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Case Report Open Access

Wegener's granulomatosis with polyangiitis presenting as a soft tissue mass and osteomyelitis: A case report

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Wegener's granulomatosis (WG) is a life-threatening and rare systemic vasculitis associated with anti-neutrophil cytoplasmic antibodies and granulomatous lesions. The disease is primarily associated with pulmonary and renal involvement. Diagnosing this disease is a challenging task because of the lack of specific histological findings and its numerous manifestations. Although WG may affect any organ, the lung is most frequently affected. Herein, we report a case of a granuloma mass in the soft tissue of the leg and chronic ulcer around the talus with fistula to the bone similar to chronic inflammatory osteomyelitis.

Keywords: Antineutrophil Cytoplasmic Antibodies; Osteomyelitis; Vasculitis; Wegener's Granulomatosis

Introduction

Wegener's granulomatosis (WG) is a systemic necrotizing vasculitis associated with anti-neutrophil cytoplasmic antibodies (C-ANCA) and granulomatous lesions. It is a severe disease that may lead to organ damage and even death in the absence of appropriate treatment [1]. WG is characterized by necrotizing granulomatosis vasculitis. Diagnosing this disease is a challenge because of the lack of specific histological findings and its numerous manifestations.

WG may affect any organ, including rare areas such as the bones, and evolve into an inflammatory mass anywhere [2]. Clinical patterns, laboratory tests, and histological evaluation are necessary for the early diagnosis of WG. The characteristic histopathological triad, i.e. vasculitis, necrosis, and inflammation, are not the same in all patients. Commonly, multiple organs are involved in the disease, but in some cases, the lung is the only involved organ [2, 3]. Herein, we report a case of WG presenting as a soft tissue mass and bone fistula similar to chronic inflammatory osteomyelitis.

Case presentation

A 32-year-old male patient with no past medical history had been suffering from loose stools without blood or fever for two months prior to hospitalization. He had a history of chronic diarrhea,

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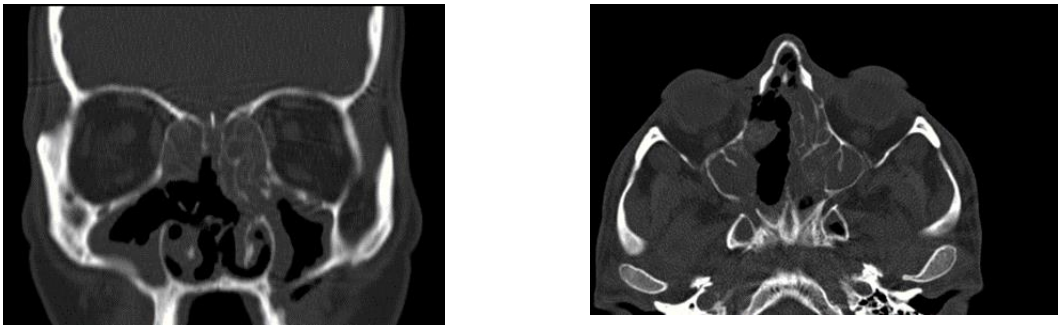
epistaxis, saddle nose, and recurrent sinusitis during the year before his hospital admission. The patient was admitted to Imam Reza Hospital affiliated with Mashhad University of Medical Sciences with deteriorating symptoms, swelling in his right ankle, and recurrence of sinusitis. Two months before hospitalization, he had undergone *endoscopy* for diarrhea. Computed tomography (CT) of the sinuses showed an increase in the thickness of the paranasal sinuses and destruction of the nasal septum and walls of the nasal cavity (Figure1). A thick-walled cavitary lung lesion and patchy ground-glass opacification (GGO) were seen on high-resolution CT (*HRCT*) of the lungs. Paranasal sinuses (PNS) biopsy was performed, which revealed the presence of necrosis and granuloma. Laboratory tests showed erythrocyte sedimentation rate (ESR) = 100. Anti-neutrophil cytoplasmic antibody (c-ANCA) was positive in immunofluorescence with a titer of 1:160. Based on his tests results, the patient was diagnosed with WG and was treated with 1 g *IV cyclophosphamide per* months for 5 months and 50 mg/d prednisolone. A few days before receiving the last dose of cyclophosphamide, the patient presented to the Emergency Department of Ghaem Hospital and was hospitalized due to aggravating headache, blood in the nasal mucus discharge, nausea and vomiting, and a fistula with effluent discharge forming from the swelling in the ankle. Duodenal biopsy showed villous atrophy and elevated intraepithelial lymphocytes (IELs). Tissue trans-glutaminase antibody (anti TTG-IgG) test was positive. The patient underwent magnetic resonance imaging (MRI) of the ankle because of the swelling, which showed edema of the talusplus soft tissue edema around the talus. No pathological evidence was found in ocular counseling, electromyography (EMG), nerve conduction velocity (NCV) and bronchoscopy were normal, and acid-fast bacteria (AFB) culture of the ankle fistula was negative. Positive rheumatoid factor (RF) with a titer of 3+ and negative antinuclear antibodies (ANA) profile were reported.

Brain MRI and magnetic resonance venography



A **B**

Figure 1. Axial (A) and coronal reconstructed (B) CT images of the paranasal sinuses show mucosal thickening, destruction of the left medial maxillary sinus wall and nasal septum perforation

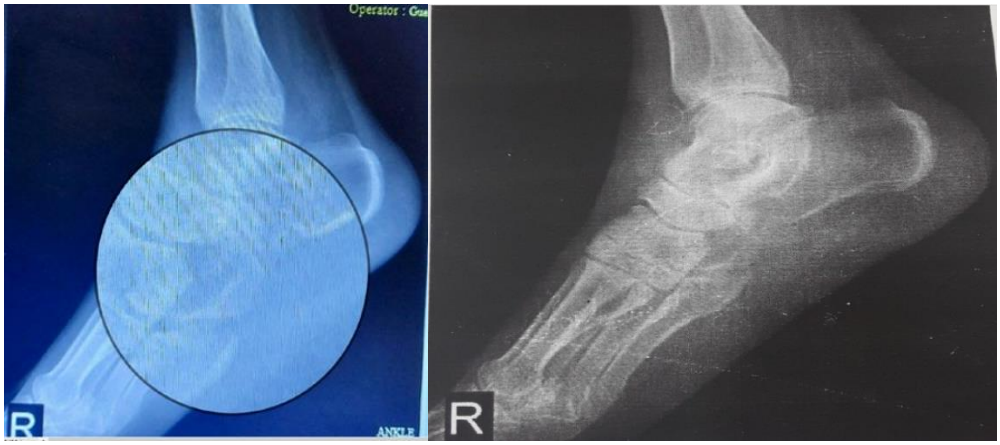


Figure 2. Lateral ankle radiographs showing a lytic lesion in the head and neck of the talus with medial ankle soft tissue swelling

(MRV), performed due to chronic headache, showed normal results. Ankle X-ray showed irregularities in the medial talus cortex (Figure 2). Ankle MRI showed a defect in the talus, possibly due to bone destruction extending into the soft tissue (Figure 3). Evidence of cellulitis was seen on the ultrasound of the ankle, while no collection was observed. Doppler ultrasonography of the lower extremities was normal. Two days later, bronchoscopy and bronchoalveolar lavage were performed. Negative results were reported in Ziehl-Neelsen staining, galactomannan measurement, PCR of tuberculus bacillus and Aspergillus in bronchoalveolar lavage fluid.

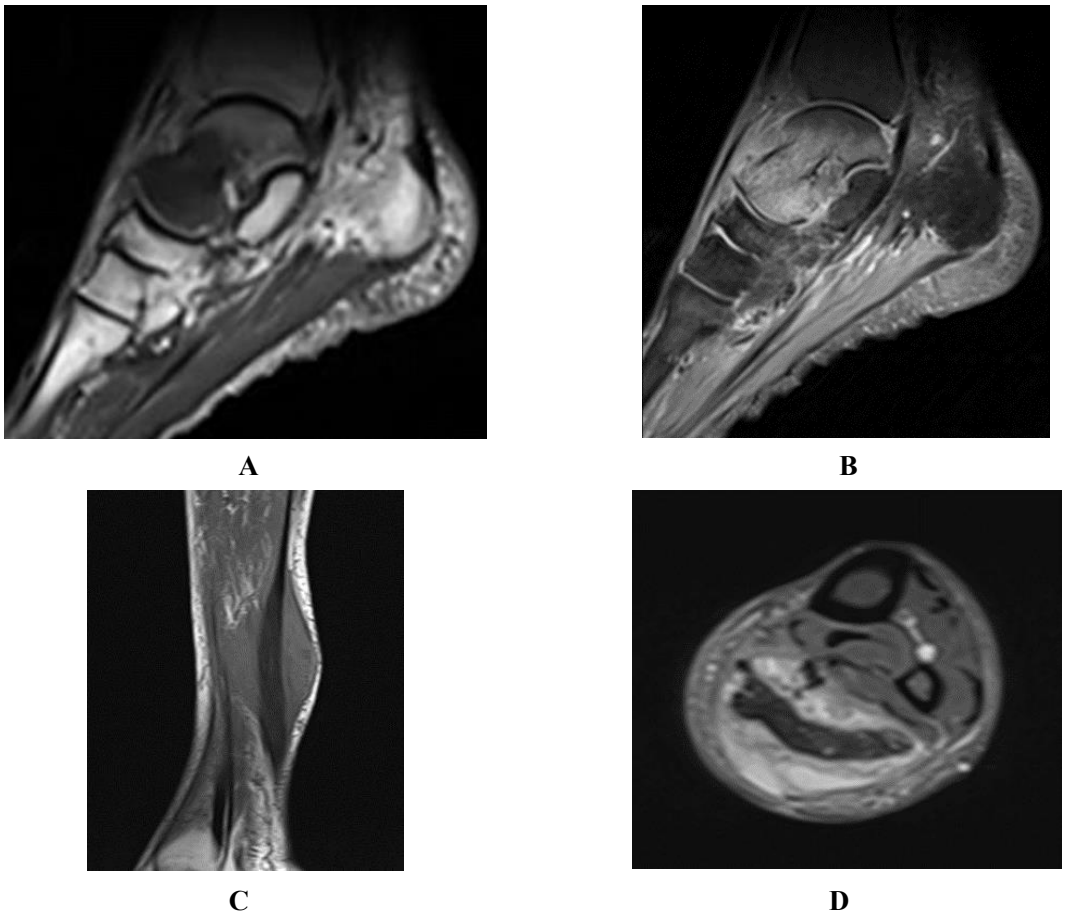


Figure 3. Ankle magnetic resonance imaging (A-D) showed a defect in the talus

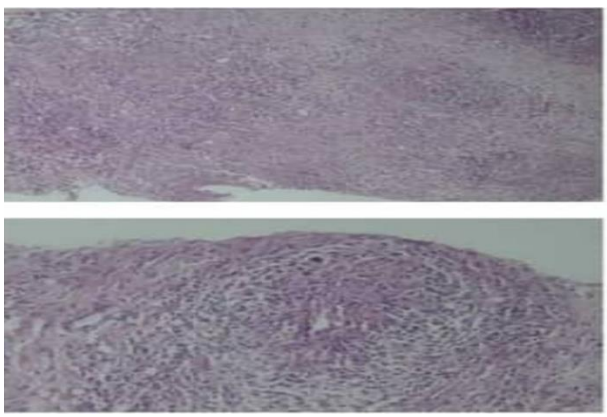


Figure 4. Biopsy of the mass behind the left leg showed the presence of leukocytoclastic vasculitis with necrosis and granuloma

Moreover, interferon gamma release assay (IGRA test), viral hepatitis test, urine analysis, and COVID-19 test were negative. A microbial biochemistry test was also performed, and *Clostridium difficult* was not found. Laboratory tests showed ESR = 112, white blood cell count (WBC) = 10.8 × 10^9 cells per liter, hemoglobin 11 = gr/dl, platelet count = 225000 per microliter, and creatinine = 0.9 gr/dl. A puncture biopsy (0.3 to 1-cm biopsy with 9 G needle) was performed on the right medial ankle, the results of which showed necrotic bone with chronic inflammation more in favor of WG. *Staphylococcus epidermidis* was detected in culture. Ankle biopsy culture was negative for tuberculosis or microbial and fungal infections. Thus, treatment with meropenem, vancomycin, and rifampin was initiated. Abdominal Doppler ultrasonography and CT angiography (CTA) were performed because of chronic abdominal pain. No evidence of thrombosis or vasculitis was seen. A mass had formed behind the left leg of the patient. Ultrasound and biopsy were performed. Ultrasound images showed thickening of the distal Achilles tendon, soft tissue edema, and hypo-intense echoic mass around the thickened tendon. Biopsy of the mass behind the left leg showed the presence of leukocytoclastic vasculitis with necrosis and granuloma (Figure 4). Methylprednisolone pulse 1000 mg/day on three consecutive days and the first course of rituximab 500 mg/weekly up to four weeks were administered, and then rituximab was prescribed for the second course. A month later, the patient returned to the hospital for re-examination and MRI showed the same defect in the talus to some extent. Granulomatous inflammation and soft tissue involvement were decreased remarkably after treatment. The patient was advised to visit six months later for the re-administration of rituximab. In follow-up, the ankle's fistula, sinusitis, and pulmonary cavitation had improved, the patient's general condition was acceptable, and he returned to normal activities.

Discussion

Herein, we reported a case of granuloma mass in the soft tissue of the leg and chronic ulcer around the talus with fistula to the bone simultaneous with chronic inflammatory osteomyelitis.

ANCA develops in patients with WG. However, its primary role in disease development is unclear. A relationship between the serum level of ANCA and disease activity in WG has been corroborated; accordingly, ANCA titers tend to be negative in cases with an inactive disease [1]. Positive C-ANCA is higher among WG patients with a higher severity of disease compared with those with limited disease [2]. The sensitivity of the approach is 90% and 60% in patients with generalized and limited WG disease, respectively [4]. Biopsy should be performed to determine the classical histopathological features of WG. Necrotizing vasculitis along with granuloma formation are the histopathologic hallmarks of WG as were observed in the current case. However, histopathologic evidence should be used along with pathological results to diagnose the disease. If the clinical picture of the patient confirms the diagnosis of WG, a complete histopathological picture is necessary [5]. Except for facial bone involvement, skeletal involvement of granulomatosis is very rare. Kim et al. reported a 54-year-old man with sternal osteomyelitis and destructive arthritis around the sternoclavicular joint. Similar to our study, antibiotics and conventional immuno-suppressive treatment were not effective. Finally, the presence of chronic granulomatous inflammation with fibrinoid necrosis had been confirmed. In our case, a lytic lesion in the head and neck of the talus andmedial ankle soft tissue swelling were observed. A bone fistula formed in the swelling of the ankle due to chronic inflammatory osteomyelitis.

There are some reports of WG with unexpected findings, including soft tissue involvement [6-9]. The disease may affect bone tissue and be observed simultaneously with chronic inflammatory osteomyelitis, as observed in our case. Sharma et al. reported a case of WG mimicking skull base osteomyelitis. The course of WG was very similar to that of skull base osteomyelitis, which could be due to pseudomonas infection. However, negative bone scan and bilateral otological features, which are uncommon in skull base osteomyelitis, led to the exclusion of skull base osteomyelitis [10].

The clinical picture of WG should be robust for

early diagnosis. The clinical course of this condition may be very similar to osteomyelitis, and it is essential to distinguish between the two conditions. The presence of infection must be rejected in WG. Although we observed Staphylococcus epidermidis in the culture and the patient was treated for the infection, the evidence of chronic granulomatous inflammation along with necrosis was in favor of WG. Therefore, we did not rule out the presence of either in favor of the other. Cyclophosphamide was administered based on pathological evidence of paranasal sinuses. The initial therapy for WG is gluco-corticoids along with cyclophosphamide that are gradually tapered during six months. In our case, 1 g IV cyclophosphamide for 5 months (each month 1 g) plus prednisolone 50 mg/d was administered. The patient's progress was suboptimal in the first hospitalization, and no improvement was observed.

Malignancies and bone-marrow toxicity are the most common severe side effects of cyclophosphamide, which are reported in 42% of patients [11]. Recently, the use of the anti–B cell antibody rituximab has increased for the treatment of patients with refractory WG [12]. Rituximab can potentially induce profound B cell depletion, and consequently, lead to the disappearance of ANCAs associated with clinical improvement [3]. Our case responded to treatment with rituximab weekly up to four doses. The agent was effective as an induction and maintenance treatment in our patient and resulted in remarkable improvement.

Conclusion

WG as a systemic disease with numerous manifestations needs a high index of clinical suspicion to ensure an accurate diagnosis. The disease could affect any organ and cause an inflammatory mass anywhere because of its granulomatous vasculitis nature. Rarely, WG may affect bone tissue and occur simultaneously with chronic inflammatory osteomyelitis. The analysis of ANCA is necessary when WG is suspected. Morbidity and mortality of the disease could be reduced with early diagnosis and treatment.

Acknowledgment

Not applicable.

Conflict of interest

The authors declare that they have no conflict of interest.

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