Case Report

Chronic Sinusitis — A Rare Initial Presentation of Childhood Granulomatous Polyangiitis

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Received: 2 April 2021        Accepted: 30 April 2021
doi: https://doi.org/10.3329/jemc.v11i2.65195

Abstract

Childhood granulomatosis with polyangiitis (cGPA), is a rare, potentially fatal necrotizing vasculitis and its clinical features overlap with infection. Clinical manifestations of cGPA varies widely from involvement of upper and/or lower respiratory tract, necrotizing glomerulonephritis and less commonly skin, central nervous system, heart, salivary gland, eye and orbit. A ten-year-old girl was admitted having chronic sinusitis and fever for three months followed by perforating palate ulcer, persistent middle ear effusion, epistaxis, nasal deformity, rapidly progressing pneumonia and necrotizing skin lesions in limbs. Investigations demonstrated high titer of cANCA and vascular granulomatous lesions that confirmed the diagnosis of cGPA. Diagnosis of cGPA at the early stage is difficult because of the nonspecific symptoms which mimic other disorders. This case highlights the difficulty in diagnosing cGPA and the potentially life-threatening consequences of failing to do so.

Key words: Childhood granulomatosis with polyangiitis (cGPA); cANCA; Necrotizing skin lesions

J Enam Med Col 2021; 11(2): 128−132

Introduction

Granulomatosis with polyangiitis (GPA), previously known as Wegener’s granulomatosis, was renamed in April 2011.1 It is a rare disease, with an estimated childhood incidence of <1 per 2 million per year.2 It is a chronic vasculitis involving small- to medium-sized arteries. It is characterized by granulomatous inflammation of the upper and lower respiratory tracts; necrotizing, pauci-immune glomerulonephritis; and vasculitis that frequently involves other organs such as eyes, ears, skin, bones, and joints.3,4 The cause of GPA is unknown; it is a systemic, autoimmune multifactorial disorder. Serum anti-neutrophil cytoplasmic antibody directed against proteinase 3 (PR3ANCA) is known to be involved in the pathophysiology of GPA; however, the precise pathophysiology related to PR3ANCA remains elusive.5 Diagnosis of cGPA at the early stage is difficult because of the nonspecific symptoms which mimic other disorders and therefore there is delay in the commencement of appropriate treatment.3,6

We describe a case of a young girl presented with chronic sinusitis and fever for three months followed by upper and lower respiratory tract infections (ear, nose, palate and lung). She gradually developed more...
symptoms of GPA. This case report emphasizes the importance of considering the diagnosis of GPA in those who present with chronic sinusitis in early stage and atypical respiratory tract infections, as early diagnosis and treatment may avoid further complications.

Case report

A ten-year-old girl was admitted with the features of chronic sinusitis (blocked nose, pain over cheek radiating to frontal region and teeth, postnasal discharge) fever and cough for three months. These symptoms were followed by purulent discharge from ear and nose for one month which was occasionally blood mixed. The girl developed productive cough and progressive respiratory distress for fifteen days prior to admission. She was also having skin lesions and oral ulcers for last seven days. Skin lesions were over the both legs, feet and hands, initially maculopapular and later on became bullous, few were deeply ulcerated. An ulceration in the soft palate gradually turned to perforation. Mother also complained of depression of nasal bridge and she thought that it might be resulted from some trauma. There was no history of contact with tuberculosis or leprosy patient.

On admission the patient was toxic, ill-looking, highly febrile and dyspnoeic. There was saddle nose deformity (Fig 1), nasal blockade with thick purulent discharge, bilateral purulent aural discharge with ruptured tympanic membrane. There was a perforating ulcerative lesion over the hard palate measuring 10 mm×07 mm (Fig 2). Skin blisters with pyoderma gangrenosum over both lower legs and feet were present (Fig 3). Chest examination revealed crepitation and ronchi over the both lung fields. There was no subglottic stenosis. Investigations showed anaemia, neutrophilic leukocytosis and thrombocytosis. X-ray and CT scan of the chest showed bilateral infiltrates and cavitations. CT scan of the sinuses revealed bilateral erosive sinusitis with polypoid thickening (Fig 4). Skin biopsy from the ulceration of foot revealed granulomatous vascular lesions. Tissue from perforated lesion over hard palate also had granuloma on histopathology. Renal function tests were normal. Anti-PR3-Ab (c-ANCA) was positive (7.86, more than 1.10 considered positive). Anti-MPO-Ab (p-ANCA) was negative. We treated the girl with broad spectrum intravenous antibiotics, nutritional support, bronchodilators, chest physiotherapy and other supportive care. We started pulse intravenous cyclophosphamide and daily oral prednisolone as induction of remission. We added cotrimoxazole with the therapy as Pneumocystis jirovecii pneumonia prophylaxis. Within one month of treatment the patient t improved and was discharged home. But around eight weeks of onset of treatment, the girl again was admitted with respiratory difficulties. We had to refer the girl to Bangabandhu Sheikh Mujib Medical University. There, the unfortunate girl died of severe respiratory complications.

Fig 1. Saddle nose deformity
Discussion

Though very rare in children, spectrum of presentations and subsequent courses in GPA is extraordinarily wide.7 This case report highlights the difficulties associated with diagnosis of cGPA. The report also emphasizes the importance of considering an atypical inflammatory aetiology when managing apparently refractory infective aetiologies. The largest cohort study on cGPA (ARCHiVe) described 130 patients.6 At disease onset, the most common constitutional symptoms observed were fatigue, weight loss and fever. These were followed by pulmonary (81%), renal (79%), and ear, nose and throat (75%) manifestations. For diagnosis of cGPA the EULAR/PRINTO/PRES criteria suggested that diagnosis of cGPA can be done in presence of any three of the following six criteria — pulmonary involvement, upper airway involvement, renal involvement, granulomatous lesions, laryngotracheobronchial stenosis and presence of ANCA (antineutrophil cytoplasmic antibody).3,8,9 At disease onset, usually there is fever with myalgias, arthralgia, anaemia and weight loss which are progressively complicated with upper/lower airway and renal disease.8 This patient developed sinusitis as the most initial symptom. Chronic sinusitis as the initial manifestation of cGPA has been reported very rarely.10 Chronic sinusitis as an initial presentation may be misleading. In a cohort study performed by Fowler et al10 eighty six percent of cGPA patients had upper airway involvement and common manifestations were recurrent otitis media, saddle nose deformity, sinusitis, subglottic stenosis, hoarseness, recurrent epistaxis etc. According to different studies pulmonary symptoms or signs were dyspnea, stridor, wheeze, cough, pyrexia, hemoptysis and thoracic pain.8,11 We found almost all the features of upper and lower airway involvement in the said case. The girl recurrently had blood-mixed aurral and nasal discharge with features of sinusitis. Oral involvement of GPA occurs in approximately 6% to 13% of patients.8 The oral manifestations of cGPA include oral ulceration of the buccal and/or lingual mucosa, floor of the mouth, posterior pharynx, tonsils and labial mucosal nodules, delayed healing of extraction wounds and oral-antral fistula.12 The presented case had extensive buccal ulcers along with a deep oroantral fistula extending from the hard palate to antrum, similar to the cases described by Allen et al12 and Kasifoglu et al13 Palpable purpura, petechiae,
acneiform lesions, pyoderma gangrenosum, deep subcutaneous nodules, vesicles, bullae and digit ischaemia are the commonest skin manifestations in children.3,7,14 This patient had erythema multiforme and bullous lesions in hands and feet which have deteriorated to develop pyoderma gangrenosum.

Confirmatory investigations are serological markers (specifically ANCA, and most commonly PR3-ANCA or cANCA), and characteristic histopathological findings (pauci-immune granulomatous inflammation of predominantly small to medium arteries, capillaries or small veins, or pauci-immune glomerulonephritis).3,7 In our case Anti-PR3-Ab (c-ANCA) was positive. Biopsy from different ulcers revealed granulomatous vascular lesions suggestive of GPA. The management of cGPA demands an interdisciplinary approach care for children, including paediatric rheumatologists, otolaryngologists, and pulmonologists and nephrologist. Patients need continuous active inquiry and follow up regarding otolaryngologic and airway symptoms. We have involved ENT, Pulmonology, Dermatology and Hematology and Nephrology departments for management of this case. Treatment regimen was divided into two steps- induction remission with glucocorticoid with cyclophosphamide (CYC) or methotrexate (three to six months), and maintenance (minimum 18 to 24 months) with glucocorticoid and methotrexate or azathioprine.3,7 The European Vasculitis Study Group (EUVAS) designed and tested a regimen to administer the CYC by intermittent intravenous pulses every 2 to 3 weeks as an alternative to oral induction therapy that uses 50% less CYC.15 D de Groot et al16 and Licidi et al17 in their meta-analysis and review has presented that pulse CYC with steroid has better remission and survival rate. This patient has been reated with pulse cyclophosphamide and prednisolone. Regarding the prognosis, children treated with prednisone and CYC over 90% of patients responded completely or partially; however, more than 50% relapsed within 5 years. Mortality rate varies according to the severity of diseases and the cause of mortality are kidney disease, respiratory illnesses and infectious illnesses.3,7,16,17 Though the initial response to induction therapy was good, our patient had very severe pulmonary complications and died. Earlier diagnosis and treatment could improve the prognosis.

Conclusion

Though rare, cGPA is a major life-threatening disease, early diagnosis and treatment may prevent life threatening consequences and irreversible organ damage. We should consider the cGPA in patients who presents with chronic sinusitis and other infectious manifestations not responding with treatment.

References


