CASE REPORT

Volume 17 Issue 1 2022

DOI: 10.21315/aos2022.1701.CR01

ARTICLE INFO

Submitted: 09/08/2021
Accepted: 15/01/2022
Online: 23/06/2022

Facial Palsy with Tongue Ulcer: A Rare Initial Presentation of Granulomatosis with Polyangiitis

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To cite this article: Nur ANZ, Mohamad MSF, Abdullah NA, Tan GC, Mawaddah A (2022). Facial palsy with tongue ulcer: A rare initial presentation of granulomatosis with polyangiitis. *Arch Orofac Sci*, **17**(1): 151–156. https://doi.org/10.21315/aos2022.1701.CR01

To link to this article: https://doi.org/10.21315/aos2022.1701.CR01

ABSTRACT

Granulomatosis with polyangiitis (GPA) is a rare multisystem disease. Although GPA is rare, it commonly presents in a localised stage where its manifestation involves the upper or lower respiratory tract before progressing to a generalised stage. Therefore, most patients with GPA will visit an oral surgeon or an otolaryngologist to seek treatment. However, the diagnosis of GPA is often delayed as GPA is not frequently considered as a differential diagnosis in common oral and facial diseases. The lack of gold standard investigation for the diagnosis of GPA makes management of this case, a diagnostic conundrum. We herein report a patient who was diagnosed with bilateral acute otitis media and left mastoiditis complicated with facial nerve palsy, and later developed tongue ulceration one month after his initial presentation. The ear, facial and oral symptoms represent a diagnostic red herring to a full-blown generalised stage of GPA.

Keywords: *Facial asymmetry; granulomatosis polyangiitis; oral ulcer; otitis media*

INTRODUCTION

Granulomatosis with polyangiitis (GPA) is an idiopathic multisystem disease characterised by the formation of necrotising granulomas and vasculitis at upper and lower respiratory tract as well as kidneys (Wojciechowska *et al.*, 2016). The incidence of GPA is approximately 5 to 10 cases per 1 million in the European continent (Wojciechowska *et al.*, 2016), and even rarer in the Southeast Asian region. Generalised GPA is reported to carry a high mortality rate, with an estimated survival of 5 months if left untreated (Wojciechowska *et al.*, 2016). Although GPA is rare, it commonly presents in a localised stage where its manifestation involves the upper or lower respiratory tract before progressing to a generalised stage (Iannella *et al.*, 2016). Therefore, the initial treatment

when the patient presents to an oral surgeon, or an otolaryngologist is often focused on the head and neck related morbidity. This causes unnecessary delay in diagnosing the disease (Srouji *et al.*, 2007; Iannella *et al.*, 2016). We herein report a patient who was diagnosed with bilateral acute otitis media and left mastoiditis complicated with facial nerve palsy, and later developed tongue ulceration one month after his initial presentation. The ear, facial and oral symptoms represent a diagnostic red herring to a full-blown generalised stage of GPA.

CASE REPORT

A 43-year-old male with no underlying illness presented with left facial asymmetry for 1 week associated with otalgia, yellowish blood stained otorrhoea, reduced hearing and tinnitus for the past 1 month. Physical examination showed facial weakness of House-Brackmann Grade II (Fig. 1a). There was tenderness of the left mastoid bone with an inflamed left tympanic membrane, which was bulging and associated with sagging of the posterior canal wall (Fig. 1b). The right tympanic membrane was also inflamed but was not bulging with normal ear canal. The patient was diagnosed with bilateral acute otitis media complicated with left mastoiditis and facial nerve palsy.

His pure tone audiometry showed bilateral conductive hearing loss worse on the left side. High resolution computed tomography scan of the temporal bone showed soft tissue density within the mastoid air cells on the left side with bilateral middle ear soft tissue densities. No apparent erosion of the facial canal was found. The patient underwent left cortical mastoidectomy to eradicate the infected mastoid air cells and right ventilation tube was placed on the right tympanic membrane to drain pus from the middle ear thus alleviate the otalgia. The patient was discharged well at postoperative day-7 with oral amoxicillin/clavulanate 625 mg BD, prednisolone 20 mg OD and was given a fortnightly follow-up.

Upon follow-up, his facial weakness completely resolved, but at the fourth post-operative week, the patient complained of a small left tongue ulcer which was associated with pain. The patient was evaluated by an oral surgeon and was prescribed triamcinolone acetate ointment with an initial impression of aphthous ulcer.

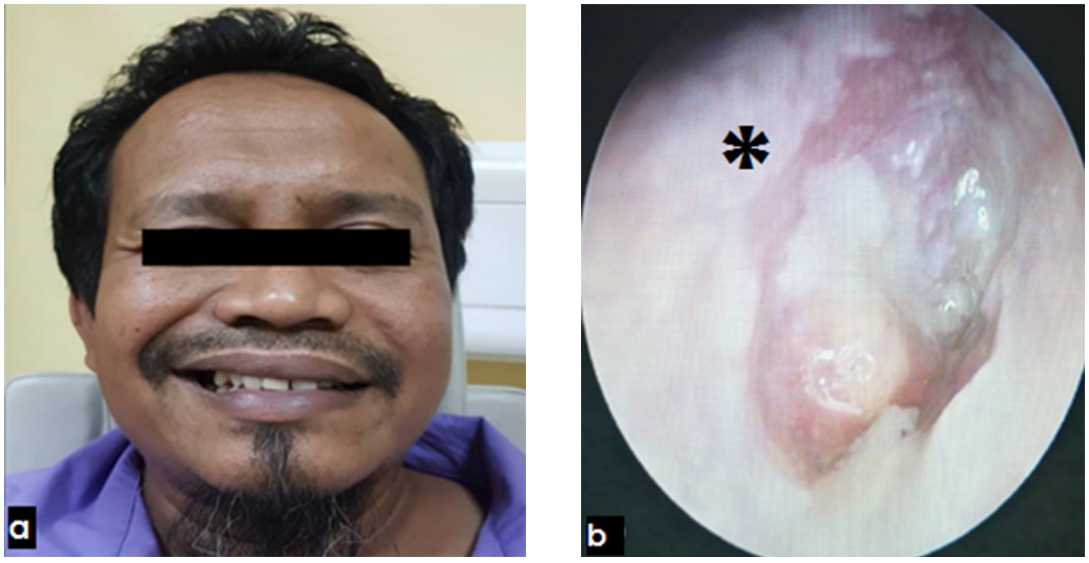

Fig. 1 (a) Left facial nerve palsy House-Brackmann Grade II. There was no obvious facial asymmetry seen at rest with slight asymmetry of left nasolabial fold on smiling. Minimal loss of left forehead wrinkle was also seen. (b) Inflamed and bulging left tympanic membrane with posterior wall sagging (*).

Unfortunately, the patient represented 3 days later with worsening tongue ulceration (Fig. 2), associated with chest pain, shortness of breath, intermittent fever, joint pains, mucoid diarrhoea and intermittent epistaxis.

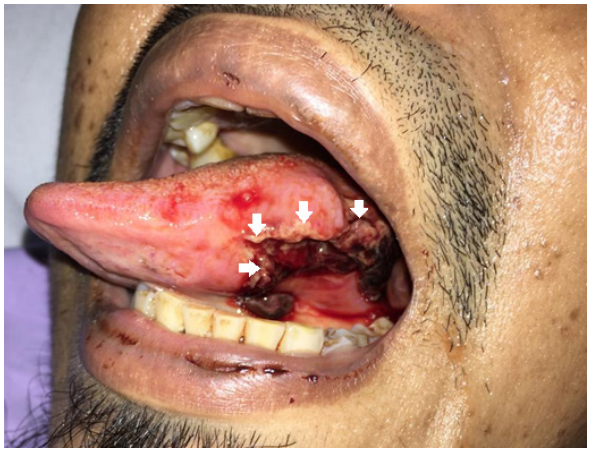

Fig. 2 A huge ulcer at the left lateral border of tongue with contact bleeding and surrounding slough (white arrow).

Histopathological examination of granulation tissue from the mastoid antrum sent during the initial cortical mastoidectomy was sought after. The specimen showed a chronic inflammatory process with presence of giant cells and central necrosis (Fig. 3), supporting a diagnosis of necrotising granulomatous inflammation. Following a multidisciplinary meeting, biopsy of the oral ulcer was deferred, in view of a high clinical suspicion of a systemic inflammatory process. The chest radiograph showed a cavitating lesion on the right upper lobe and consolidation on the right lower lobe of the lungs. Subsequent echocardiography showed minimal pericardial effusion with good left ventricular function. Sigmoidoscopy and colonoscopy were performed during admission in view of patient had few episodes of haematochezia in ward and biopsy showed moderate colitis. Bronchoscopy and bronchial alveolar lavage were performed, and samples were sent for *Mycobacterium tuberculosis* DNA. The patient progressed further with purplish skin rash over trunk, upper limbs and lower limbs suggestive of vasculitis and ischaemia of toes and fingers. Following a multidisciplinary team discussion, the patient was empirically treated as disseminated tuberculosis (pulmonary, mastoid, pericarditis and colitis) with differential of GPA. He was started on a combination isoniazid 375 mg/rifampicin 750 mg/ethambutol 1375 mg and pyrazinamide 2000 mg OD therapy but unfortunately, he deteriorated from pulmonary haemorrhage with respiratory failure and acute kidney failure requiring artificial ventilation and haemodialysis support. At day-3 of admission, the antineutrophil cytoplasmic antibodies (ANCA) result was reported positive with a negative *Mycobacterium tuberculosis* DNA supporting a diagnosis of GPA. Anti-tuberculous therapy was immediately stopped, and intravenous methylprednisolone 50 mg OD was commenced. Intravenous rituximab and cyclophosphamine was later started in view of initial poor response to methylprednisolone as a single therapy. He subsequently showed slow but progressive improvement in his respiratory, hemodynamic and kidney status with combination immunosuppressive therapy.

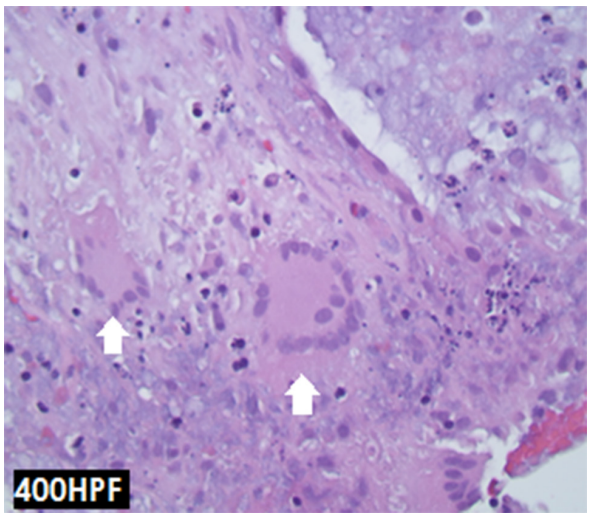

Fig. 3 Histopathological examination of the granulation tissue from left mastoid antrum showing a chronic inflammatory process. Two multinucleated giant cells (white arrows) and epithelioid histiocytes were seen in 400 high-power field (HPF).

After 7 weeks of admission, the oral ulcers showed signs of healing and the patient no longer required haemodialysis support. He was discharged with a tapering dose of oral prednisolone and 3 weekly intravenous cyclophosphamides. At 12 months following diagnosis, oral ulcers were completely resolved, and he remains asymptomatic of renal failure. At 18 months following the initial presentation, the patient is still on immunosuppressive therapy.

Ethics Statement

This report was approved by the institutional Ethical and Review Board (Ref. No.: FF-2021-192, dated 13th March 2021). The patient was provided with a written consent for publication of this manuscript and use of the clinical images herein.

DISCUSSION

GPA or historically known as Wegener granulomatosis is a rare multisystem disease (Wojciechowska *et al.*, 2016), especially in the Southeast Asia region. The European Vasculitis Study Group (EUVAS) classified Wegener granulomatosis into localised, early systemic and generalised stage (Iannella *et al.*, 2016). In the localised stage, manifestation is restricted to the upper or lower respiratory tract, whereas in the early systemic stage any organ except the kidney may be affected. The generalised stage of GPA presents with kidney involvement with or without organ failure (Iannella *et al.*, 2016). GPA has been reported to progress from its localised to generalised stages within a variable period of time (weeks to years). However, in some cases, the disease may remain stagnant in the localised or early systemic stage without any apparent progression (Iannella *et al.*, 2016).

Majority of patients with GPA present in a localised stage through involvement of facial and oral manifestations (Iannella *et al.*, 2016). Sinonasal involvement is the most common manifestation of GPA in head and neck region (Wojciechowska *et al.*, 2016), and it occur in up to 85% of patients. Additionally, 19% of patients present with otologic involvement as their first symptom (Wojciechowska *et al.*, 2016). GPA can involve either or a combination of the external, middle, or inner ear. Patient may present with chronic otitis media and conductive hearing loss, as seen in our case. Otitis media in GPA is secondary to Eustachian tube dysfunction from nasopharyngeal involvement (Wojciechowska *et al.*, 2016).

A combination of ulcerative oral lesion and facial nerve palsy, occurring in the same patient is a rare presentation of GPA. In only about 5%–6% of patients with GPA, oral cavity lesions were the presenting complain (Wojciechowska *et al.*, 2016). Similarly, the incidence of facial nerve palsy in GPA is reported to be low, between 5% to 8% (Iannella *et al.*, 2016). Facial nerve palsy presenting without an associated middle ear pathology occurred in about 10% of GPA cases (Iannella *et al.*, 2016). It is thought that vasculitis of the superficial petrosal branch of the middle meningeal artery and posterior auricular artery supplying the facial nerve contributed to the facial nerve damage in the absence of middle ear involvement (Iannella *et al.*, 2016). However in most cases, facial palsy appeared in the localised stage of GPA and were associated with middle ear or temporal bone diseases (Iannella *et al.*, 2016). Even though facial and oral manifestation is commonly the first manifestation of GPA, oral cavity pathologies usually present late in the disease (Lalla *et al.*, 2020). As seen in our case, oral ulcer presented late preceding the otitis media and facial nerve palsy.

Tuberculous infection is endemic in Southeast Asia, particularly in Malaysia. In most cases where a necrotising granulomatous inflammation is seen pathologically, a diagnosis of tuberculosis is entertained first, compared to rare

immunologic conditions such as GPA. The diagnostic difficulties faced in managing this case is partly explained by inability to exclude tuberculous infection in the earlier course of the disease. *Mycobacterium tuberculosis* infection is difficult to demonstrate in both microbial and histopathological specimens (Purohit & Mustafa, 2015). Microbial specimens such as Zeihl-Neelsen (ZN) stain and culture have low sensitivity, but high specificity compared to histopathological specimens, which demonstrated a high sensitivity but low specificity (Purohit & Mustafa, 2015). ZN stain has limited diagnostic value with reported sensitivity of only up to 40% (Purohit & Mustafa, 2015). Even though isolation of *Mycobacterium tuberculosis* by culture is considered "gold standard" for diagnosing extrapulmonary tuberculosis, it is not 100% sensitive (Purohit & Mustafa, 2015). Currently a new molecular diagnostic test for *Mycobacterium tuberculosis* DNA is available. This test demonstrated better sensitivity that sputum smear microscopy and similar specificity with sputum culture, but with faster results (Piatek *et al.*, 2013).

In our case the patient initially presented with localised GPA with upper respiratory tract symptoms and the diagnosis of GPA was only arrived at after the patient presented with generalised GPA. The diagnosis of GPA was very challenging and had to be made based on clinical presentation of systemic disease suggesting vasculitis, positive ANCA and histologic evidence. Since its introduction in 1990, the American College of Rheumatology 1990 Criteria for the Classification of Wegener Granulomatosis has been widely used by the clinicians to distinguish GPA with other types of vasculitis (Leavitt *et al.*, 1990). Four criteria were aligned where the presence of two or more criteria is associated with a sensitivity of 88.2% and a specificity of 92.0% in diagnosing GPA. The criteria are nasal or oral inflammation (painful or painless oral ulcer or purulent or bloody nasal discharge); abnormal chest radiograph (nodules, cavities, or fixed infiltrates); granulomatous inflammation on biopsy; and abnormal urine sediment (red cell cast or >5 red blood cells per high power field) (Leavitt *et al.*, 1990). Our case met three of these criteria where patient has painful oral ulcer, cavitating lesion in his chest radiograph at the right upper lobe and granulomatous inflammation on the mastoid tissue specimen.

In a case of bilateral acute otitis media in a previously healthy individual, suspicion of other cause of the disease such as tuberculosis and autoimmune disease should be considered. This is especially when it is associated with other symptoms such as facial nerve palsy and oral ulcer. Early diagnosis and treatment of GPA is crucial as it can prevent irreversible end organ damage and reduce mortality (Wojciechowska *et al.*, 2016). Srouji *et al.* (2007) reported a delay in diagnosis of GPA patients with head and neck manifestations. Awareness among oral surgeons and otolaryngologists on this rare disease is important, therefore should be highlighted. If left untreated, up to 80% of the patients die within one year with renal disease as the most common cause of death (Iannella *et al.*, 2016; Panupattanapong *et al.*, 2018). In our case, the patient was diagnosed with multiorgan involvement, 3 months following his initial presentation and survived the disease with favourable outcome. While cure remains elusive in this disease, relapses often require immunosuppressive therapy (Panupattanapong *et al.*, 2018).

CONCLUSION

Facial asymmetry is a common complication of ear diseases, making a diagnosis of GPA rarely considered in its early management. Albeit rare, progression of the patient's symptoms later clinched its diagnosis. This case demonstrates that early suspicion of GPA in patients presenting with oral and facial manifestation is paramount to initiate diagnostic investigations and improve patient outcome.

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