Granulomatosis with Polyangiitis, Presenting with Saddle Nose and Rash: A Case Report

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ABSTRACT:

Granulomatosis with polyangiitis is included in the group of antineutrophil cytoplasmic antibody-associated vasculitis that is pathologically characterized by necrotizing granulomatous inflammation and small to medium-sized vasculitis in multisystem organ.

Our report is about a 31-year-old female with prior history of scleritis, subglottic stenosis and chronic sinusitis presented with recurrent skin lesions on extremities for 1 month. Clinical examination revealed saddle nose deformity with multiple localized erythematous infiltrative papules on both elbows and extensor surface of forearms. Multiple discrete ulcerated papules and nodules on both thighs were demonstrated. Based on 2202 criteria developed by ACR/EULAR including clinical examination, laboratory finding, imaging and histopathology, she is diagnosed with granulomatosis with polyangiitis.

Key words: Granulomatosis with polyangiitis (GPA), antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), saddle nose deformity, skin lesions

Introduction

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of muti-organ vasculitis involving small to medium-sized vessels with subsequent tissue damage. This group includes granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA)[1]. GPA is an uncommon immunologically mediated systemic disease that is pathologically characterized by necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract and necrotizing vasculitis[1].

Case report

A 31-year-old female presented with recurrent skin lesions on extremities for 1 month.

In the past 10 years, she has developed recurrent nasal congestion and epistaxis. Physical examination showed small perforated nasal septum. Computed tomography of the lungs showed a tiny nodule on the left upper lung field.

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Six years prior, she was diagnosed with scleritis and subglottic stenosis. She had progressive dyspnea, which did not respond to steroid inhaler. Thus, tracheostomy was placed. In the following year, chronic sinusitis was diagnosed. Computed tomography of paranasal sinus showed mucosal thickening and total opacity of maxillary sinus. She had no prior history of tissue biopsy.

One month prior, skin lesions started to develop. Clinical examination revealed saddle nose deformity without nasal discharge and mild conjunctival injection. Her lungs were clear. S1 and S2 were heard on cardiac auscultation. There was also no edema. The skin lesion showed multiple localized erythematous infiltrative papules on both elbows and extensor surface of forearms. (Figure 1-A, B, C) Multiple discrete ulcerated papules and nodules on both thighs were demonstrated. (Figure 1-D,E) A skin biopsy specimen taken from the affected area on left forearm showed scattered foci of degenerated collagen in the dermis surrounded by palisades of histiocytes, neutrophils, and nuclear dusts, consistent with palisaded neutrophilic and granulomatous dermatitis. (Figure 2-A,B,C) Histopathology from left thigh revealed focally fibrinoid change of vessels, rare nuclear dusts, and extravasated erythrocytes, consistent with small vessel vasculitis. (Figure 3-A, B)

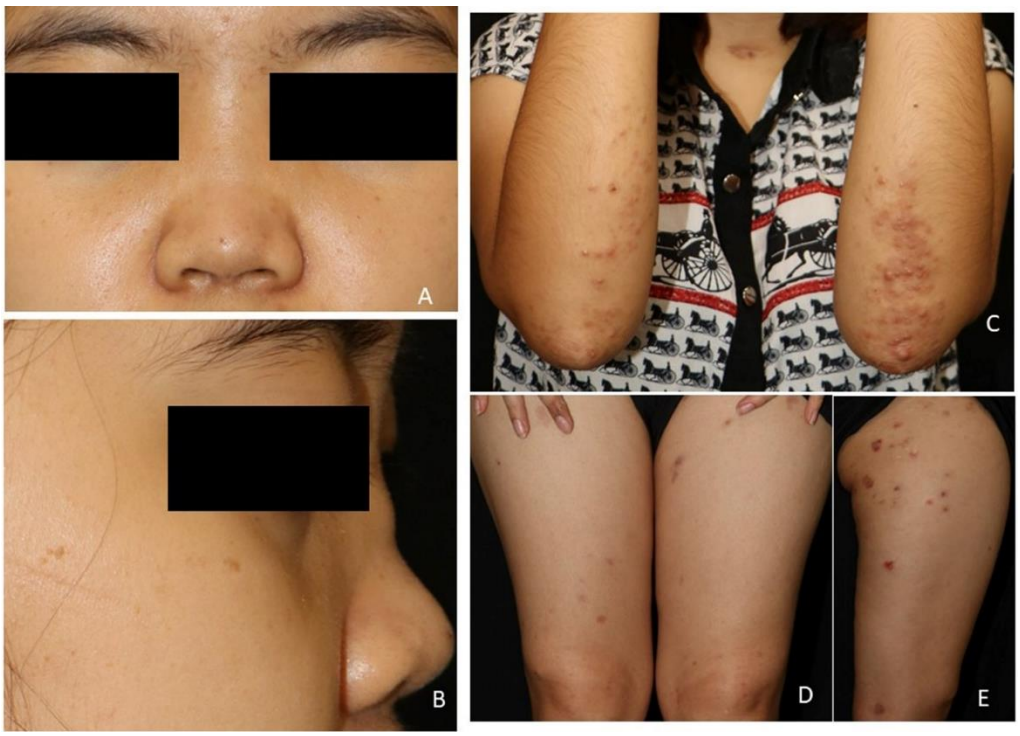

Figure 1 Saddle nose deformity, multiple localized erythematous infiltrative papules on both elbows and extensor surface of forearms. (A, B, C) Multiple discrete ulcerated papules and nodules on both thighs (D, E).

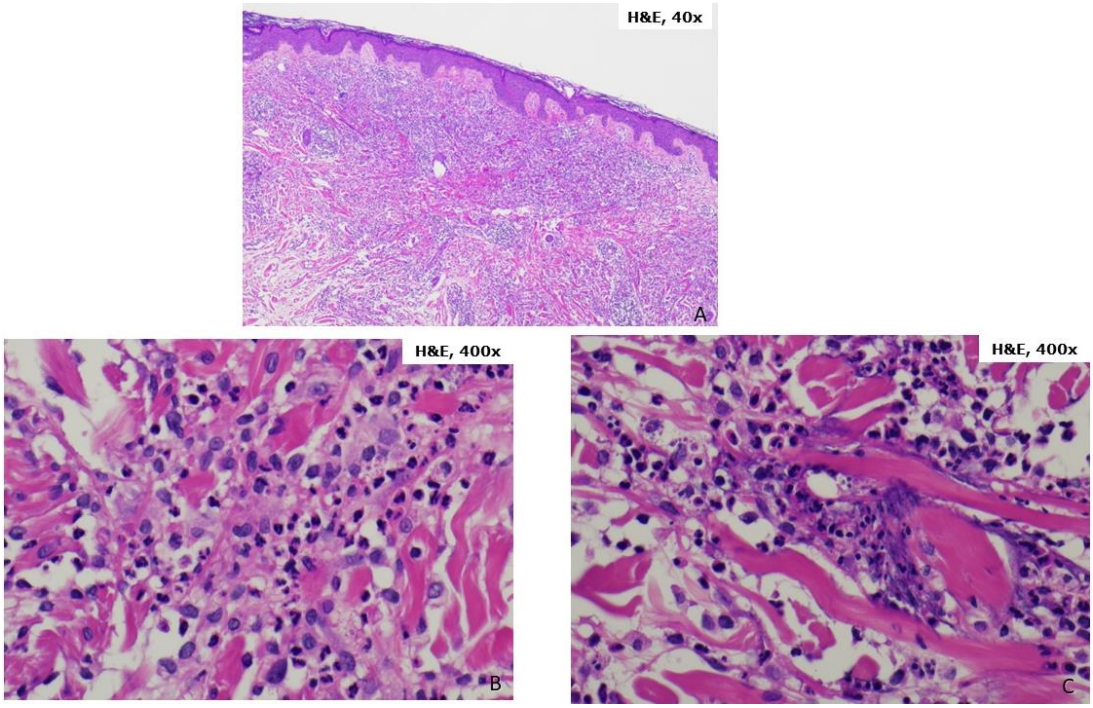

Figure 2 Scattered foci of degenerated collagen fibers in dermis associated with histiocytes, neutrophils, nuclear dusts, lymphocytes, consistent with palisading necrotizing granuloma pattern (H&E, A: original magnification X40, B and C: original magnification X400)

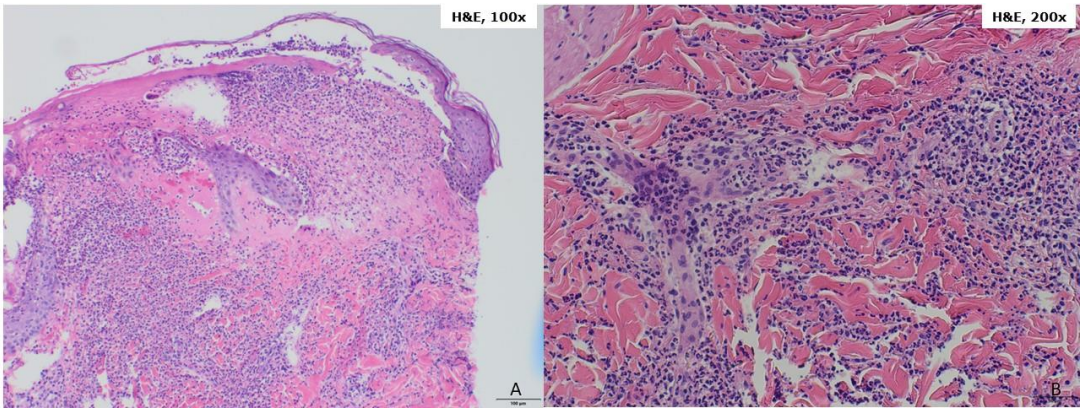

Figure 3 Focally fibrinoid change of vessels, rare nuclear dusts, and extravasated erythrocytes, consistent with small vessel vasculitis (H&E, A: original magnification 100x, B: original magnification X200)

Laboratory investigations showed positive for pANCA and anti-MPO, and negative for cANCA and anti-PR3. ESR was 63 mm/hr (0-20 mm/hr), and CRP was 4.1 mg/dL (0-1 mg/dL). Urine protein was negative with 0-1 cells/HPF of WBC and 2-3c ells/HPF of RBC

in urine analysis. Glomerular filtration rate (GFR) was 130.29 ml/min/1.73m^2. Other laboratory results were unremarkable. Granulomatosis with polyangiitis (GPA) was diagnosed. Mycophenolate mofetil 1,000 mg/day, oral prednisolone 15 mg/day, and 0.1% fluorometholone eyedrop were prescribed with gradual clinical response.

During the next three months, the patient developed increasing size of multiple painful erythematous papules with some pustules on buttocks and legs. One week after oral dicloxacillin was prescribed, the lesions subsided.

Discussion

Granulomatosis with polyangiitis (GPA), formerly named Wegener's granulomatosis, is an uncommon systemic disease characterized by necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract, and necrotizing vasculitis affecting predominantly small to medium vessels[1,2]. The incident rate is 0.4-11.9 cases per million person-years, predominate in European countries and seldom observed in East Asian countries[3]. Common clinical manifestations include destructive sinusoidal lesions, pulmonary nodules, and pauci-immune glomerulonephritis[4]. The upper airway is involved in 70-100% of cases. Nasal cavity and paranasal sinuses are the most common sites of head and neck area involvement. The most common features of nasal involvement are blood-stained rhinorrhea, crusting, and nasal obstruction. Septal perforation is the most common feature of damage as we found in this case[5]. Prevalence of subglottic stenosis was 6-23% as also presented in this case[5]. GPA can also affect the eyes, skin, joints, and nervous system[5]. There are various dermatological manifestations including palpable purpura, petechiae, subcutaneous nodules, digital gangrene, livedo reticularis/racemose, pyoderma gangrenosum-like ulcers, hemorrhagic blisters, and papulonecrotic lesions[6]. Histopathology findings including leukocytoclastic vasculitis, granulomatous inflammation with/without vasculitis, necrobiotic granuloma, palisaded neutrophilic and granulomatous dermatitis (PNGD) have been described[6,7]. GPA is most commonly associated with cytoplasmic ANCA and antibodies to proteinase3 (PR3)[4]. PR3-ANCAs are present in about two-thirds and MPO-ANCAs are also present in up to one-quarter of patient with GPA. Therefore, patients diagnosed with GPA can be negative for both type of ANCAs[8]. Positive ANCA serology is not essential for diagnosis of GPA if clinical and histological evidence can support the diagnosis[5]. There is no special diagnostic test for GPA. Diagnosis for GPA is based on a combination of the clinical manifestation which suggest a diagnosis of vasculitis, positive cANCA serology and histological evidence of necrotizing vasculitis, necrotizing glomerulonephritis or granulomatous inflammation from relevant organ biopy[5]. Recently in 2022, American College of Rheumatology (ACR)/European Alliance of Association for Rheumatology (EULAR), developed weighted criteria by threshold scores that is higher sensitivity and specificity than the previous use of 1990 ACR classification criteria. The recent criteria are beneficial for diagnosis of early-stage disease, which is essential to prevent long-term complications[9]. Based on the 2022 ACR/EULAR criteria, clinical criteria, laboratory, imaging, and biopsy criteria were included, our patient is definitely diagnosed with granulomatosis with polyangiitis (GPA) by the total score of 9 as shown in Table 1.

Table 1 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for granulomatosis with polyangiitis[9]

Clinical criteria	
*Nasal involvement**:** bloody discharge, ulcer, crusting, congestion, blockage, or septal defect/perforation	**+3**
*Cartilaginous involvement: inflammation of ear or nose cartilage, hoarse voice, stridor, endobronchial involvement, saddle nose deformity	**+2**
Conductive sensorineural hearing loss	**+1**
Laboratory, imaging, and biopsy criteria	
Positive test for cytoplasmic antineutrophil cytoplasmic antibodies (cANCA) or antiproteinase3 (anti-PR3) antibodies	**+5**
*Pulmonary nodules, mass or cavitation on chest imaging	**+2**
*Granuloma, extravascular granulomatous inflammation, or giant cell on biopsy	**+2**
*Inflammation, consolidation, effusion of the nasal/paranasal sinuses, or mastoiditis on imaging	**+1**
Pauci-immune glomerulonephritis on biopsy	**+1**
*Positive test for perinuclear antineutrophil cytoplasmic antibodies (pANCA)	**-1**
Blood eosinophil count $\geq 1x10^9$/liter	**-4**
A score of $\geq$ 5 is needed for classification of granulomatosis with polyangiitis	
**criteria included of this patient*	

The patient'scores included 3 scores of nasal involvement, 2 scores of saddle nose deformity, 2 scores of pulmonary nodules on chest imaging, 2 scores of extravascular granulomatous inflammation on biopsy, 1 score of paranasal sinuses effusion with minus 1 score of positive pANCA. Treatment depends on organ involvement, the activity and severity of disease[4]. Physician should be also concerned about superimposed infection of cutaneous lesions, especially in flare up of rashes as this patient. However, the presenting of skin ulcer did not encourage routine administration of topical or systemic antibiotics. Systemic antibiotics recommended only in the presence of significant infection such as erythema in the surrounding skin, increasing pain, progressive increase in ulcer size, pus discharge, hotness or edema[6]. There is no evidence of suspected active renal involvement. Therefore, no currently renal biopsy is needed in this patient. 10-year survival rate is estimated to be 60-70% compared to 40% with renal involvement[5]. Since GPA patients with skin lesions were more prone to have severe systemic manifestations and multiple organ involvement[6]. Regular follow-up is essential and should follow the standard guideline of management. These include measures to induce remission of new-onset organ threatening, remission of relapses and measures to maintain remission[6].

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