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Case Report

Ophthalmology Section

Oculomotor Nerve Palsy as a Rare Presentation and First Sign of Multiple Myeloma

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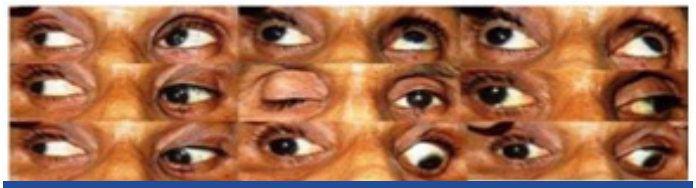
ABSTRACT

Acquired oculomotor nerve palsy has varied aetiologies like vascular (diabetes, heart disease, atherosclerosis and posterior communicating artery aneurysm), space occupying lesions or tumours, inflammation, infection, trauma, demyelinating disease like Multiple sclerosis, autoimmune disorders such as Myasthenia gravis, postoperatively as a complication of neurosurgery, cavernous sinus thrombosis etc. Cranial Nerve palsies as one of the first symptoms of multiple myeloma have been reported sparsely in literature. We report a case of a 60-year-old woman who developed sudden onset right-sided pupil sparing oculomotor nerve palsy along with a tender swelling at right sternoclavicular joint. Cranial and orbital magnetic resonance imaging and cerebrospinal fluid examination demonstrated no abnormalities. Immunological investigations and histopathological analysis of sternoclavicular joint swelling confirmed the diagnosis of IgG type multiple myeloma. After confirmation of diagnosis we started her with appropriate chemotherapy, after which the palsy resolved within one month. The cause of the palsy was probably due to nerve ischemia due to hyper viscosity of the serum.

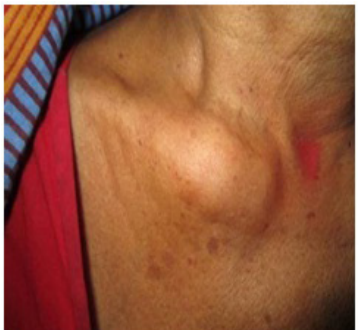
Keywords: Hyperviscosity, Plasmacytoma, Third nerve palsy

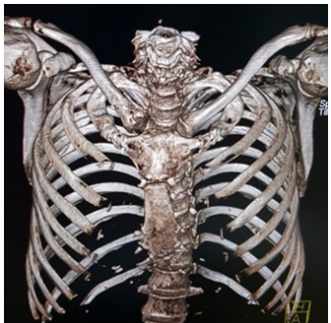
CASE REPORT

A 60-year-old woman presented to out-patient department with complaints of headache for several days duration and double vision that had developed the day before. Her medical history was unremarkable. On examination (after taking written consent) her visual acuity was 6/36 in right eye and 6/12 in left eye; colour vision and field of vision were within normal range. Pupils were equal in size, round, normally reacting to light and absence of any relative afferent pupillary defect. There was severe ptosis and limitation of adduction, depression and elevation in her right eye which was suggestive of third cranial nerve palsy [Table/Fig-1]. Anterior segment was within reference ranges in both eyes. Dilated fundus examination showed bilateral minimal tortuousity of retinal veins. Physical examination revealed a swelling in the medial end of right clavicle near the sternoclavicular joint [Table/Fig-2] which she mentioned to have been present for six months duration. The mass was approximately 5x4 cm, bony hard and tender. Neurologic evaluation had normal results except for the right sided third cranial nerve palsy. Her blood pressure was 130/70 mm Hg, and her pulse rate was 68/min. Suspecting hyper viscosity syndrome we immediately requested haematological parameters which showed a serum viscosity of 3.5Cp, accelerated ESR (100 mm/h), severe normocytic normochromic anaemia with rouleaux formation (haemoglobin level of 10.10 g/dL), and a normal fasting blood glucose level (89mg/dL), normal serum urea (21mg/dl) and creatinine (0.7mg/dl), serum calcium was 8.5mg/dl. Chest X-ray examination revealed an expansile osteolytic lesion in the medial one third of right clavicle along with a pathologic fracture. CT Scan chest revealed a minimally displaced fracture at medial end of the right clavicle [Table/Fig-3]. Results of contrast magnetic resonance imaging of her brain and orbits were normal. Serum levels of total blood protein (10.60 g/dL), immunoglobulin A (5.27gm/dL) immunoglobulin G (3.08gm/dl) with a M-Spike were noticed, and Bence Jones proteins were found during urine analysis. Tc 99m MDP3 Phase bone scan of the skull region and whole body skeletal imaging were performed showing low grade malignant process involving medial part of right clavicle and sternoclavicular joint [Table/Fig-4]. No distant metastases were seen. Aspiration cytology of right sternoclavicular joint swelling was done (after taking patient's informed and written consent) which showed numerous Marschalko-type plasma cells with eccentric nuclei and basophilic cytoplasm mixed with small plasma cells with dense round nuclei (lymphoplasmacytic) suggestive of low grade multiple myeloma [Table/Fig-5]. However, immunohistochemistry and bone

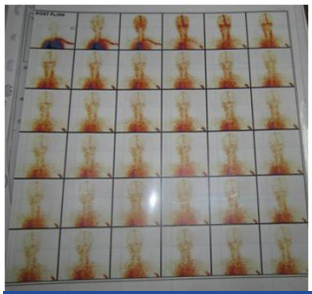


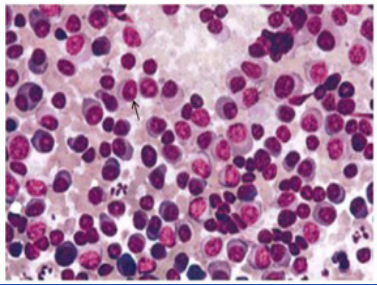
[Table/Fig-1]: Ptosis and limitation of elevation, depression, and adduction of the right eye consistent with third cranial nerve palsy.



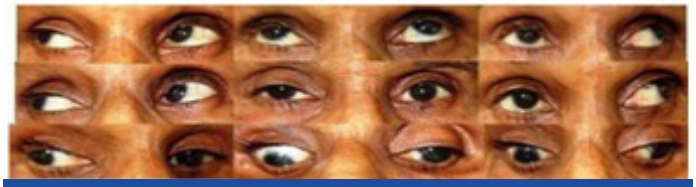


[Table/Fig-2]: Swelling in the medial end of right clavicle near the sternoclavicular joint.
[Table/Fig-3]: CT Scan chest revealed a minimally displaced fracture at medial end of the right clavicle.

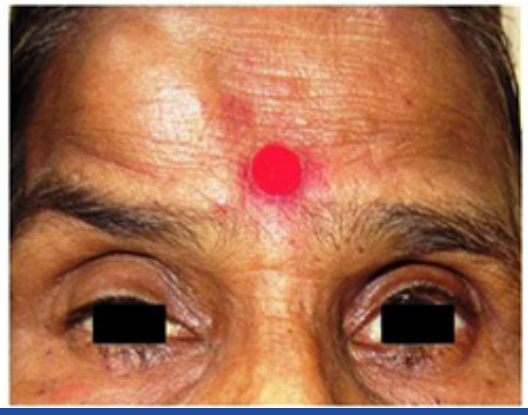




[Table/Fig-4]: Tc 99m MDP3Phase bone scan of the skull region and whole body skeletal imaging were performed showing low grade malignant process involving medial part of right clavicle and sternoclavicular joint.
[Table/Fig-5]: Aspiration cytology of right sternoclavicular joint swelling showed numerous Marschalko-type plasma cells with eccentric nuclei and basophilic cytoplasm mixed with small plasma cells with dense round nuclei (lymphoplasmacytic) suggestive of low grade multiple myeloma.



[Table/Fig-6]: Resolution of her ophthalmoplegia and ptosis three months after commencement of treatment.



[Table/Fig-7]: Soft tissue mass over her right side forehead developed 5 months later.

marrow biopsy was not done due to local unavailability and financial constraints. Chemotherapy with CTD regimen {Cyclophosphamide (400mg once weekly), Thalidomide (50mg once daily X^2 weeks then 100mg once daily), and Dexamethasone (20mg once daily once a week)} was initiated after routine blood investigations. She responded well. To our surprise, within a month of commencement of treatment, her ophthalmoplegia and ptosis resolved completely [Table/Fig-6]. Unfortunately she developed another soft tissue mass over her right side forehead within five months period which gradually increased in size [Table/Fig-7]. She was on regular follow-up with us with no ocular relapse for two years and died thereafter due to gradual decline in her general condition.

DISCUSSION

Multiple myeloma and Plasmacytoma are characterised by a gamut of the same pathology, only that Multiple myeloma indicates a disseminated disease whereas plasmacytomas refers to the localized disease. The most common presenting symptom of Multiple myeloma is bone tenderness, frequently involving the spine or chest, others being pathologic fractures, compression in the spinal cord, anaemia, infections, neurologic symptoms, weakness, hypercalcemia, and renal failure. Sundaresan N et al., very early in 1977 reported the first case of plasmacytoma of the sphenoid sinus presenting initially with third nerve palsy [1]. A review article by Omoti AE et al., published that apart from cranial nerve palsies, the various ophthalmic manifestations seen in multiple myeloma are, conjunctival and corneal crystalline and non-crystalline deposits, scleritis and episcleritis, lid ecchymosis, xanthomatosis, ciliary body cysts, ciliochoroidal effusion, uveal plasmacytomas, secondary glaucoma, hyper viscosity retinopathy, retinal vasculitis, neuro sensory retinal detachment and retinal pigment epithelium detachment, proptosis etc [2]. Yilmaz SG et al., have reported a patient with anterior uveitis, bilateral disc edema and subretinal mass surrounding around the optic nerves which on investigating proved to be having multiple myeloma [3]. On searching the available literature on cranial nerve involvement in multiple myeloma we found out that the most common cranial nerve involved were oculomotor, abducens, and hypoglossal nerves, and site of involvement being lesions in skull base [4-10]. Kashyap R et al., had reported two patients, one with diagnosed multiple myeloma under chemotherapy developed abducens palsy as a result of insufficient chemotherapy, another patient who presented with third nerve palsy and later detected to have a skull base plasmacytoma [4]. Singh T et al., described a 49-year-old man who presented with multiple Cranial nerve palsy (right third, sixth, ninth, tenth and twelfth Cranial Nerves) and on further work up revealed an extra axial mass at the base of the skull involving the right side of clivus, dorsum sellae, sphenoid, and extending up to right cerebellopontine angle. The patient recovered within one month of initiation of chemotherapy [5]. León-Ruiz et al., have mentioned that isolated, complete and fluctuating third cranial nerve palsy in their patient with IgA-kappa multiple myeloma as extremely rare condition and after receiving chemotherapy and autologous stem cell transplantation, she attained complete remission [6]. Feletti A et al., described two patients with oculomotor and abducens nerve involvement as uncommon initial manifestations of a parasellar extramedullary plasmacytoma [7]. Tucker D et al., reported a 63-year-old lady undergoing chemotherapy for multiple myeloma presenting with acute onset hypoglossal nerve palsy due to multiple soft tissue masses involving the base of the skull including the hypoglossal canal [8]. Movsas T et al., have reported two patients with sixth nerve palsy as an initial manifestation of intracranial plasmacytoma and multiple myeloma [9]. Roever AC et al., have mentioned a patient who presented with third nerve palsy 3 months after resection for a soft tissue mass at sternum, histopathologically proven as a plasmacytoma and at the same time skull lesions and intracranial mass involving sphenoid sinus were also diagnosed [10].

All these cited case reports bring light to the varied neuro-ophthalmic involvement in multiple myeloma whether as an initial manifestation or during the course of the disease. Ocular involvement in Multiple myeloma may be due to direct infiltration of orbital tissue or compressive effects of extramedullary plasmacytomas or by causing hyper viscosity syndrome, or by deposition of immunoglobulin light chain in ocular tissues. All the above cited case reports were caused by direct mass effect that caused the cranial nerve palsies and not the hypercoagulable state and this is the uniqueness which we report in this case. The indexed case presented with a complete ptosis and ophthalmoplegia without pupillary involvement suggestive of isolated third cranial nerve palsy and absence of any other neurological manifestations instead she revealed a soft tissue mass in the sternoclavicular region. This mass was initially thought to be a solitary extramedullary plasmacytoma but after further investigations proved to be a disseminated multiple myeloma. Blood investigations revealed that she was suffering from hyper viscosity syndrome as clinical sequelae of increased serum viscosity due to increased circulating serum immunoglobulins at the time of presentation. However, she did not have other constitutional and cardiorespiratory symptoms. The hyper viscosity leads to abnormal microcirculation in the cranial nerves (oculomotor nerve in our case) and causes paresis. There is no exact cut-off value of serum viscosity to prove as hyper viscosity since different patients are symptomatic at different values. The treatment of hyper viscosity is related to the treatment of the cause if applicable. Hence, we started her on chemotherapy which gradually restored the function of the damaged oculomotor nerve and her ptosis and ophthalmoplegia recovered within a month. This case may look speculative since her age was also a risk factor for microvascular third nerve palsy. But micro vascular cranial nerve palsy does not resolve so early which was seen in this case. The present case is one of the few reported cases of isolated third nerve palsies associated with multiple myeloma but the unique feature was that it was accompanied by a swelling which could have been left undiagnosed, had it been overlooked without keen clinical suspicion of an Ophthalmologist.

CONCLUSION

In the elderly population, cranial nerve palsies are mostly due to ischemic cause but when there are absence of any vascular risk factors such as diabetes or hypertension and the presentation of a significant bony swelling near clavicle, it could be associated with

any malignant or non-malignant tumour. Fine needle aspiration biopsy remains the initial diagnostic approach to solve this dilemma. Histopathology and immunohistochemistry clinches the diagnosis and other supportive investigations should be pursued to confirm the diagnosis. Early diagnosis and institution of chemotherapy helps increase survival rate in such patients.

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