation products and dysmorphic erythrocytes cylinders in urine.

The mortality rate is high among untreated WG patients. Average life expectancy is 5 months in untreated patients, and survival rate with treatment at the end of the first year is 90%; it is 87% at the end of the second year and 76% at the end of the fifth year (15). That means early diagnosis and treatment is very

important for the patients with WG.

Due to the fact that it is a necrotizing vasculitis disease, the treatment should immediately start with pulse steroid infusion. The usual treatment is given for 24 months; oral prednisolone 1 mg/kg/day, cyclophosphamide 2mg/day/kg. Moreover, trimethoprim-sulfametoxazol is suggested in order to prevent s.aureus colonization and relapses (20).

WG requires a differential diagnosis than microscopic polyangiitis, Churg Strauss Syndrome and anti-GBM or Goodpasture Syndrome, systemic lupus erythematosus (SLE) and rheumatoid arthritis.

Since the pathological findings are similar to microscopic polyangiitis or Churg Strauss Syndrome, it the best to make the diagnosis with the collaboration between pathology and clinician in clinic harmonization (15).

The chronic and severe arthritis and arthralgia findings and localizations at the beginning require a differential diagnosis of rheumatoid arthritis and ankylosing spondylitis; and bilateral malar rush on the face and SLE alike involvement require a differential diagnosis of Systematic Lupus Erythematosus.

Finally, the Wegener diagnosis is made by evaluating the clinic findings, serological and radiological findings and pathology of the patient together. Since the mortality is rather high for the patients who apply to the emergency department with severe upper and lower respiratory findings and telescopic urine findings, we think that it could be a practical and lifesaving treatment method to start the pulse steroid treatment by making the diagnosis of 'unspecified vasculitis' -on condition that sepsis is ignored- without waiting for the serology and pathology results.

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