

Case Report

Granulomatosis polyangiitis: an otorhinolaryngological perspective

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ABSTRACT

Granulomatosis with polyangiitis or Wegeners granulomatosis is a rare entity, however is known to have specific otorhinolaryngological manifestations. Initial clinical manifestations could be subtle but deteriorate rapidly with an underlying active autoimmune process which can be life threatening in severe subglottic stenosis. We report a case of Granulomatosis with polyangiitis in an adolescent girl initially presented with otitis media refractory to treatment and epistaxis and rhinitis and eventually with the progression of disease presented with subglottic stenosis. Diagnosis was made by anti-neutrophil cytoplasmic antibody proteinase 3 (ANCA-PR3) positive status and histological confirmation by nasal biopsy, elevated C-reactive protein (CRP) levels and renal involvement with evidence of microalbuminuria. She underwent dilatation of the subglottic stenosis twice, with resection of the stenotic mass by coblation. The diagnostic and therapeutic challenges faced are emphasized in this report.

Keywords: Granulomatosis polyangiitis, Wegeners, Subglottic stenosis, ANCA-PR3

INTRODUCTION

Granulomatosis with polyangiitis (GPA) is an uncommon immunologically mediated systemic disease of unknown aetiology. It is characterised by an inflammatory reaction pattern necrosis, granulomatous inflammation and vasculitis that occurs in the upper and lower respiratory tracts and kidneys. GPA is an autoimmune multisystemic small-vessel vasculitis that is included in the group of anti-neutrophil cytoplasmic antibody (ANCA) associated small-vessel vasculitides.¹

Classic otorhinolaryngologic symptoms may be the initial clinical manifestation of GPA because the upper respiratory tract is involved in 70-100% of cases.² The nasal cavity and the paranasal sinuses are the most common sites of involvement in the head and neck area (85-100%), whereas otological disease is found in approximately 35%.

Commonly underdiagnosed and treated in line of symptomatic management could lead to failure of early

intervention and possible poor outcomes. We report a case of an 11 years old girl with granulomatosis with polyangiitis with an initial presentation of epistaxis and ear discharge and later with significant subglottic stenosis.

CASE REPORT

11 years old girl came with history of blood-stained nasal discharge and intermittent epistaxis spontaneous in nature, treated elsewhere with topical nasal spray, however did not resolve with medications. She developed purulent discharge from both the ears, intermittent moderate in amount, non-foul smelling not blood tinged. She had no history of tinnitus, hearing loss. There was no previous history of ear trauma or ear surgery. Anterior rhinoscopy revealed blood clots in both nasal cavities with fragile nasal mucosa. Posterior rhinoscopy was suggestive of adenoid hypertrophy. Sinuses were non tender; pharynx and neck were normal. Otoscopic examination showed purulent non foul-smelling discharge in external auditory canal, tympanic membrane was congested, mastoid tenderness was absent and facial nerve was normal. Ear

swab sent for culture and sensitivity was suggestive of methicillin-resistant *Staphylococcus aureus* (MRSA) and was treated accordingly with sensitive oral and topical antibiotics with regular aural toileting. Nasal swab was also found to be MRSA positive. She was posted for nasal biopsy for the confirmation of diagnosis as granulomatosis with polyangiitis. She was evaluated for anti-neutrophil cytoplasmic antibody proteinase 3 (ANCA-PR 3), anti-neutrophil cytoplasmic antibody myeloperoxidase (ANCA-MPO), tuberculosis polymerase chain reaction (TB-PCR), complete blood count (CBC), erythrocyte sedimentation rate (ESR) and c-reactive protein (CRP). She was found to be ANCA-PR 3 positive, with microalbuminuria and a positive nasal biopsy that confirmed the diagnosis of granulomatosis with polyangiitis. She was started on a course of steroids and mycophenolate mofetil (MMF). She was on regular follow up with the constant monitoring of CRP levels.

She then developed intermittent history of noisy and laboured breathing after a year since the initial manifestation, not associated with fever/nasal or ear complaints. Laryngoscopy revealed narrowing of the subglottis-grade 2 Cotton's classification. She underwent bronchoscopy under spontaneous ventilation- biopsy was taken from the stenotic segment and sent for histopathological examination. Subglottic region was dilated endotracheally resulting in significant widening of the subglottic region (Figure 1 and 2).

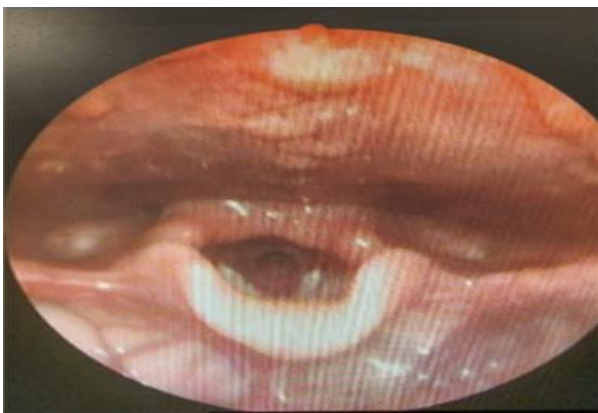


Figure 1: pre-operative image of after 1 month.



Figure 2: Post-operative image of subglottic stenosis.

Histopathological examination (HPE) of the tissue from the subglottic region showed hyperplastic squamous mucosa with dense inflammatory cell infiltrate of lymphoplasmacytic cells and neutrophils. Neutrophilic exocytosis and intraepithelial microabscesses were found.

She was then started on cyclophosphamide and oral steroids for the control of the ongoing systemic disease process. However, she developed noisy breathing with respiratory distress. On laryngeal endoscopy a moderately severe narrowing the subglottis-grade 3 Cotton's classification was noted suggestive of an ongoing autoimmune process.

Computed tomography (CT) chest was suggestive-circumferential soft tissue thickening causing near complete stenosis/narrowing at the level of glottis, minimally extending superiorly into the supraglottis. Mild circumferential soft tissue thickening along the proximal portion of subglottic region.

She was then started with rituximab and steroids prior to the dilatation of the stenotic segment which recurred again compelling need for a definitive procedure to secure the airway was considered (Figure 3 and 4).

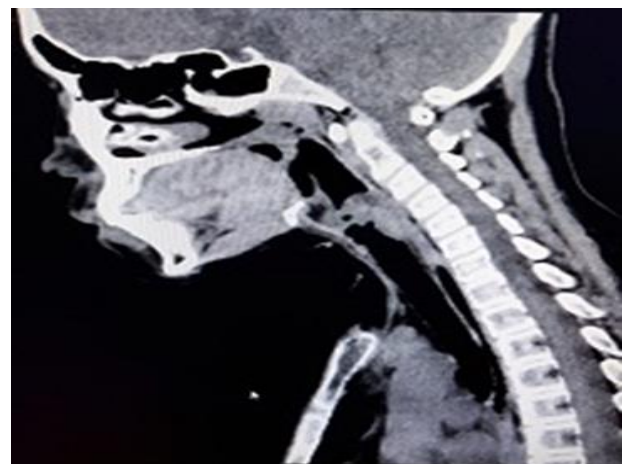


Figure 3: Sagittal section-stenotic segment just below the glottis.

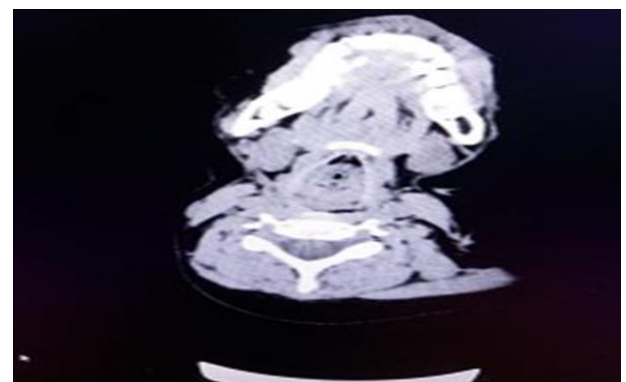


Figure 4: Axial section-stenotic segment just below the glottis.

Patient then underwent fibreoptic flexible bronchoscopy and resection the subglottic stenotic segment with coblation followed by topical triamcinolone application. She continued immunosuppressants for the control of the systemic disease during follow up.

DISCUSSION

Classic otorhinolaryngologic symptoms may be the initial clinical manifestation of GPA because the upper respiratory tract is involved in 70-100% of cases. Otolological involvement may occasionally be the first and only sign of GPA, mastoiditis may be the first manifestation of GPA.³ Fauci et al reported that 25% of patients with GPA presented with serous otitis media and that 6% of patients presented with hearing loss as the initial sign of the disease.⁴

Early diagnosis is essential to prevent long-term complications. Otolological involvement can be seen in up to 40% of patients who require early appropriate treatment to prevent permanent sensorineural hearing loss or permanent facial nerve paralysis. Primary otological presentation occurs in 20-25% of patients, and diagnosis can be difficult when the disease is limited to this locoregional phase. Kempf reported that approximately half of patients with GPA developed otological manifestations in the early stage of the disease.⁵

Otolological involvement involves serous otitis media, the most frequent manifestation, which results from Eustachian tube obstruction and nasopharyngeal involvement; chronic otitis media, which is caused by primary involvement of the middle ear and mastoid cavity; sensorineural hearing loss, the aetiology of which is unknown but is considered to involve either: vasculitis of the cochlear vessels and deposition of the immune complexes in the cochlea; pressure on the acoustic nerve by granulomatous lesions or toxic effects of inflammatory by-products arising from the middle ear through the round window, which adversely affect the vasa nervorum and the cochlear vessels and vertigo, thought to be due to either: immune complex deposition in the vestibular portion or manifestation of central nervous system involvement caused by a polyneuritis; and facial nerve palsy, which is seen in 8-10% of cases and is usually associated with otitis media. In the majority of cases, facial paralysis improves with cytotoxic therapy.⁶⁻⁸

Conductive hearing loss, sensorineural hearing loss or mixed hearing loss can be observed at different clinical phases. Conductive hearing loss is caused by granulation and effusion in the middle ear, obstruction of the Eustachian tube, effusion in the middle ear caused by vasculitis in the middle ear mucosa.

Sensorineural or mixed hearing loss is caused by inflammation in the inner ear, often it is a reversible hearing loss and it had not progressed to complete deafness.

In the head and neck region, biopsies from the paranasal sinuses showed higher positive rates for GPA. Therefore, it is recommended that biopsy specimens be taken from the paranasal sinus or nose.

It has been reported that cytoplasmic-ANCA (c-ANCA) is highly specific for active GPA and that c-ANCA titres are directly related to GPA disease activity. Delays in diagnosis and initiation of therapy negatively affect the prognosis for hearing loss. Therefore, it is important to start treatment before irreversible change occurs in the middle and inner ears.

The most common anatomical site for manifestation of lesions in GPA is the upper airway. The most common features of nasal disease activity are crusting, blood-stained rhinorrhoea and nasal obstruction. Septal perforation is the most common feature of damage (24%). The acute pain, fever and mucopurulent discharge were reported in 10% of the patients and the area most affected was the maxillary sinus. The most common organism identified is *Staphylococcus aureus* which has previously been associated with GPA activity and relapse.

The prevalence of subglottic stenosis was 23%, while in the reported series it was in the range of 6-23%. Patients with subglottic stenosis were younger than those with a normal subglottis and 60% were women. As in other case studies, stridor and reduced exercise tolerance were often the presenting symptoms.⁹

CONCLUSION

Subglottic stenosis of a severe degree in a pediatric patient associated with an underlying autoimmune etiology can pose serious challenges in treatment. A multidisciplinary approach involving the paediatricians, anaesthetists and otolaryngologists which included management of the autoimmune process with immunosuppressants-cyclophosphamide, oral glucocorticoids and rituximab were administered preoperatively. Surgical modality of dilation of the stenosis was done twice, followed by excision of the stenotic segment was done with coblation and intralesional steroid injections.

Granulomatosis with polyangiitis though a rare condition, must be sought with an eye of suspicion in patients presenting with symptoms involving the ear, nose and upper airway that is refractory to conservative management. Appropriate tests to confirm the diagnosis will aid in early recognition of the disease and timely institution of treatment can slow down the pathogenic process and progression to systemic severe disease and improve the prognosis.

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