Oculo-otological Manifestations in a Case of Granulomatosis with Polyangiitis

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Abstract
A 44 year old lady presented with acute onset of loss of vision in the right eye and cough with mucopurulent expectoration for two months. Ophthalmic examination revealed central retinal artery occlusion (CRAO). Chest radiograph showed multiple cavitatory nodules with fluid levels. Sputum was negative for AFB and ANCA was strongly positive suggestive of a diagnosis of Granulomatosis with Polyangiitis (GPA). Within the next few weeks the patient had rapid deterioration due to left eye CRAO, progressive bilateral hearing loss, facial palsy and retro orbital mass. The aggressive disease responded well to steroids and cyclophosphamide.

Introduction
Granulomatosis with polyangiitis is an ANCA-associated small vessel vasculitis characterised by granulomatous necrotising inflammatory lesions of the upper and lower respiratory tract and also ocular and otological involvement. Eye involvement is frequent and may range from mild conjunctivitis to dacrocystitis, scleritis, episcleritis, granulomatous uveitis, ciliary vessel vasculitis and retro-orbital mass. Retinal vasculitis is rarely seen. Otological involvement may occasionally be the first and only sign of the disease with presentations like serous otitis media, sensorineural hearing loss, otalgia and otorrhoea with middle ear involvement. We present a case of GPA with rapidly progressive oculo-otological manifestations which were much more florid than the pulmonary symptoms.

Case History
A 44 year old post-menopausal lady residing in rural Maharashtra, farmer by occupation presented to the ophthalmology department with sudden onset loss of vision in the right eye. She also had 2 month history of moderate grade fever, cough with mucoid expectoration. Initial ophthalmologic examination revealed the presence of pale disc with pale retina, attenuated arterioles with cattle trucking in veins and ghost vessels. A cherry red spot was also seen on the macula. A diagnosis of central retinal artery occlusion was made and right eye anterior chamber paracentesis was done under local anaesthesia. Patient was started on aspirin, vasodilators (pentoxiphylline, xanthinol nicotinate), oral acetazolamide, topical dorzolamide, antibiotics, and labetolol and referred to us for her systemic complaints.

On presentation to us patient had tachycardia, with a pulse rate of 120 beats per minute, other vitals were stable. Respiratory system examination revealed the presence of vesicular breath sounds, with coarse crepitations in bilateral infra-axillary and infrascapular areas. Rest of the systemic examination was unremarkable. Preliminary investigations revealed a haemoglobin of 8.6 g%, ESR of 55 mm at the end of first hour, TLC of 36,700/mm³ with 88% polymorphs and 12% neutrophils, a platelets count of 4.0 lakhs/mm³. Her BUN was 9.0 mg/dl with a serum creatinine of 0.9 mg/dl. Blood sugar levels, liver function tests, complete lipid profile were within normal limits. ECG showed the presence of sinus tachycardia. A chest radiograph (Figure 1) was performed which showed the presence of multiple cavitatory nodules with fluid levels in bilateral lung fields, largest in the right parahilar region. The preliminary differential diagnoses were multiple lung abscesses of possible bacterial, mycobacterial or fungal etiology, cavitatory metastasis or granulomatosis with polyangiitis (Wegener’s granulomatosis). Sputum examination was negative for acid fast bacilli by Ziehl Neelsen staining as well as NAA method. Sputum culture yielded growth of Klebsiella pneumoniae sensitive to amikacin and piperacillin+tazobactum. Sputum mycobacterial culture and fungal culture were negative. Sputum cytology showed numerous WBCs with few alveolar macrophages, without any atypical cells. A high resolution CT was done (Figure 2) which showed presence of multiple cavitatory lesions.

Her serum C reactive protein levels were 155.0 mg/L. Urine examination was negative for protein, casts or active sediments. HIV, HBsAg and anti-HCV markers were negative.

Fig. 1: Chest X-ray PA view s/o multiple cavitatory nodules with fluid levels in bilateral lung fields

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ANA, anti-ds DNA were negative. C3 and C4 complement levels were normal. Samples were sent for anti-neutrophil cytoplasmic antibodies. 2D-echocardiography showed an ejection fraction of 60%, with a structurally normal heart. There were no thrombi or vegetations. Carotid arterial doppler revealed no e/o plaque or thrombus in bilateral carotid arteries. CT guided biopsy of lung lesions showed the presence of organizing haemorrhage within the lung parenchyma, without any evidence of malignancy. Patient was started on IV antibiotics (piperacillin+tazobactum and amikacin), Inj. dexamethasone 4 mg od. Acetazolamide 250 mg tds, along with aspirin, vasodilators, topical antibiotics, labetolol and dorzolamide were continued. 6 days after the initial presentation, patient complained of sudden onset vision loss in left eye. Fundus examination was s/o ill-defined margins of disc with attenuated arterioles, dilated tortuous veins with cattle trucking, ghost vessels and the presence of a cherry red spot (Figure 3).

The impression was that of left central retinal artery occlusion. MRI Brain with MRA showed presence of chronic ischemic changes in periventricular white matter, minimal T2 hyper intense signal in the left optic nerve s/o neuritis with diminished calibre of right optic nerve s/o atrophy. In lieu of optic neuritis, patient was started on Inj. Methylprednisolone 1g for three days i/b oral prednisolone 1mg/kg. Meanwhile patient’s ANCA titres came positive with titres 1:40 (+4), cytoplasmic pattern by immunofluorescence. Anti-PR-3 ANCA levels were strongly positive by E.I.A with titres of 186.38 RU/ml (negative <20 RU/ml). ENT examination showed normal nasal cavities, nasopharynx, external auditory canal and tympanic membrane. Diagnostic nasal endoscopy showed normal mucosa with no e/o granulation. A screening CT scan of the paranasal sinuses showed mild thickening of mucosa of the left frontal sinus, with normal maxillary, ethmoid and sphenoid sinuses. A final diagnosis of granulomatosis with polyangiitis was made and patient was started on pulse cyclophosphamide therapy and was discharged on oral prednisolone.

Twenty days later this patient presented with progressive bilateral hearing loss and left facial asymmetry of 7 days duration. On examination patient had left infranuclear facial palsy and bilateral conductive hearing loss, which was subsequently confirmed by pure tone audiometry (mild to moderate in right ear and moderate to severe in left ear). Otoscopic examination showed presence of an intact, bulging tympanic membrane.

HRCT of the temporal bone suggested fluid in the middle ear with intact ossicular chain. A diagnosis of serous otitis media was made and patient underwent myringotomy with grommet insertion. Subsequently, a second pulse of cyclophosphamide was administered and patient was discharged on oral glucocorticoids and advised to return after a month for the third cycle.

Subsequently our patient did not follow up as per our advice. She came back to us only 3 months later, that too after stopping all medications and treatment by various alternative medicine practitioners. This time she presented with weakness in left hand since one week which was causing her difficulty in buttoning and unbuttoning clothes, difficulty in making a fist with the left hand and thus causing difficulty in doing household chores. She also had diplopia and that she had difficulty in seeing sideways objects necessitating that she turn her head around every time. On examination there was lagophthalmos, hypertropia and restricted extra ocular movements in bilateral eyes. Bilateral LMN type facial paralysis and a weak left hand-grip were also present. Sensory loss was also noted over medial aspect of left hand. Fundus examination showed bilateral optic atrophy.

A CT scan of the orbit showed the presence of a 10*20 mm well circumscribed intraconal mass in the left orbit extending upto the orbital apex and orbital canal leading to the compression and displacement of the optic nerve (Figure 4).

A MRI was performed which showed the presence of a left orbital mass, which was intraconal in location compressing the optic nerve and pushing it medially. The mass showed dark signal on T2 and T1, with brilliant post-gadolinium enhancement. Similar enhancing ill-defined masses were seen along bilateral cavernous sinuses with extension along the petrous apex to involve the medial pterygoids and parapharyngeal space as well as both pterygopalatine fossae. There was also an ill-defined T2/flair hyperintense lesion 1cm in diameter in the right half of posteroinferior cerebellum projecting into the 4th ventricle. The lesion showed restricted diffusion and post-contrast enhancement. MR Spectroscopy revealed a lactate peak in the lesion (Figure 5).

A nerve conduction study was also performed which showed reduced CMAPs in left median, left ulnar, bilateral common peroneal nerves and reduced SNAPs in left median nerve suggestive of mononeuritis
Discussion

Granulomatosis with polyangiitis (previously Wegener’s granulomatosis) is a multisystem autoimmune disorder associated with antineutrophil cytoplasmic antibodies (ANCA), predominantly c-ANCA or PR3-ANCA. It predominantly affects the upper and lower respiratory tracts and kidneys. However, it is also known to involve eyes, ears, heart, gastrointestinal system, central and peripheral nervous systems. The pathology of GPA comprises of necrotizing granulomas and vasculitis of small to medium sized blood-vessels. Our case is atypical as it had predominant ophthalmologic and otologic involvement with bilateral central retinal artery occlusion at the initial presentation, orbital, nasopharyngeal and cavernous sinus pseudotumors, cavitatory lung lesions, bilateral facial nerve palsy, mononeuritis multiplex, cerebellar granuloma, and the conspicuous lack of renal involvement till date.

Ophthalmologic involvement occurs in 28-58% of patients of GPA.3,4 Ocular GPA can either manifest de novo, as disease spread from contiguous structures such as the sinuses, or as a part of systemic GPA. Ocular inflammation can occur with or without systemic manifestations. Ocular manifestations may be the initial presentation of GPA in 8-16% of patients and visual loss occurs in up to 8% of patients. Eye involvement can be in the form of keratitis, conjunctivitis, scleritis, episcleritis, uveitis, retrobulbar granulomatous disease, ocular palsies, lacrimal duct obstruction, optic neuritis and retinal vascular occlusions. Our patient had bilateral central artery occlusion, optic neuritis and left orbital pseudotumor.

The ear may be involved in nearly 40% of patients of GPA. Otologic involvement may be in the form of otitis media; usually of serous type, granulomatous involvement of middle ear and mastoid mucosa, tympanic membrane perforation, inflammation of the auricle etc.5 Conductive as well as sensorineural hearing loss can occur and may lead to profound deafness.6 Facial nerve palsies are also common, caused by either necrotizing vasculitis of the vasa nervorum or neuritis due to granulomatous involvement of the middle ear. Our patient had bilateral severe otitis media with facial paralysis.

Nervous system involvement is seen in a significant proportion of patients, either the peripheral nervous system (PNS) involvement due to vasculitis or with central nervous system (CNS) involvement due to infiltrating granulomatous manifestations (10–45%).7 Peripheral neuropathy, cranial neuropathy, external ophthalmoplegia, cerebrovascular events, seizures, cerebritis, spastic paraparesis, temporal arteritis, Horner’s syndrome, and papilledema have been known to occur.8 Peripheral neuropathy could either present as mononeuritis multiplex, distal symmetrical polyneuropathy or unclassified peripheral neuropathy. Cranial neuropathies frequently involved the second, sixth, and seventh cranial nerves, occasionally with simultaneous multiple cranial nerve involvement.

Apart from cavitatory lung lesions and predominant ophthalmologic and otologic involvement, our patient had mononeuritis multiplex and granulomatous lesion in right postero-inferior cerebellum. Additionally she also had inflammatory granulomatous masses in the left orbit, bilateral cavernous sinuses and pterygopalatine fossae. However, there was no evidence of renal involvement till date. Renal involvement could occur in due course and hence patient needs regular evaluation for the same.

Conclusion

Predominant oculo-otological involvement as an initial presentation of GPA can of ten confound the diagnosis.

References