

Temporal arteritis with focal pachymeningitis: a deceptive association

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ABSTRACT

Temporal arteritis is an immunological disorder mostly affecting the elderly population. This frequently occurs in association with other rheumatological diseases of the elderly. The symptoms of Temporal arteritis overlap with other symptoms of commonly occurring diseases in that population. Focal pachymeningitis in association with temporal arteritis is a rare finding and a literature review revealed less than ten cases of similar associations being published. In such instances, this finding can be mistaken for aseptic meningitis and treated erroneously. We present our case, discuss the management and summarize a review of literature about focal pachymeningitis along with temporal arteritis which was managed successfully with steroids and Tocilizumab.

Keywords: giant cell arteritis, pachymeningitis

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INTRODUCTION

Temporal arteritis (TA) also known as Giant cell arteritis (GCA)/Horton's disease is a disease of the elderly. It commonly presents as headache of varied intensity. This preferentially involve major branches of the aorta most commonly the extra cranial branches of the carotid arteries. TA may be mistaken for other disorders causing headaches. This disease is more common in the European countries where it occurs frequently in association with polymyalgia rheumatica. It is less often seen in Japan. The association of TA with Focal pachymeningitis has been reported sparsely. It may present with varied manifestations and abnormalities in the Cerebrospinal fluid. It can be misdiagnosed as aseptic meningitis if not promptly investigated. We present the challenges we faced in a patient with TA, who had focal pachymeningitis and CSF abnormalities.

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CASE REPORT

A 53-year-old man was admitted in our hospital with intense pain in the right eye which began five days before his admission. There was no itching or redness of the eye at that time. There was no history of visual loss or blurring of vision. There was no history suggestive of any other neurologic deficit. On examination he was fully conscious and oriented. General examination was uneventful. There were no thickened arteries in the scalp. Cranial nerve examination was normal. Motor and sensory systems were normal. There were no cerebellar signs. He was examined by ophthalmologist and there were no conclusive findings to suggest any local disease. Fundus examination was normal. He was examined clinically and was found to have no other focal neurologic examination. He had no pain in the joints suggestive of polymyalgia rheumatica. There was no neck stiffness. This pain in the right eye lasted for 2 weeks after which it subsided. One week later, he began to have headache of severe intensity. This was also associated with mild fever. Routine blood examination was done which showed a moderate rise of total White blood cells viz., 12900 cells/mm³, ESR was 104 mm/1st hr, and C-Reactive Protein was 29.34. A lumbar puncture was done which show increased cell count of 45/mm³ with 100% lymphocytes, Protein was 46mg/dl, and sugar 59 mg/dl. In view of the abnormal Cerebrospinal fluid count a possibility of meningitis was suspected. CSF was tested for herpes simplex antigens with PCR technique but it was found to be negative. Cultures were also sent for bacteriology which turned out to be negative.

A repeat CSF study was done after five days which showed a mild decrease in the cell count to 26/ul (100% lymphocytes), along with sugar 71 mg/dl and protein of 31 mg/dl. Cultures were again repeated but turned out to be negative. CT scan of the brain with contrast was done along with angiogram which did not show any intracranial abnormalities and normal calibre of both the superficial temporal arteries as well as the intracranial arteries.

Magnetic resonance imaging of the brain with contrast was done along with magnetic resonance angiogram. There was focal enhancement of the Dura over the left frontal, temporal and the occipital region suggestive of pachymeningitis. A PET CT scan was done which did not show any abnormal uptake.

He was diagnosed as a case of possible temporal arteritis and a biopsy of the temporal artery was advised. In the meantime he was started on steroids, Methyl Prednisolone 1000 mg/day for



Fig. 1 CT brain with Contrast, CT Angiogram

Fig. 1a: CT Brain with contrast – Normal Study

Fig. 1b: CT angiogram showing normally filling intracranial vessels

Fig. 1c: 3D reconstructed CT angiogram showing normal filling of the temporal arteries

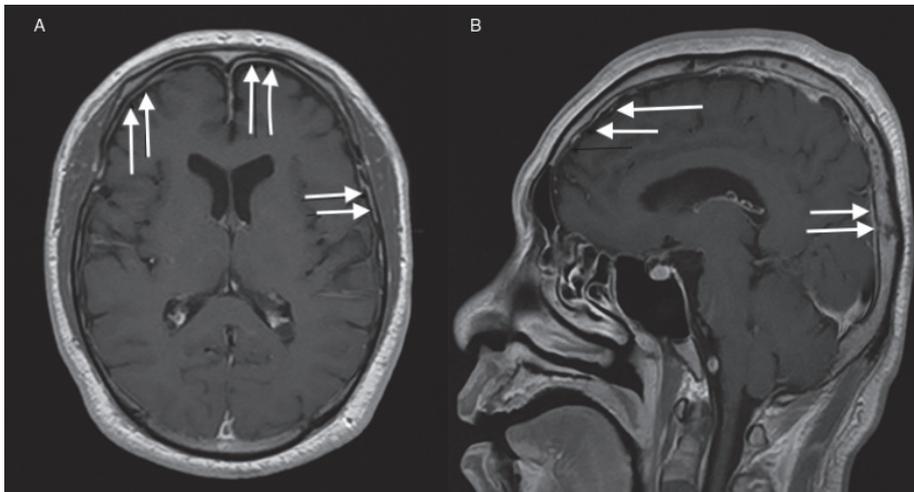


Fig. 2 MRI brain with Contrast

Fig. 2a: Magnetic Resonance Imaging T1 Weighted image with contrast Axial section showing focal enhancement of the dura in the frontal and the temporal region

Fig. 2b: Magnetic Resonance Imaging T1 Weighted image with contrast Sagittal section showing focal enhancement of the dura in the frontal and the occipital region

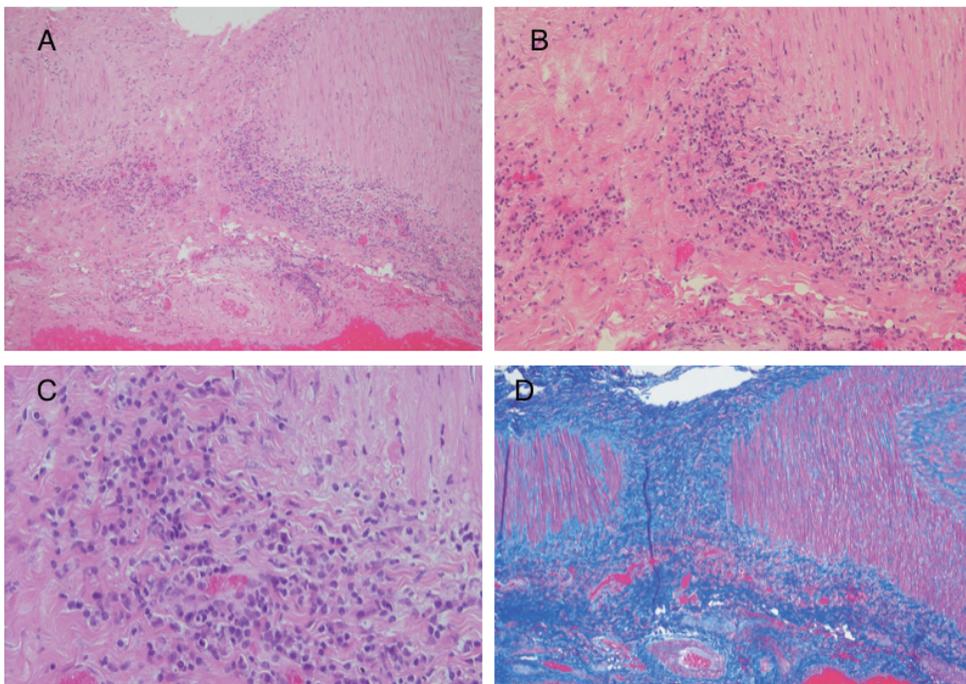


Fig. 3 Photomicrographs of slides

Fig. 3a: Photomicrograph – H & E stain x10 showing dense fibrosis and inflammation within the walls of the artery

Fig. 3b: Photomicrograph H & E stain x 10, showing medial fibrosis with inflammatory infiltrates

Fig. 3c: Photomicrograph H & E x 40, showing lymphocytes, plasma cells and neutrophils in the media

Fig. 3d: Photomicrograph x40, Trichrome Azan stain to visualise Fibrocollagen

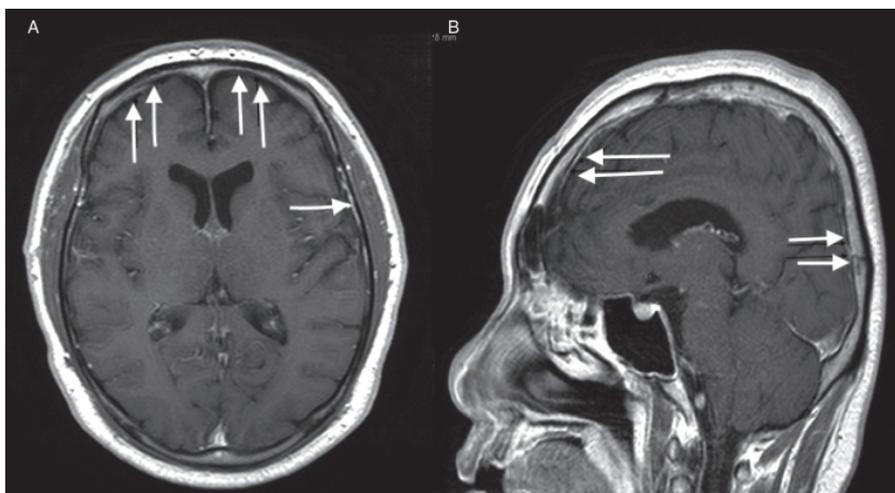


Fig. 4 Post Steroid MRI brain

Fig. 4a: MRI Brain – After one month of steroid and Tocilizumab

T1W axial scan with contrast showing marked reduction in enhancement of part of the dura over the frontal region compared to scan taken as in Fig 2a. However the temporal region dura shows modest decrease in the enhancement pattern

Fig. 4b: T1W sagittal scan with contrast showing resolution of the enhancement of the part of the dura shown in Fig 2b

three days which was followed by prednisolone 60mg/day after which there was mild relief of headache. A CSF study was repeated after three days which showed a decrease in cell count to 19/ml, Protein 32 mg/dl and glucose 67 mg/dl. At biopsy, one centimetre of the superficial artery was excised and sent for histopathological examination. The histopathological examination showed the vessel wall had fibrously thickened intima and adventitia with infiltration of lymphocytes and neutrophils. There were no Giant cells seen suggestive of temporal arteritis.

After two weeks of starting steroids his symptoms improved and thereafter he was started on monoclonal antibody Tocilizumab after which his symptoms subsided totally. One month after the treatment a repeat MRI brain with contrast was taken which showed that there was marked reduction in the focal enhancement of the dura.

DISCUSSION

Temporal arteritis /Giant cell arteritis is a disease of the elderly. This involves vasculitis of the medium and large sized arteries, in which there is a favoured tropism for the branches of the aorta particularly the carotid arteries.¹ The American college of rheumatology have published diagnostic criteria for GCA, according to which age is the strongest factor for the development of this disease.² This is attributed to the aging of the immune system and the blood vessel wall, which is the normal site for dendritic cells.¹ There are regional variations in the occurrence of this disease where the population residing in North America and Scandinavia are the most commonly affected.³ Japan has a relatively low incidence of TA/GCA. A nationwide survey conducted in 1998 suggested a prevalence of 1.4 per 100,000 population with an average age of onset at 71.5 years.⁴ Our patient was relatively young than in whom this disease typically

manifests. Such reports, although sparse have been published in the literature.⁵

There are varied symptomatic presentations of TA published in the English literature. The typical presentation is with unilateral headache with jaw claudication. Systemic symptoms most frequently associated with TA are fever and weight loss. In Japanese study the patients usually had fever and weight loss in 43.9% of the surveyed patients. In addition, pain in the temporal region and temporal artery was noted in 57.6% and 58.5% of population.⁴ Visual disturbances have been reported often in patients with TA/GCA. Ocular manifestations in TA/GCA is commonly due to anterior ischemic optic neuropathy.⁶⁻⁸ Rare cases of severe acute loss of vision has been reported with TA/GCA.⁹ The other uncommon ophthalmic presentations reported in the literature vary from eye pain, third nerve palsy,¹⁰ corneal ulcerations¹¹ and orbital cellulitis.¹²

Several theories have been put forth in the etiopathogenesis of TA/GCA. In addition to environmental factors like seasonal changes and geographic distribution, infectious origin of this disease have also been postulated.¹³ Infectious epidemics with mycoplasma pneumonia have been correlated with rising incidence of GCA in Denmark.¹⁴ But until now no particular organism has known to be regarded as a specific pathogen in the pathogenesis of this disease. The dendritic cells residing in the mural layers of the arteries along with the critical mediators of host protective immunity are the main players in the development of vasculitis. This can be inferred by the large quantity of inflammatory infiltrates in the wall of the biopsy specimen. The lack of Giant cells may be seen in 50% of cases of TA.¹⁵

Pachymeningitis has been seen in association with diseases of rheumatological, infectious as well as autoimmune origin. The association of pachymeningitis with TA/GCA has been reported sparsely in the literature.¹⁵⁻²⁰ The thickening of the dura adjacent to the inflamed temporal artery has been attributed to the pain described by the patients in such association. The enhancement of the dura seen on contrast MRI is seen due to the leaky inflamed arteries supplying the dura in the presence of inflammation.¹⁵ In our patient, one month after the treatment this enhancement was not seen which was an indirect evidence that the inflammation had subsided.

The diagnosis of GCA in association with pachymeningitis has to be viewed with a high level of suspicion. Investigations pertaining to systemic large vessel vasculitis as well as autoimmune diseases should be sent to confirm the diagnosis. Our patient had all investigations within normal range. The only abnormal investigation was the examination of cerebrospinal fluid which showed pleocytosis. This would at times mislead the physician towards a diagnosis of aseptic meningitis. CSF abnormalities in TA/GCA have been reported in the literature.²¹⁻²⁵ In most of the cases this abnormality was limited to raised protein and abnormal lymphocyte count. In our patient, protein was mildly elevated along with mononuclear cells which initially prompted us to think in the lines of aseptic meningitis. However, as the CSF cultures and PCR tests were all negative, we persisted with a diagnosis of TA/GCA. Such instances have been reported in the literature where successive testing of CSF has shown to normalise with treatment with steroids.²¹

The imaging in TA/GCA must include all basic investigations as this can involve all the systemic arteries although it has a predilection for the branches of the carotid. Magnetic resonance imaging with contrast is a vital investigation to detect GCA related stroke syndromes.²⁶ In addition, angiography may be done to detect intracranial vasculitis and related stenosis. The role of Positron emission tomography scan is an upcoming investigation in the imaging of GCA. The role of 18-F Fluro deoxy glucose (¹⁸F-FDG) PET in japan was only approved recently in April 2018 but was limited in localisation and activity of large vessel vasculitis diagnosed through other modalities of investigation.²⁷ Our patient had undergone angiography as well as PET scan both of which were normal.

The gold standard considered for the diagnosis of TA/GCA is temporal artery biopsy. However, there are reports that suggest that this may be necessary only when diagnosis is inconclusive or in

patients who have a strong contraindication for steroids.²⁸ The sensitivity of temporal artery biopsy in diagnosis of TA/GCA is 70% to more than 90%. Hence a negative biopsy doesn't rule out the disease and treatment should be started on strong suspicion if indicated clinically.^{29,30} Recently Bowling et. al., had questioned the necessity for invasive biopsy in view of new diagnostic tests like high resolution Magnetic resonance imaging. Ultrasound scan and PET CT.³¹ Our patient had a positive biopsy even when he was started on steroids which consolidated the diagnosis of TA/GCA. The treatment with steroids has not shown to alter the result of biopsy in specimen.^{32,33}

The definitive management of TA/GCA is with Steroids. There is no standard dose recommendation for beginning glucocorticoids therapy but it varies from one country to another. Our patient was started on 1000 mg/day x 3days followed by a maintenance dose of 60 mg/day of Prednisolone which was continued for 2 weeks. Such high doses are usually effective in active control of inflammation followed by a tapering phase where the doses are gradually reduced.³ Other drugs used in the management of GCA are Methotrexate,³⁴ Cyclophosphamide,³⁵ Azathioprim, Hydroxychloroquine and Infliximab.³⁶ Recently Tocilizumab has been shown to be a promising drug in the management of GCA resistant or intolerant to steroids.³⁷

Our patient was treated with Pulse therapy of prednisolone followed by Tocilizumab which proved to be very effective in alleviation of pain. This improvement was mirrored in the MRI taken on follow up after one month which showed a marked reduction in the frontal and moderate reduction in the temporal dura.

CONCLUSION

TA/GCA in association with focal pachymeningitis is a rare presentation. CSF abnormalities can occur in GCA which may lead to suspicion of aseptic meningitis. Investigations should be planned, and other causes for pachymeningitis should be carefully excluded thereof.

CONFLICT OF INTEREST

The authors hereby declare that there is no conflict of interest for any of the authors.

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