Case Report

Acne fulminans in a young man with granulomatosis with polyangiitis (Wegener's granulomatosis): A chance association or marker of serious systemic disease?

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Abstract

A 19-year-old man with granulomatosis with polyangiitis (Wegener's disease) presented with hemorrhagic facial nodules mimicking severe inflammatory acne (acne fulminans) as one of the first symptoms of the disease. The lesions were earlier treated as nodulocystic acne with isotretinoin without any benefit. Complete resolution was seen with pulsed methylprednisolone and oral prednisolone and mycophenolate mofetil thereafter. He also developed acute onset of severe pustular eruption of the face and a destructive ulcer of the auricle on two separate occasions. Facial lesions mimicking severe inflammatory acne, not responsive to standard treatment, may be a marker for more severe systemic disease such as Wegener's disease/granulomatosis with polyangiitis.

Key words: Acne fulminans, face, granulomatosis with polyangiitis, inflammatory nodules, ulcers, Wegener's disease, granulomatosis with polyangiitis

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Introduction

Granulomatosis with polyangiitis affects mainly the upper and lower respiratory system and kidneys; however, many organs including skin may be involved. About 15% of the patients have cutaneous manifestations that are specific to granulomatosis with polyangiitis. Facial involvement with pyoderma-like lesions or ulcerations and especially involvement of the periauricular area are thought to be specifically suspicious for the disorder.

Case Report

A 19-year-old man was admitted with severe joint pains and fever with bleeding from "boils" on the face of a few days' duration. The lesions were painful, engorged with blood and had appeared in crops. In the past 2 years, he had developed painful bleeding nodular lesions on the face on and off, for which he was seen by a dermatologist and treated with a course of minocycline and topical clindamycin, without much effect. He had also received a course of 20 mg of isotretinoin per day for about 8 weeks, without much improvement. There was history of nasal polypectomy, a few months before presentation. He also had fleeting joint pains involving the ankles and knees and a history of purpuric eruption on the legs that cleared spontaneously. He complained of severe fatigue and had lost 7 kg body weight in the past 2 months. There was no cough or hemoptysis.

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On examination, there were multiple crusted nodules on the face, many of which were breaking down, leaving bleeding ulcers with ragged edges [Figure 1a and b]. A provisional diagnosis of acne fulminans versus hemorrhagic nodules related to a systemic disease, mimicking nodular acne was entertained. He had a total white blood cell count of 11,200 cells/mm^3, an erythrocyte sedimentation rate of 40 mm/1st hour and a C-reactive protein of 80 mg/L. His rheumatoid factor, antinuclear antibody studies, hepatic and renal profile were normal. His cytoplasmic antineutrophil cytoplasmic antibody was reported as 2+ on ethanol-fixed slide by immunofluorescence. PR3 (main antigen of cytoplasmic antineutrophil cytoplasmic antibody) was strongly positive at 9.73 by ELISA.

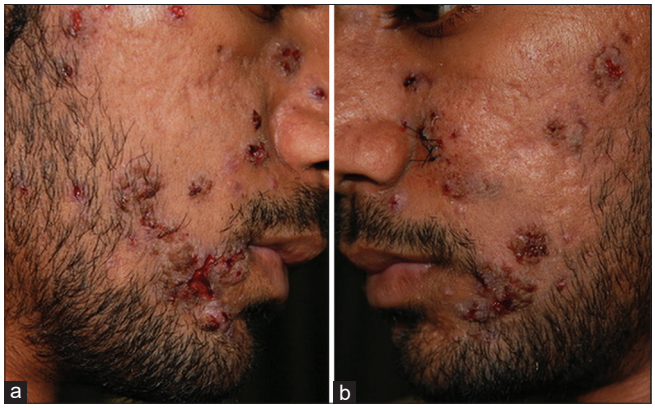

Figure 1 (a and b): Hemorrhagic nodules mimicking nodular acne, some breaking down with crust formation and some juxtaposed with preexistent scars of acne

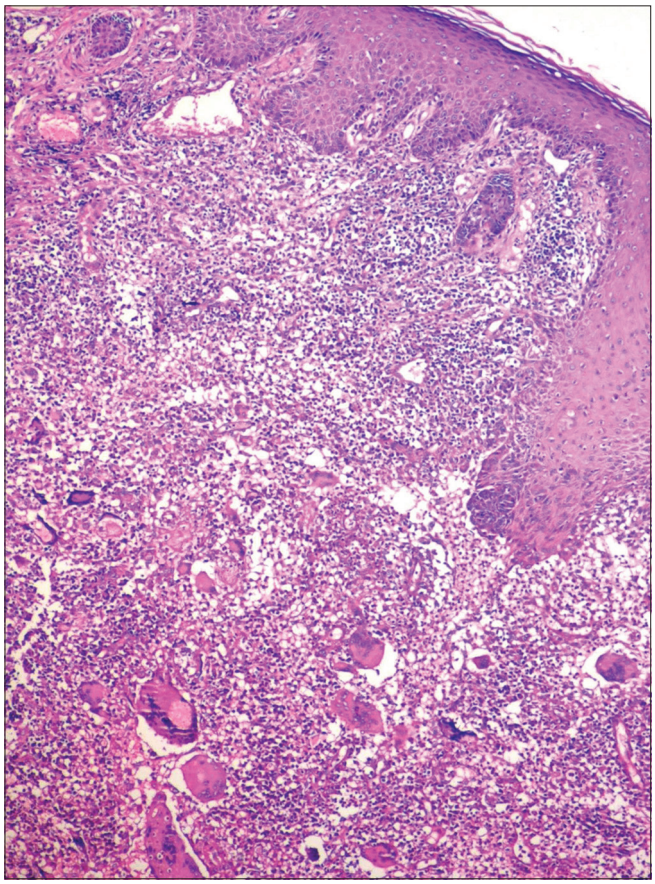

Figure 2a: Irregular epidermal and follicular infundibular epithelial hyperplasia with diffuse dermal infiltrate that has many giant cells (H and E, 100×)

Commonly documented skin manifestations of granulomatosis with polyangiitis like papules, nodules on the limbs, palpable purpura, ulcers, oral ulcers, gingivitis etc., were absent. Two skin biopsies taken from the edge of an ulcerated nodule showed irregular epidermal and follicular infundibular epithelial hyperplasia with diffuse dermal infiltrate containing lymphocytes and numerous giant cells [Figure 2a]. Follicular epithelium was hyperplastic with a dense dermal infiltrate of lymphocytes with several giant cells [Figure 2b]. Against the backdrop of granulomatous inflammation with multiple giant cells were also some granulomas showing a central fibrinoid degeneration [Figures 2c and 2d]. Computed tomography scan of paranasal sinuses and chest showed mucosal thickening of both ethmoid and maxillary sinuses and the nasal mucosa and discrete multiple angiocentric nodular opacities, respectively [Figure 3]. His eyes, central nervous system and heart examinations were normal. His urine routine examination, urine 24-hour protein, serum creatinine and blood urea nitrogen were normal.

Clinicopathological correlation suggested a diagnosis of granulomatosis with polyangiitis presenting with hemorrhagic facial nodules mimicking nodular acne. He responded dramatically to methylprednisolone pulse of 500 mg administered intravenously for 5 days with topical mupirocin for 15 days for the lesions [Figure 4a and 4b]. He was later treated with 60 mg of prednisolone and 2 g of mycofenolate mofetil. In the fifth month of treatment, he developed acute onset of painful pustular lesions studding his face and ulceration of the lobule of the ear

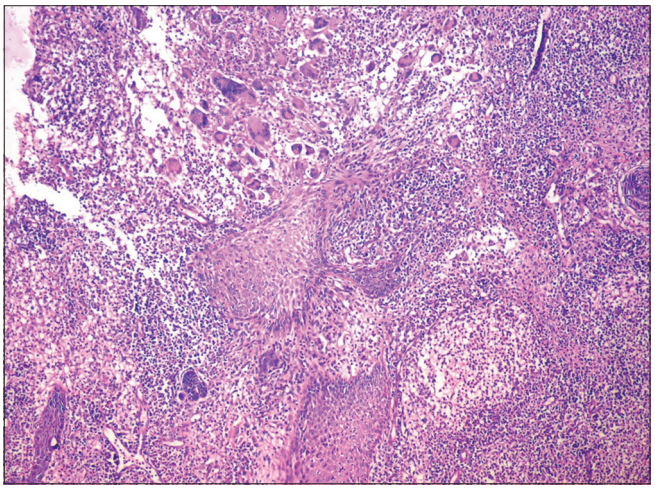

Figure 2b: Hyperplastic follicular epithelium with dense dermal infiltrate of lymphocytes with several giant cells (H and E, 100×)

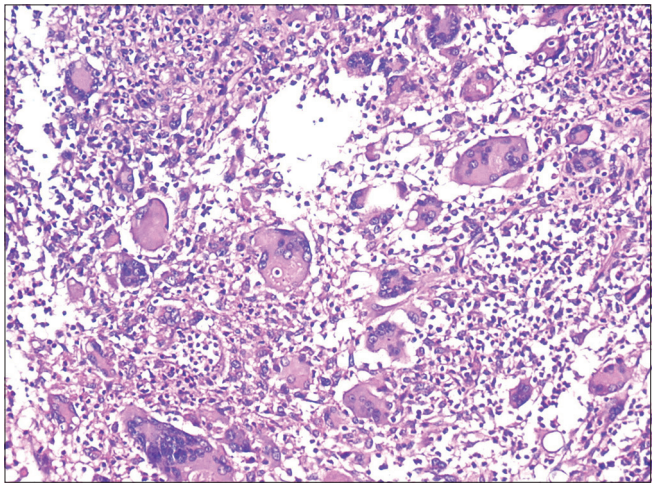

Figure 2c: Granulomatous inflammation with numerous giant cells (H and E, 400×)

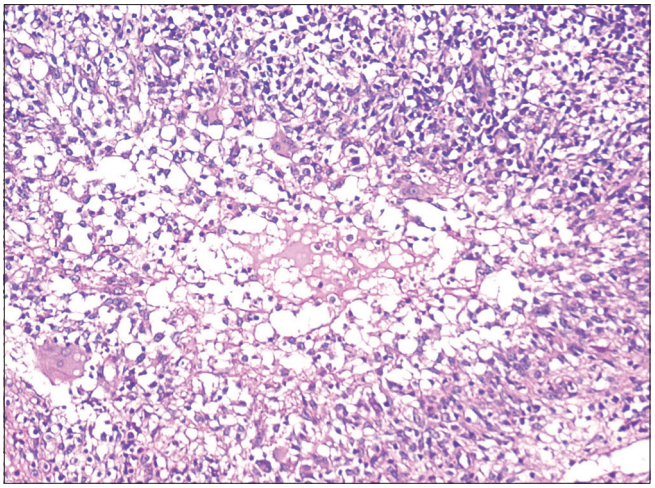

Figure 2d: Granuloma with central fibrinoid necrosis (H and E, 400×)

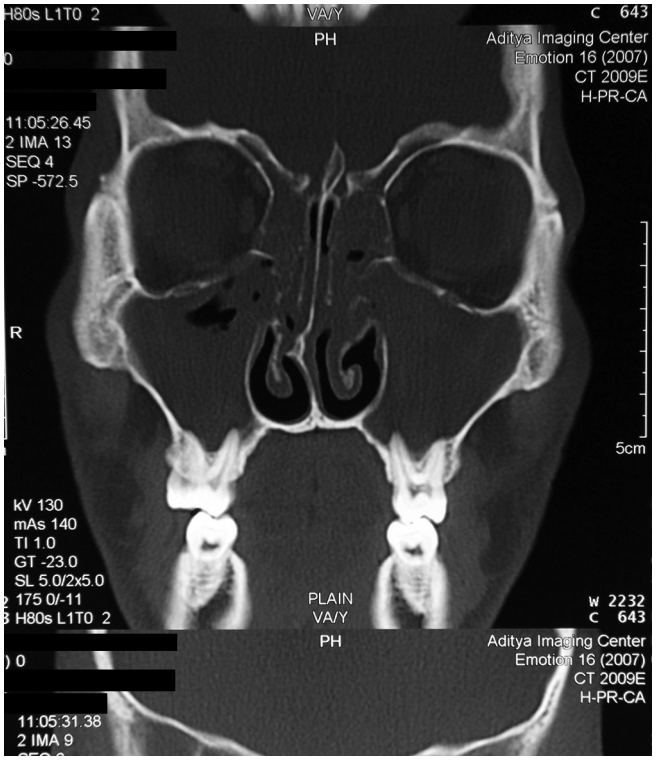

Figure 3: Diffuse mucosal thickening involving both maxillary sinuses with blockage of osteomeatal complexes. Mucosal thickening is seen involving bilateral ethmoid sinuses too

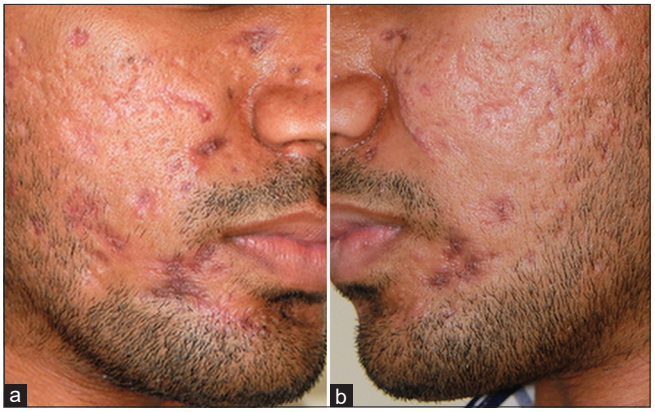

Figure 4 (a and b): Healed lesions after pulsed methylprednisolone therapy

[Figure 5a and 5b]. Prednisolone was again increased to 80 mg and the lesions resolved in 3 weeks. He continued to be well with no complaints 12 months after starting therapy except for inflammatory acne-like facial nodules off and on that resolved spontaneously.

Discussion

Granulomatosis with polyangiitis, previously known as Wegener's disease, is a rare multisystem disease. It is a form of small to medium vasculitis, and although it can affect any organ it most frequently targets the respiratory system and kidneys.[1] The peak incidence of the disorder which has been cited as between ages of 45 and 50 years has been shown to be increasing in child and adult population.[1-3] Data on the disorder in pediatric age group are sparse, but it is said to occur most commonly in the second decade.[1] Skin is involved in 35%–50% of patients with Wegener's granulomatosis[3-5] About 15% of patients have cutaneous lesions specifically associated with the disorder if one disregards those occurring secondary to infections, treatment or coexisting dermatoses unrelated to it.[1-3] Skin manifestations of the disorder include palpable purpura, cutaneous nodules, subcutaneous nodules, papules, vesicles, petechiae, urticarial lesions, panniculitis, pyoderma gangrenosum–like lesions and Raynaud's disease.[3-5] They are seldom seen to dominate the clinical picture.[4] Acneiform lesions have been reported in association with the disorder in patients younger than 20 years of age. They are often the first presenting symptom in this age group.[1,6-8] Cutaneous lesions have been noted more frequently in multiorgan disease.[1,2] Skin lesions are thought to run their course parallel to the systemic disease and generally respond to treatment of the

disorder.[3-5] Our case gave history of developing painful acne-like eruptions on his back at 17 years of age which spontaneously resolved with scarring. He then developed facial nodules with systemic signs and symptoms that were treated by a dermatologist unsuccessfully. He had nasal symptoms which were diagnosed and treated as sinusitis and nasal polyposis and was eventually operated upon just a few months before the nodular eruption. There is only one previous report of hemorrhagic acneiform nodules occurring in a teenager in English literature but that patient seems to have had very mild lesions compared with ours.[6] Interestingly, that patient also developed an acute pustular eruption and a destructive ulcer of the auricular lobule. Facial involvement with pyoderma-like lesions or ulcerations and especially involvement of the periauricular area are thought to be specifically suspicious for Wegener's granulomatosis [Figure 5b].[2,9] Over 50% of skin biopsies in granulomatosis with polyangiitis may yield nonspecific findings.[4,10] Necrotizing vasculitis, granulomatous vasculitis, extravascular palisading granulomas and leukocytoclastic vasculitis are most commonly reported.[1,4,10] While evidence of some form of vasculitis helps in a definitive diagnosis of the disorder, it is not always the case and absence of it does not rule out granulomatosis with polyangiitis. Erythema nodosum–like septal granulomatous inflammation and acneiform granulomatous folliculitis have been reported.[1]

Table 1: Other conditions presenting with severe acne

Syndrome	Components	Type of acne	Associated findings
SAPHO	Synovitis, acne, pustulosis, hyperostosis, osteitis	Sudden-onset hemorrhagic acne on face and chest like acne fulminans or even conglobate type	Neutrophilic palmoplantar pustulosis
PAPA	Pyogenic arthritis, pyoderma gangrenosum, acne	Severe nodulocystic conglobate type	Inflammatory bowel disease
PASH	Pyoderma gangrenosum, acne, HS	Moderate to severe truncal acne and HS	Overactivation of innate immune system with increased IL1 levels and sterile neutrophilic cutaneous lesions
SAHA	Seborrhea, acne, hyperandrogenism, androgenetic alopecia	Moderate to severe nodulocystic	Hirsutism
HAIR AN	Hyperandrogenism, acne, insulin resistance, acanthosis nigricans	Moderate nodulocystic acne	Other autoimmune diseases like Graves' disease, Hashimoto's thyroiditis
Late-onset congenital adrenal hyperplasia	Precocious puberty, irregular menses, infertility, acne in some cases	Severe, refractory or atypical acne	
APERTS syndrome	Craniosynostosis, early epiphyseal closure, characteristic facies, acne early in puberty	Moderate to severe acne at unusual sites like forearms and buttocks	Palmoplantar hyperkeratosis and acral hypopigmentation

IL: interleukin, HS: hidradenitis suppurativa

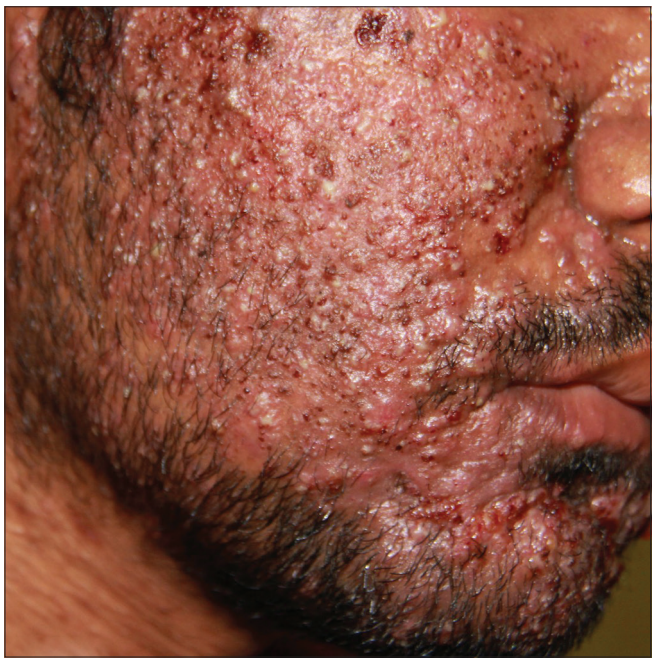

Figure 5a: Acute pustular eruption on face in second episode while on treatment

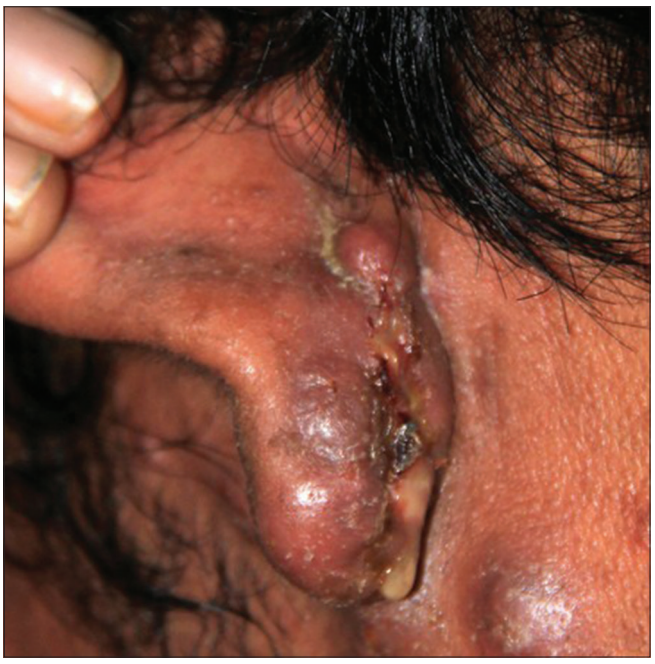

Figure 5b: Ear lobule ulceration in second episode while on treatment

Granulomatous pathology is also encountered not infrequently and represents tissue damage. It is said to be seen most often in non-purpuric lesions.[11] Our patient's skin biopsy from the facial nodules showed dense granulomatous infiltrate with plenty of lymphocytes and several giant cells but no evidence of vasculitis. A granuloma with central fibrinoid necrosis was also seen. This case underscores the importance of meticulously investigating patients presenting with severe acne-like lesions with associated musculoskeletal, upper airway, pulmonary or renal involvement with a high index of suspicion granulomatosis with polyangiitis. The knowledge of possibility of various presentations of acne-like lesions occurring on the face also reduces the chances of treatment with unnecessary antibiotics and topical drugs for acne. Table 1 shows a number of other conditions, mainly syndromes, that present with acne as a significant component.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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