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Case Report

An atypical presentation of granulomatosis with polyangiitis: A case report ☆,☆☆

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ABSTRACT

Granulomatosis with polyangiitis (GPA) is a systemic vasculitis that is associated with antineutrophil cytoplasmic antibodies (c-ANCA). It classically presents with sinonasal, pulmonary and renal involvement. We are presenting a case of a 32-year-old male who presented with septal perforation, crusting and nasal obstruction. He had been operated on twice for sinonasal polyposis. Relevant investigations revealed that he was actually suffering from GPA. The patient was started on remission induction therapy. A combination of methotrexate and prednisolone was started with a 2-weekly follow-up. The patient had experienced his symptoms for 2 years before presentation. This case highlights the importance of correlating ENT and pulmonary symptoms to reach the correct diagnosis.

Introduction

Granulomatosis with polyangiitis (GPA), formerly Wegener's granulomatosis, is a c-ANCA-associated systemic vasculitis that classically affects upper airways, lungs and kidneys [1]. The disorder is thought to be immune-mediated due to the presence of anti-neutrophil cytoplasmic antibodies (ANCA). These antibodies are involved in neutrophil activation, which results in the production of inflammatory cytokines and free radicals. This is the underlying cause of granulomatous necrotizing vasculitis, a pathognomonic histological feature of granulomatous polyangiitis [2]. It is a rare disease with an incidence rate of 12.8 cases per 1,000,000 person-years in the adult population and 1.8 cases per 1,000,000 person-years in the pediatric population [3].

The disease process can involve multiple organ systems. The localized and non-severe forms of the disease involve the

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upper respiratory tract. The systemic, severe forms involve the lungs, kidneys, CNS and skin. c-ANCA is classically raised in active systemic disease. It may be negative in localized forms of the disease, making its diagnosis difficult. The classic symptoms of granulomatous polyangiitis include nasal obstruction, nasal discharge, epistaxis and crusting. The extensive disease process can lead to septal perforation and saddle-nose deformity [4]. Pulmonary involvement can result in cough, hemoptysis and exertional dyspnea. Renal involvement results in progressive glomerulonephritis and renal failure, the most common cause of death due to GPA. The disease process can also involve the orbit causing episcleritis, dacryoadenitis, orbital myositis and proptosis. Rare clinical manifestations include gingival hyperplasia and angular stomatitis, called "strawberry gums" [1].

Diagnosis is confirmed on biopsy with raised c-ANCA levels. A negative c-ANCA, however, does not exclude the disease [5]. Treatment includes remission induction therapy followed by remission maintenance therapy. A combination of corticosteroids and immunosuppressants [6] (cyclophosphamide, methotrexate and rituximab) are used to treat this disease. Relapse and flares can occur during treatment and are usually controlled by corticosteroids.

Fig. 1 – Lateral view shows saddle-nose deformity.

Case presentation

The 32-year-old male patient presented to the ENT OPD Mayo Hospital Lahore with active complaints of nasal obstruction, nasal discharge, myalgias and frontal headache for 1.5 years. The Patient was vaccinated for COVID-19 and was tested negative for COVID-19 at the time of admission. The patient's symptoms started 2 years back when he first experienced pain over the temporal and occipital regions of the head. The pain remained for 5-7 days, after which he experienced bleeding from bilateral nasal cavities. These clots were dark-coloured and foul-smelling. He experienced a similar episode of nasal bleeding 4-5 months later. After the second episode, he had a nasal obstruction. He took medications from a local doctor, but these did not alleviate his symptoms. At this time, he started feeling progressive exertional dyspnea and arthralgias. His first CT scan of the nose and paranasal sinuses was done on June 7, 2021 in a private hospital to determine the cause of nasal obstruction. The CT scan showed sinonasal disease. The sinuses' involvement was minimal. He was diagnosed with sinonasal polyposis at the same private hospital. He was operated on in a private hospital for sinonasal polyposis on June 22, 2021. His complaint of nasal obstruction remained after the operation.

His second CT scan of the nose and paranasal sinuses was done on August 22, 2021. The CT scan showed extensive sinonasal involvement, suggesting that the disease process is progressive. The patient was again operated on for sinonasal polyposis in another private hospital on August 24, 2021. A biopsy sample was obtained and sent to Agha Khan Pathology Lab. The results showed chronic necrotizing granulomatous inflammation with no superadded fungal infection or suspicion of malignancy.

The patient lost the records of both operations. His active complaints remained after the surgical procedures. He started experiencing progressive nasal obstruction and foul-smelling nasal discharge. These symptoms were associated with pain around the eyes and knees. He kept taking medications and nasal sprays from local healthcare. By mid-2022, he noticed a whistling sound in the nasal cavity while expiring. He felt difficulty breathing during any physical activity. A mild cough had also started by this time. There was no associated fever or dysuria. The patient finally presented to the ENT department of Mayo Hospital Lahore with these complaints.

On examination, the patient had a saddle-nose deformity (Fig. 1). Nasal speculum examination (Fig. 2) showed septal perforation in the cartilaginous septum with no involvement of the bony septum. He had nasal crusting bilaterally and mild left-sided DNS.

The patient was admitted to the ENT ward. Suspecting a granulomatous disease of the nose, we ordered a fresh CBC, ESR, serum c-ANCA levels, urine examination and a high-resolution CT chest. The reports showed raised ESR (35, normal up to 10). Serum c-ANCA levels were more than 200 U/mL (the normal level is less than 10 U/mL). Urine chemistry was positive for proteins +1 and hemoglobin +3. The patient had no history of diabetes or hypertension. A high-resolution CT chest showed pulmonary consolidation and ground glass haze bilaterally (Fig. 3).

These investigations and the biopsy report confirmed our suspicion that the patient suffers from granulomatous polyangiitis. Opinion was obtained from the pulmonology and nephrology departments regarding patient management.

The patient was started on combination therapy of methotrexate and prednisolone for 6 months. The dosage included methotrexate 15 mg once a week with continued folic acid supplementation and prednisolone 5 mg/kg/d with gradual tapering. Tab Septra (TMP/SMX) was also included in the

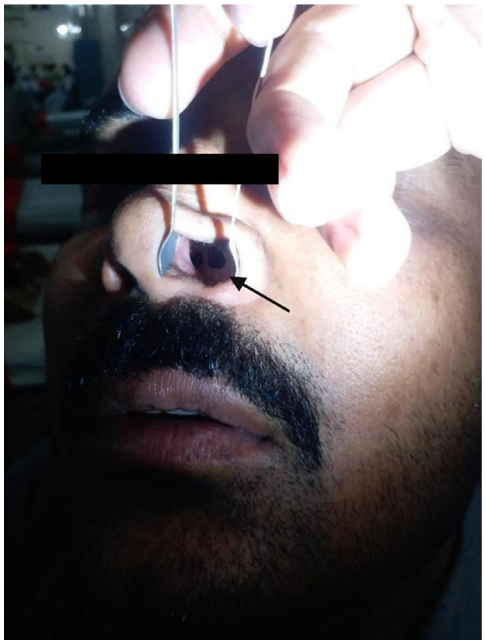

Fig. 2 – Nasal speculum examination shows septal perforation.

treatment regimen, to be taken on alternate days. Calcium supplementation and omeprazole were also part of the treatment regimen. The patient remained on a 2-weekly follow-up.

Discussion

GPA is a rare immune-mediated systemic disease associated with necrotizing vasculitis in small to medium-sized vessels [7]. This case of granulomatosis with polyangiitis represents an atypical presentation where the patient has been mistakenly diagnosed with sinonasal polyposis and operated on twice. The patient's symptoms of nasal discharge and epistaxis were mistakenly associated with nasal polyps. The CT scans at 2 months showed progressive sinonasal disease, an important indication of the disease's progressive nature. The biopsy report confirmed the underlying granulomatous disease process. The patient's ENT and pulmonary symptoms were not correlated, leading to a different diagnosis and management. Although saddle-nose deformity and septal perforation presented late in the disease process, this case highlights the importance of correlating varied clinical presentations owing to the variable nature of granulomatosis with polyangiitis. c-ANCA levels usually correlate to the active disease process and decline during remission. The patient was planned to be started on combination therapy of cyclophosphamide and prednisolone, but methotrexate was opted for due to the non-availability of cyclophosphamide. Rituximab is a monoclonal anti-CD20 antibody superior to cyclophosphamide in remission induction and azathioprine in remission maintenance [8]. It also has fewer side effects and a low frequency of relapses. Rituximab is now recommended as a first-line drug for patients with systemic disease. Tab TMP/SMX was also included in the patient's treatment regimen. It is effective in remission induction and maintenance in patients with disease localized to the ear, nose and throat [9]. The possible mechanism is its action against Staphylococcus aureus. Chronic nasal carriage of Staphylococcus aureus is thought to be a significant factor in relapses [10]. This factor is clinically supported by the foul-smelling nasal discharge, indicating a superadded bacterial infection.

The prominent clinical manifestations in this patient were saddle-nose deformity and septal perforation. The incidence of saddle-nose deformity and septal perforation in GPA is approximately 20% and 30%, respectively [11]. These deformities do not occur in every case of GPA involving the nose. Only 2 cases report a septal abscess associated with GPA [12,13]. In some cases, GPA can present with subglottic stenosis, a life-threatening complication of granulomatous inflammation [14]. In such cases, the initial manifestations are stridor, tachypnea and cyanosis. An emergent tracheostomy may be needed in such cases. Subglottic stenosis may remain even after remission, and endoscopic or laser treatment may be

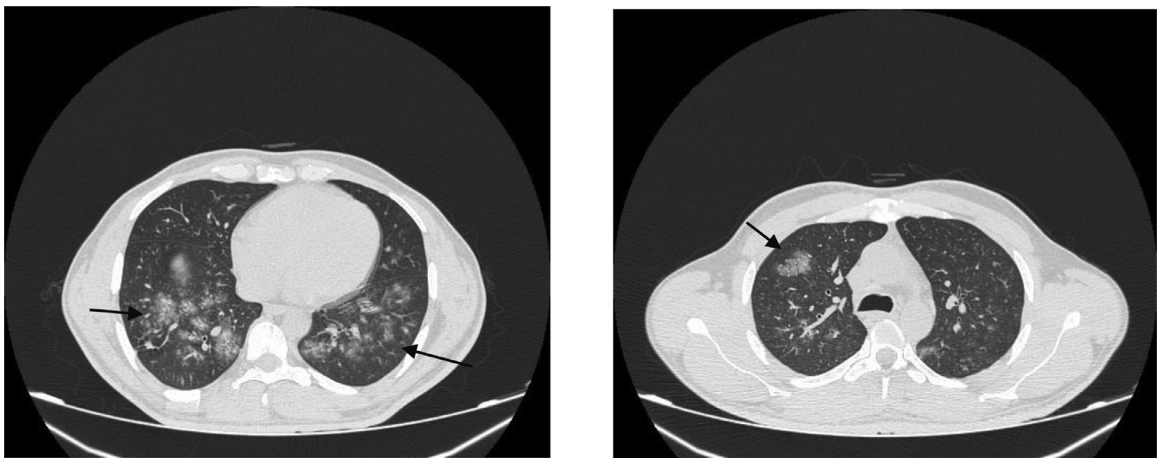

Fig. 3 – HRCT chest axial images show multifocal consolidation areas bilaterally. Areas of ground glass haze are seen in both lung fields.

required [1]. There are some cases of GPA where pulmonary involvement is predominant. A case report describes an adolescent male with excavated pulmonary nodules who was later diagnosed with GPA [15]. The initial manifestations can also be ocular in nature. There are cases reported with episcleritis and conjunctivitis as the initial clinical features of GPA [16,17]. A case of septal perforation associated with unilateral facial nerve palsy has also been reported [18]. This case is a rare presentation of GPA where a patient has been mistakenly diagnosed with sinonasal polyposis due to sinonasal disease seen on CT scans and overlapping clinical features. Following careful clinical examination and relevant investigations, the correct diagnosis was made. Surgical treatment of nasal deformities is done after a long period of remission. It includes the insertion of the silastic button and reconstruction of the dorsum of the nose with costal cartilage [19].

Conclusion

GPA is a rare disease with varied clinical presentations. It mostly affects the upper and lower airways and the kidneys, but other systemic manifestations can also be the initial manifestation. The correlation of nasal, pulmonary and renal symptoms is important to reach the correct diagnosis. Biopsy and c-ANCA levels confirm the diagnosis. The management includes a combination therapy of corticosteroids and immunosuppressants with regular follow-up.

Ethical approval

For this case ethical approval was not required from hospital, and we have patient father consent form.

Patient consent

Written informed consent was obtained from the parent of patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

REFERENCES

[1] Sattui SE, Lally L. Localized granulomatous with polyangiitis (GPA): varied clinical presentations and update on treatment. Curr Allergy Asthma Rep 2020 9;20(10):56.

[2] Comarmond C, Cacoub P. Granulomatosis with polyangiitis (Wegener): clinical aspects and treatment. Autoimmun Rev 2014;13(11):1121–5.

[3] Panupattanapong S, Stwalley DL, White AJ, Olsen MA, French AR, Hartman ME. Epidemiology and outcomes of granulomatosis with polyangiitis (GPA) in pediatric and working-age adults populations in the United States: analysis of a large national claims database. Arthritis Rheumatol Hoboken NJ 2018;70(12):2067–76.

[4] Grygiel-Górniak B, Limphaibool N, Perkowska K, Puszczewicz M. Clinical manifestations of granulomatosis with polyangiitis: key considerations and major features. Postgrad Med 2018;130(7):581–96.

[5] Lutalo PMK, D'Cruz DP. Diagnosis and classification of granulomatosis with polyangiitis (aka Wegener's granulomatosis). J Autoimmun 2014;48–49:94–8.

[6] Puéchal X. Granulomatosis with polyangiitis (Wegener's). Joint Bone Spine 2020;87(6):572–8.

[7] Lee SW, Park YB. Classification of antineutrophil cytoplasmic antibody-associated vasculitis. J Rheum Dis 2019;26(3):156–64.

[8] Hassan RI, Gaffo AL. Rituximab in ANCA-associated vasculitis. Curr Rheumatol Rep 2017;19(2):6.

[9] Cohen Tervaert JW. Trimethoprim-sulfamethoxazole and antineutrophil cytoplasmic antibodies-associated vasculitis. Curr Opin Rheumatol 2018;30(4):388–94.

[10] Zycinska K, Wardyn KA, Zielonka TM, Demkow U, Traburzynski MS. Chronic crusting, nasal carriage of Staphylococcus aureus and relapse rate in pulmonary Wegener's granulomatosis. J Physiol Pharmacol 2008;59(Suppl 6):825–31.

[11] Cannady SB, Batra PS, Koening C, Lorenz RR, Citardi MJ, Langford C, et al. Sinonasal Wegener granulomatosis: a single-institution experience with 120 cases. Laryngoscope 2009;119(4):757–61.

[12] Ishikawa T, Suzuki J, Shirai T, Koizumi S, Tsuchiya Y, Hishinuma K, et al. Presence of Phlebitis in aseptic nasal septal abscess complicated with ulcerative colitis; possible association with granulomatosis with polyangiitis: a case report. Tohoku J Exp Med 2022;258(1):29–34.

[13] Sasawaki M, Omura K, Ebihara T, Otori N. A case of granulomatosis with polyangiitis (GPA) where a multicystic nasal septal abscess aided in the diagnosis. Case Rep Otolaryngol 2022;2022:7415498.

[14] An J, Song JW. Life-threatening subglottic stenosis of granulomatosis with polyangiitis: a case report. Med Kaunas Lith 2021;57(5):423.

[15] Arfaoui H, Elkihal H, Jabri H, Elkhattabi W, Afif H. Adolescent with severe granulomatosis with polyangiitis: a case report. Pan Afr Med J 2021;38:285.

[16] Ciotoracu AC, Dimăncescu MG, Mitulescu TC, Haralambie CI, Iorga AM, Busuioc C, et al. A clinical case of recurrent episcleritis as the initial manifestation of granulomatosis with polyangiitis. Romanian J Ophthalmol 2021;65(4):386–90.

[17] Nejabat M, Mahmoudi Nezhad GS, Shenavandeh S, Ashraf MJ, Jalalpour MH. Conjunctivitis as a manifestation of Wegener's Granulomatosis. J Curr Ophthalmol 2018;30(3):268–72.

[18] Zaeri B, Khan S, Hegazy A, Al Ghanim N. Granulomatosis with polyangiitis presenting with unilateral facial nerve palsy and nasal septum perforation. BMJ Case Rep 2021;14(1):e236469.

[19] Unadkat SN, Pendolino AL, Kwame I, Swift A, Pusey C, Gantous A, et al. Nasal reconstructive surgery for vasculitis affecting the nose: our two-center international experience. Eur Arch Oto-Rhino-Laryngol 2020;277(11):3059–66.