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Neurofibroma Arising In the Parotid Gland- A Rare Case Report

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ABSTRACT
Neurofibromas of salivary gland are very rare and account for only 0.4% of all salivary gland neoplasms. Plexiform type of neurofibroma is predominantly seen in a scenario of neurofibromatosis 1 association, but solitary plexiform neurofibroma has also been occasionally reported. We present a report of this variant in a 17 year old male who presented with a slow growing painless swelling in the right pre auricular region for 8 months duration. Microscopic examination and immunostaining of the tumor confirmed the diagnosis of plexiform neurofibroma. We report this case in order to emphasize the importance of correctly recognizing this rare entity due to several reasons; including the difficulty in its complete excision, and a potential for malignant transformation in 10% cases. Therefore, correct diagnosis and a timely treatment with follow up are a necessity for this tumor.

INTRODUCTION

Tumors of neural origin (like neurofibromas) are rare in salivary glands.[1] Plexiform neurofibromas are benign neoplasms of Schwann cells of peripheral nerve sheath, which rarely involve the salivary glands. They are more commonly seen in the orbit, neck, back, and inguinal region. It is an infrequent growth presenting either as a solitary mass or as multiple lesions frequently in the background of NF1, also known as Von Recklinghausen's disease. NF1 is well known to be an autosomal dominant genetically inherited disease caused by a germline mutation in the NF1 tumor suppressor gene which is located at 17q11.2, and which encodes for the protein neurofibromin. The condition has a range of clinical manifestations: from pain, disfigurement and neurological deficits to even life threatening complications.

This report describes the extremely rare occurrence of a solitary plexiform neurofibroma localized to the parotid gland in the absence of neurofibromatosis syndrome. It is important to note here that though majority of plexiform neurofibromas occur as a component of NF-1, they are not considered pathognomonic of neurofibromatosis, as several earlier researchers have reported cases of isolated plexiform neurofibroma without NF-1. [2-4] However, association with NF1 has a prognostic implication; as patients with plexiform neurofibromas associated with NF1 have been found to have a higher mortality rate in comparison to patients without NF1 and demonstrating asymptomatic plexiform neurofibromas[5]. The current mainstay of treatment for plexiform neurofibroma, though difficult, is complete excision of the tumor; as it is prone to recurrence and malignant transformation.

CASE PRESENTATION

A 17 year old male presented to the surgery outpatient department with swelling in the right side of the face that had been present for eight months. The swelling had gradually increased in size. On physical examination, a right sided pre auricular swelling measuring 6x5cm was noted which was freely mobile, non tender and firm in consistency. Overlying skin was normal. On systemic examination, there were no other swellings anywhere else on the body. Café-au-lait spots and axillary freckles were absent. A family history of NF was absent.

INVESTIGATIONS

Laboratory investigations were within normal limits. CT scan showed a large round hypoattenuated mass lesion with well defined margins arising from right parotid gland without involvement of bone (Figure A). Fine needle aspiration cytology was found to be inconclusive. Surgery was further done and the tumor was removed.

Gross examination of the resected specimen showed an unencapsulated , firm, grey-white piece of tissue measuring 5x4.5x3 cm (Figure B). It comprised of an irregular, prominently enlarged nerve with tumor nodules. The cut section was lobulated, with a white, hyalinised appearance. On examination under low-power magnification (10X), the parotid gland mass was nodular and showed numerous thickened nodular nerve bundles with adjacent serous salivary gland. A tortuous mass of expanded nerve branches was seen cut in various planes of section with anastomosing network pattern (Figure C). On high power, the tumor was seen to be comprised of wavy serpentine nuclei with pink cytoplasm and a myxoid background, with areas of collagen bundles. Infiltration by few mast cells was also seen. S-100 immunostain showed cytoplasmic positivity (figure D). Hence, a diagnosis of plexiform neurofibroma was obvious on microscopic examination.

DIFFERENTIAL DIAGNOSIS:

Plexiform schwannoma can be a close mimicker sometimes, because of the presence of plexiform or network like anastomosing focal areas. However presence of well encapsulated lesion grossly along with certain microscopic features like verocay bodies, dimorphic growth pattern of antoni A and B areas and hyaline thickening of vessels are unique to schwannoma which helps in differentiating these two entities. Also plexiform schwannoma arises more frequently in superficial dermis or subcutaneous tissue unlike neurofibroma. Malignant transformation in schwannoma is an exceptionally rare event, in contrast to plexiform neurofibromas which have 2-5% tendency for malignancy.

Other common tumors of the parotid (like pleomorphic adenoma, warthin`s tumor etc.) can also cause a confusion clinically. Another important but uncommon differential can be soft tissue tumors arising from the adjacent areas. These can be ruled out on imaging and gross examination of the resected specimen as they

would be seen to arise from the adjacent tissue rather than from the parotid itself.

OUTCOME AND FOLLOW UP

After surgery the patient recovered well and was discharged in good condition. The patient was followed up for 1 year with no recurrence.

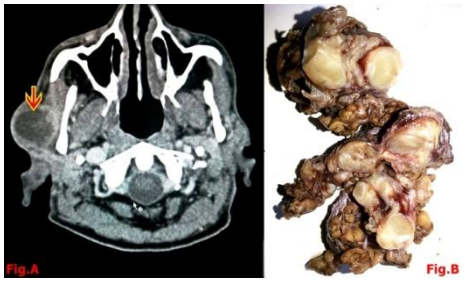

FIGURE A: CT scan showing well defined hypoattenuated mass (red arrow) arising in the parotid gland.

FIGURE B: Typical gross appearance of multinodular growth with homogenous cut section.

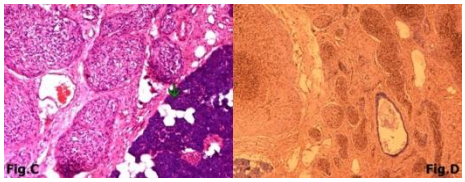

FIGURE C: Section of neurofibroma showing plexiform pattern consisting of spindle shaped cells in a collagenous stroma within normal serous salivary gland (green arrow) (H&E, x40).

FIGURE D: Section showing S100 positivity (H&E, x40).

DISCUSSION

Neurofibromas are benign tumours that originate from the nerve tissue. They may be solitary or multiple, sporadic or associated with neurofibromatosis I or II syndromes. According to the World health organization, neurofibromas are classified into two broad categories- dermal and plexiform neurofibroma, both being included as grade 1 tumours. Dermal neurofibroma involves a single peripheral nerve, while plexiform type involves multiple nerve bundles.

Plexiform neurofibromas are typically slow growing, painless and locally infiltrative tumors.[6] They represent 14% of all benign mesenchymal tumours and 10% of non-epithelial salivary gland tumours. [7] The common sites of occurrence are orbit, face, neck, retroperitoneum, inguinal region, chest or abdomen. They are often found in young children, sometimes as a congenital lesion. The clinical signs and symptoms are varied depending on the site of the tumor and the subsequent involvement of surrounding structures, ranging from pain and disfigurement to neurological deficits.

Plexiform neurofibroma of parotid gland is extremely rare. Majority of tumours of parotid gland are benign and the most common parotid gland tumour is pleomorphic adenoma.[8-10]

Plexiform neurofibromas are one of the most common and debilitating complications of neurofibromatosis 1 syndrome. So once this diagnosis is made, a diligent search for any 2 of 7 more clinical features should also be done in the patient; namely, 6 or more café-au lait spots, lisch nodules, axillary freckles, 2 cutaneous neurofibromas or 1 plexiform neurofibroma, sphenoid wing dysplasia, optic nerve gliomas and any first degree relative affected by NF1.[11] The NF1 gene mapped to chr 17q11.2, encodes for neurofibromin, which has growth regulatory properties and is normally expressed in neurons, Schwann cells, glial cellsand melanocytes.[12] The non-myelinated Schwann cells, which usually encapsulate small diameter PNS axons with their cytoplasmic processes and constitute the remak bundle, on undergoing biallelic inactivation of NF1 gene lead to the neoplastic proliferation in neurofibroma.[13]

Computed tomography (CT) imaging may show multilobulated masses that may appear as a 'bag of worms.' A characteristic 'branching ' hypoattenuated mass on CT , with branching tubular masses extending into adjacent tissue, could virtually be diagnostic.[14] Grossly,

plexiform neurofibromas are not encapsulated and typically appear as an intrafascicular diffuse tortuous nodular growth along multiple branches of more proximal nerves, resulting in a "string of onion" appearance. Histopathologically , there is diffuse cylindrical enlargement of multiple fascicles of the nerve and its contiguous branches. They are usually uniformly hypocellular with a myxoid matrix or fine fibrillary collagenous matrix containing Schwann cells, nerve fibers, mast cells and perineurial, endoneurial fibroblasts. The schwann cells are spindle shaped with scanty but extremely thin elongated eosinophilic fibrillary cytoplasm with wavy or comma shaped nuclei. It has been hypothesized that the neoplastic non-myelinated Schwann cells secrete many chemoattractants which recruit various cell types. The role of mast cells in neurofibroma formation is to secrete mitogens necessary for favorable tumour microenvironment. A thorough histopathological examination with immunohistochemistry for S100 suggesting neural origin is essential for a confirmatory diagnosis of plexiform neurofibroma. Surgical excision is the treatment of choice.

Although they are benign, neurofibromas have a 2%–5% potential for malignant transformation. [15] Accelerated growth can also be seen during early childhood, puberty and pregnancy without malignant transformation. Alarming signs including rapid increase in size, change in the consistency, increasing intensity of pain or neurological symptoms, should warrant immediate medical attention and alert the clinician towards progression of malignancy. Recurrence of the tumor is seen in about 20% of the patients after complete resection and it increases to 44% with subtotal resectioN.[16-17]

LEARNING POINTS

- Plexiform neurofibroma, although rare, should be considered in the differential diagnosis of isolated salivary gland swellings. A lack of suspicion would lead one to miss out on this entity as it is of neurogenic origin rather than salivary gland origin.
- Suspicion for NF-1 should be worked out, as plexiform neurofibromas associated with NF-1 have a high mortality rate.
- Long-term clinical follow-up is mandated because of a proven risk of recurrence and probable occurence of malignant transformation.

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