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# A RARE CASE OF LIMITED GRANULOMATOSIS WITH POLYANGIITIS PRESENTING AS BILATERAL PAROTITIS

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## ABSTRACT

*Background:* Granulomatosis with polyangiitis (GPA) is a rare autoimmune vasculitis affecting small and medium-sized vessels, commonly involving the respiratory tract and kidneys. Salivary gland involvement, particularly bilateral parotitis, is an uncommon presentation of GPA.

*Case Report:* We report the case of a 38-year-old Asian male who presented with left ear pain and parotid swelling after a water park visit. Initially treated with antibiotics for suspected otitis externa, his symptoms worsened, leading to bilateral parotitis, facial palsy, and otomastoiditis. Imaging revealed parotid abscesses and lab results showed elevated antineutrophil cytoplasmic antibodies (ANCA), specifically cytoplasmic ANCA directed against proteinase 3, confirming the diagnosis of GPA. Cultures and autoimmune workups for other causes, such as Sjogren's syndrome and immunoglobulin G4-related disease, were negative. Treatment with high-dose corticosteroids and methotrexate resulted in significant clinical improvement.

*Conclusion:* This case highlights the importance of considering GPA in atypical presentations such as parotitis, even in the absence of renal involvement. Early diagnosis and appropriate immunosuppressive therapy are critical to prevent further complications in multisystem involvement.

## KEYWORDS

Limited granulomatosis with polyangiitis, parotitis, bilateral parotitis

## LEARNING POINTS

- This case highlights the importance of recognizing atypical manifestations of granulomatosis with polyangiitis (GPA), such as bilateral parotitis, which aids in diagnosing and treating rare presentations more effectively.
- It emphasizes the need to expand differential diagnoses of salivary gland involvement, guiding the distinction of GPA from other similar conditions when antibiotics fail.
- By highlighting a rare presentation of GPA, this case improves diagnostic understanding in autoimmune diseases, enabling earlier interventions and leading to better patient outcomes.

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## INTRODUCTION

Granulomatosis with polyangiitis (GPA) is an autoimmune vasculitis that commonly affects small and medium-sized vessels, primarily the nasopharynx, lung, and kidneys, presenting as necrotizing granulomas and focal necrotising glomerulonephritis. It is often associated with autoantibodies against neutrophilic cytoplasmic components (ANCA), specifically cytoplasmic-ANCA (C-ANCA) directed against proteinase-3 (PR3). Autoimmune conditions present a challenge for accurate diagnosis due to their potential overlap. Salivary gland involvement is commonly observed in patients diagnosed with Sjogren's syndrome, immunoglobulin G4 (IgG4-related) disorders, and sarcoidosis[1]. However, its rarity in GPA is what rendered our case particularly intriguing. We present a case involving a middle-aged Asian male whose diagnosis of GPA stemmed from an unusual manifestation, showcasing bilateral parotitis, otomastoiditis, and facial palsy.

## CASE DESCRIPTION

A 38-year-old Asian male with a history of allergic rhinitis and a positive QuantiFERON test, who recently visited a water park, presented to a walk-in clinic with complaints of pain in his left ear. It was presumed to be otitis externa, and he was prescribed neomycin/polymyxin/hydrocortisone otic solution, which yielded no benefit. He presented a week later to his primary care provider's office with worsening symptoms and a tender left preauricular lymph node and was prescribed ibuprofen and oral ciprofloxacin. With no relief despite the addition of antibiotics, the patient went to the otolaryngology clinic and was diagnosed with left-sided otitis externa and left parotitis. He was prescribed amoxicillin/clavulanic acid, fluconazole, tramadol and a methylprednisolone dose pack. Despite multiple courses of antibiotics, the patient did not improve and subsequently started having right parotid involvement, coercing the patient to present to the emergency room. His vitals were normal, and he was afebrile. On physical examination, the left external auditory canal was mildly erythematous with a small volume of yellow debris/drainage, and the left tympanic membrane was coated with white debris. In contrast, the right external auditory canal and tympanic membrane were normal. The facial nerve was intact bilaterally. Anterior rhinoscopy revealed a normal midline septum with no mucopurulence or polyps. On oral examination, no purulence was expressed from Stenson's duct bilaterally. Neck examination revealed bilateral parotid gland enlargement with induration and tenderness, and there was swelling and tenderness of the bilateral preauricular area *(Fig. 1)*. Otherwise, no lymphadenopathy was palpated. Laboratory results are shown in *Tables 1-5*. Computed tomography (CT) soft tissue neck with contrast revealed bilateral parotitis with a concomitant 22 mm right parotid gland abscess. Fluid throughout the left middle ear and in left mastoid air cells was consistent with otomastoiditis. Dense secretions and mucosal thickening were present throughout the left maxillary sinus, indicative of severe left maxillary sinusitis. Left ear culture was obtained, and aspiration of the bilateral parotid gland was performed. Cultures were negative, and acid-fast bacilli (AFB) culture and stain were negative as well. He was treated with intravenous (IV) vancomycin and ampicillin/sulbactam. He had mild improvement and was subsequently discharged home on oral levofloxacin and metronidazole.

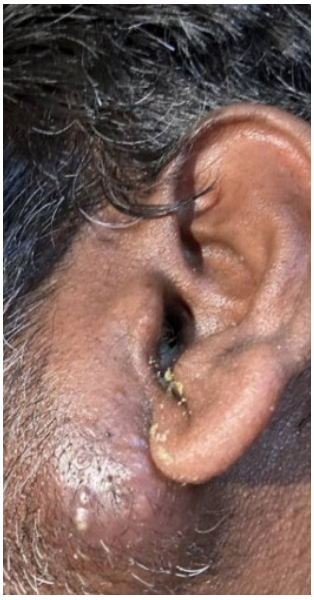

*Figure 1. Swelling and tenderness of the preauricular area.*

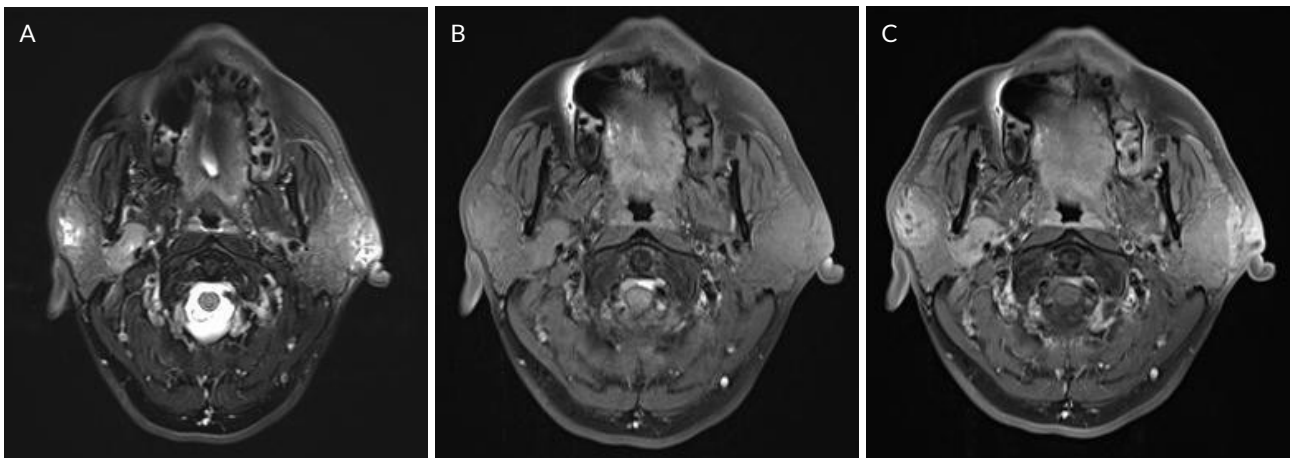


*Figure 2. Magnetic resonance imaging of A) T2, B) axial pre-contrast and C) axial post-contrast soft tissue.*

| Labs | Values |
|---|---|
| White blood cell count (x10$^3$/µl) | 12.7 |
| Haemoglobin (g/dl) | 13.2 |
| Platelets (x10$^3$/µl) | 321 |
| Creatinine (mg/dl) | 0.8 |
| Blood urea nitrogen (mg/dl) | 67 |
| Sodium (mmol/l) | 140 |
| Potassium (mmol/l) | 3.9 |
| Calcium (mg/dl) | 9.2 |
| Bicarbonate (mmol/l) | 25 |
| Syphilis | Negative |
| Human immunodeficiency virus test | Negative |

*Table 1. Lab values during the first admission.*

| Labs | Values |
|---|---|
| White blood cell count (x10$^3$/µl) | 7.2 |
| Haemoglobin (g/dl) | 13.2 |
| Platelets (x10$^3$/µl) | 338 |
| Creatinine (mg/dl) | 0.8 |
| Blood urea nitrogen (mg/dl) | 9 |

*Table 2. Lab values after re-admission.*

| Microbiology | Values |
|---|---|
| AFB culture and stain | Negative |
| Tissue culture and Gram stain | Negative |
| Fungal culture and stain | Negative |
| *Bartonella henselae* IgG, and IgM | Negative |
| VDRL test | Negative |
| Mumps IgM | Negative |
| Lyme disease *(Borrelia burgdorferi)* | Negative |

**Abbreviations:**
AFB, acid-fast bacilli; VDRL, venereal disease research laboratory

*Table 3. Microbiology labs.*

However, the patient was readmitted three days later with worsening symptoms, persistent drainage at the site of needle aspiration from the left parotid and new left facial nerve palsy. His vitals were normal. Repeat labs are shown in *Table 2*. Magnetic resonance imaging (MRI) soft tissue neck with contrast *(Fig. 2)* revealed bilateral parotitis, small subcutaneous fluid lateral to both parotid glands (1.4 x 0.7 cm on the left and 1.2 x 0.5 cm on the right), which may represent an abscess, reactive lymph node involving the deep lobe of the right parotid gland with the probable central suppurative or necrotic centre, left maxillary, anterior ethmoid, and frontal sinusitis, with left otomastoiditis. He underwent urgent left myringotomy with tympanostomy tube placement, left maxillary antrostomy, and biopsy of the parotid. This was to help decompress the left facial nerve. There was significant purulence of the left middle ear, inflamed nasal mucosa and maxillary sinus and necrosis of the parotid gland. He was treated with linezolid and piperacillin-tazobactam by infectious disease and infectious workup including *Bartonella henselae* IgG, and IgM, venereal disease research laboratory (VDRL) test, mumps IgM, Lyme was negative *(Table 3)*. Cultures from the operating room were negative for AFB culture and stain, fungal culture and stain, tissue culture and Gram stain. Rheumatology was consulted as cANCA was positive at 1:40 (cut off <1:20), and PR3 was positive at 438 (cut off 0-19). Further autoimmune workup revealed normal or negative angiotensin-converting enzyme, Vitamin D 1,25-dihydroxy, immunoglobulin profile and IgG subclasses *(Table 4)*. A biopsy of the left maxillary sinus showed marked acute inflammation associated with tissue necrosis, and left parotid tissue showed marked acute and chronic inflammation. Stains for fungi and AFB were negative. He was given pulse steroids in the hospital of 500 mg solumedrol on day 1 and 1000 mg on days 2 and 3. His symptoms improved, and his inflammatory markers

| Labs | Values |
|---|---|
| C-ANCA | 1:40 |
| PR3 | 438 |
| Anti SS-A | Negative |
| Anti SS-B | Negative |
| ANA | Negative |
| Angiotensin-converting enzyme | Negative |
| Immunoglobulin profile and IgG subclasses | Negative |

**Abbreviations:**
C-ANCA, cytoplasmic ANCA; ANCA, antineutrophil cytoplasmic antibodies; PR3, proteinase 3; ANA, antonuclear antibody.

*Table 4. Autoimmune labs.*

| Labs | Before treatment | After treatment |
|---|---|---|
| C-reactive protein (mg/l) | 41.9 | 11.2 |
| Erythrocyte sedimentation rate (mm/hr) | 50 | 24 |

*Table 5. C-reactive protein and erythrocyte sedimentation rate levels before and after treatment.*

improved from a sedimentation rate of 50 mm/hr to 24 mm/hr and C-reactive protein improved from 41.9 mg/l to 11.2 mg/l *(Table 5)*. He was later discharged on prednisone 60 mg, trimethoprim/sulfamethoxazole prophylaxis and started on methotrexate outpatient. Within 1 month of discharge, his sinusitis, parotitis, and otomastoiditis resolved, and facial nerve paralysis improved.

## DISCUSSION

Granulomatosis with polyangiitis is a rare autoimmune condition affecting small vessels. It is suggested that the annual incidence of GPA ranges from 10 to 20 cases per million people, with geographical factors playing a significant role. Specifically, higher rates are observed in colder regions. This condition tends to affect older individuals more than children, with the highest frequency observed in the age range of 64 to 75 years, and there does not seem to be sex predilection[2]. The exact origins of GPA remain unclear, although the link between the disease's pathophysiological changes and ANCA has been firmly established. Currently, it is understood that various genetic and microbial elements contribute to initiating the disease and influencing its severity. It is believed that the inflammatory foundation of GPA is indicated by ANCA positivity[3]. It has been observed that in Asian patients with GPA, ANCA may predominantly stem from antibodies targeting myeloperoxidase. In contrast, in Caucasian patients, there is a prevalence of anti-PR3-ANCA, even when the vasculitis is not specifically GPA[4]. Characteristic traits of GPA include focal necrosis, necrotizing granuloma, pauci-immune vasculitis primarily involving the vasculature in the nasopharynx, pulmonary and renal entities and less frequently involves the skin, cardiac, central nervous, and gastrointestinal system[5]. The upper respiratory tract is commonly involved in over 90% of cases, while the lower respiratory tract is affected in 15 to 50% of patients. Scleritis affects about half of the patients, and there is renal involvement in 10 to 20%. Skin manifestations like purpura, nodules, ulcers, and granulomas are present in 50 to 60% of cases. Nervous system involvement, mostly peripheral neuropathies affecting the facial nerve, is observed in 30 to 40% of patients. Cardiovascular disorders like pericarditis or valve lesions occur in less than 10% of patients, while musculoskeletal symptoms like myalgia and/or arthralgia are reported in 70% of cases [6-9]. Based on earlier studies, the occurrence of salivary gland complications in GPA at any stage of the illness varies between less than 1 to 3%[10,11]. Chandwar et al., through their review of 50 GPA cases involving salivary gland complications, noted a slight predominance in males[1].

Initially, our patient presented with ear pain and discharge after a visit to a water park, symptoms that might have been dismissed as a typical ear infection were it not for the simultaneous involvement of the parotid gland. Despite multiple rounds of antibiotics, the symptoms persisted, suggesting a more complex underlying condition requiring further diagnostic evaluation. Furthermore, facial nerve involvement, indicated by facial palsy, added to the intricacy of the case. Co-occurrence of facial palsy, bilateral parotitis, left sinusitis, left otomastoiditis, and negative cultures, an inadequate response to both oral and intravenous antibiotics, coupled with positive C-ANCA, anti-PR3, elevated inflammatory markers, and improvement with systemic steroids, strongly supported a diagnosis of GPA, presenting in an atypical manner. Intriguingly, the absence of renal involvement in our patient diverged from the typical presentation of GPA, which often includes pauci-immune glomerulonephritis. Currently, we continue to follow up our patient to monitor his prognosis as it was seen from previous observations that salivary gland involvement is associated with a better prognosis, minimal renal, and rarely central nervous system involvement. Even though, in our case, the parotid biopsy revealed inflammatory changes with necrosis, specific vasculitic findings were not observed. Given the patchy distribution of vasculitis, biopsies may not always capture these changes. Additionally, the positive C-ANCA result supports a diagnosis of vasculitis, emphasizing the importance of integrating biopsy, clinical, and laboratory findings for accurate assessment. Treatment options are chosen based on categorizing patients into limited or severe disease. Treatment involves immunosuppressive agents in two phases: induction and maintenance. Cyclophosphamide with glucocorticoids has been proven effective for induction of remission. According to the RAVE trial[12] rituximab was found to be non-inferior to cyclophosphamide for induction and it is also superior in treating relapsing cases. Methotrexate is an option for non-severe cases. Maintenance therapy aimed at preventing relapse includes methotrexate, azathioprine, or rituximab. Additional treatments such as mycophenolate mofetil and intravenous immunoglobulin show efficacy, while trimethoprim-sulfamethoxazole is used in limited GPA without renal involvement[2].

Unusual manifestations of rare autoimmune disorders frequently lead to diagnostic delays. However, maintaining a high level of suspicion and exercising caution are essential. Bilateral parotitis accompanied by facial nerve palsy is a rare manifestation of GPA. Testing for C-ANCA and considering a diagnosis of GPA becomes imperative when patients present with salivary gland involvement, mainly if initial evaluations yield negative results and there is a lack of response to empiric treatments. Timely identification and intervention are essential in averting severe multisystem complications.

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