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Pathology

PRIMARY NEUROENDOCRINE CARCINOMA OF THE PAROTID GLAND WITH FOCAL SQUAMOID DIFFERENTIATION : A RARE AND CHALLENGING CASE.

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ABSTRACT Primary neuroendocrine tumors are extremely rare in the salivary gland. A thorough workup is mandatory to exclude metastasis and to prevent its misdiagnosis. We present a case of a 48 year old female who was referred to our hospital for recurrent swelling in the right parotid region. Superficial parotidectomy was done outside and differential diagnosis of large cell Non-Hodgkins lymphoma and Mucoepidermoid carcinoma was given. Radiological findings showed recurrence of the lesion in right parotid gland. Ultrasound guided fine needle aspiration was performed in our hospital and was suggestive of poorly differentiated malignancy. Her old histopathology slides from superficial parotidectomy were reviewed and was reported as Poorly differentiated carcinoma, likely Mucoepidermoid type. Total right parotidectomy was performed in our hospital and histopathology revealed differential diagnosis of -High grade mucoepidermoid carcinoma associated with marked small cell differentiation and Primary small cell/ neuroendocrine carcinoma with focal squamoid differentiation were given. Immunohisto chemistry was done for confirmation.

Although the diagnosis of primary neuroendocrine tumor of the salivary gland was very challenging, a complete workup of the case, proper identification of the tumor on light microscopy and further immunohistochemistry helped us to diagnose the tumor accurately.

KEYWORDS : Neuroendocrine, salivary, immunohistochemistry, parotidectomy

INTRODUCTION

Neuroendocrine tumors (NETs) comprise a heterogeneous group of malignancies from cells derived from the neural crest with neuroendocrine differentiation. Neuroendocrine tumor of the head and neck are very rare. They are usually seen in the lungs and also occur in other locations like thymus, stomach, gall bladder, urinary bladder and uterine cervix but occurs rarely in the salivary gland.[1] Neuroendocrine tumors in head and neck pose a diagnostic and therapeutic challenge in the routine practice. Since they rarely occur in the salivary gland a thorough workup of the case is mandatory to rule out metastasis from other parts of the body.

According to the recent classification of neuroendocrine tumors of the lungs, they are divided into 4 types namely - well differentiated-carcinoid tumor, moderately differentiated- atypical carcinoid tumor, poorly differentiated small cell type- small cell carcinoma and poorly differentiated large cell type-large cell neuroendocrine carcinoma.[2]

We herein report a rare case of primary neuroendocrine tumor of the parotid in a 48 years old female.

CASE REPORT

A 48 year old female came to our hospital with complains of swelling in right submandibular region since 3 months. Patient had a history of superficial parotidectomy in some other hospital 4 months back, where the report given had 2 differential diagnosis, highly suspicious of Non-Hodgkin's lymphoma and Mucoepidermoid carcinoma. Immunohistochemistry was advised for confirmation. Patient was a known case of chronic obstructive pulmonary disease since many years and was on medications for the same.

On clinical examination a residual endophytic type of growth was felt so the patient was advised USG-FNAC. Other investigations done were- complete blood count, liver function test and kidney function test which were within normal limits. HIV, Hbs and HCV were non-reactive. Ultrasound abdomen and pelvis and chest X-ray showed no abnormality. Contrast enhanced computed tomography of the face showed an ill-defined lobulated heterogeneously enhancing lesion in the right parotid region. Few heterogenously enhancing right level II lymphnodes showed cortical thickening which were suspicious. The impression given was residual lesion in a known case of carcinoma right parotid-post lumpectomy.

We performed ultrasound guided fine needle aspiration from the lesion and the Giemsa stained smears studied were suggestive of 'Poorly differentiated malignancy', differential diagnosis of Small cell carcinoma and Non-Hodgkins lymphoma were given (Figure 1). Histopathology and immunohistochemistry correlation was advised.

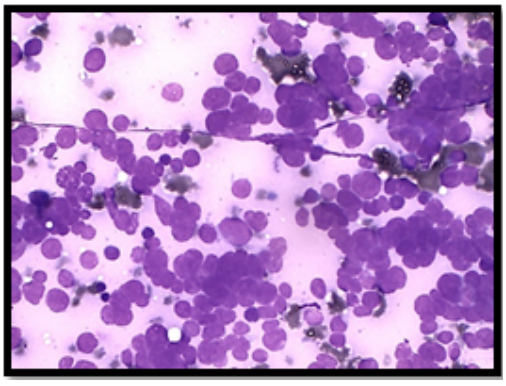

Figure 1: Cellular smears showing loose moulded aggregates and dissociative tumor cells with high N:C ratio, round nuclei, coarse clumped chromatin and negligible cytoplasm in a haemorrhagic background, Giemsa 400x.

The previous blocks and slides were retrieved from the institute where the patient was operated earlier. After reviewing the slides the impression given was 'Poorly differentiated carcinoma, likely mucoepidermoid type'. Patient was taken up for total parotidectomy with lymphnode dissection.

Grossly, the parotid specimen was received in multiple pieces that were grey white, soft, friable and altogether measured 6x5.5x3 cm. 7 lymphnodes were sent, largest measured 1x0.5x0.5cm, cut surface of all grey white, firm. The sections were studied and revealed a malignant tumor with no lymphovascular emboli or perineural invasion. 9 lymphnodes were identified microscopically and showed no evidence of tumor. The differential diagnosis given were- 1.Highgrade mucoepidermoid carcinoma associated with marked small cell differentiation, 2.Primary small cell/ neuroendocrine carcinoma with focal squamoid differentiation (Figure 2).

Immunohistochemistry was done and the markers pancytokeratin, HMWCK, CD56, synaptophysin and Ki-67 were positive while LCA and chromogranin A were negative (Figure 3a,3b,3c,4a,4b). At present patient is on Cisplastin and her health is improving.

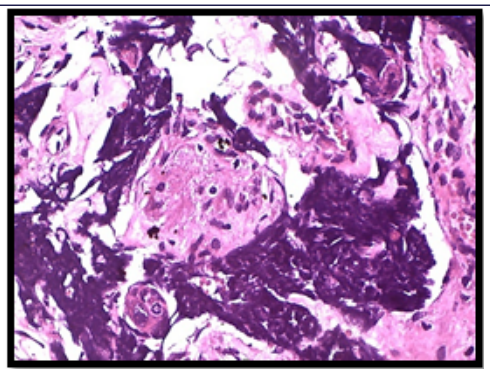

Figure 2:Diffusely infiltrating nests of neoplastic keratinized squamous cells with intervening solid sheets of small sized hyperchromatic tumor cells with frequent crushing artefact & obscured cytomorphological features, Hematoxylin & Eosin 400x.

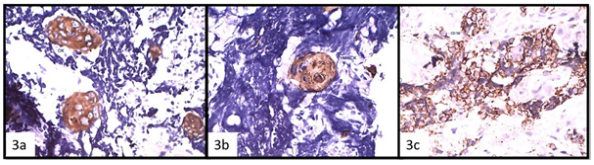

Figure 3a: Positive in squamous nests, PANCYTOKERATIN 400X
Figure 3b: Positive in squamous nests, HMWCK 400x
Figure 3c: Positive for tumor cells, CD56 400x

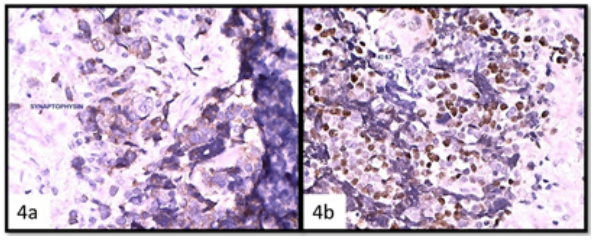

Figure 4a: Positive for tumor cells, SYNAPTOPHYSIN 400x
Figure 4b: Positive for tumor cells(20% of cells) Ki67 400x

DISCUSSION

Neuroendocrine tumors are rare tumors having an incidence of 5.76 new cases per 100,000 people, occurring mostly in the gastrointestinal tract and the lungs.[3] They are extremely rare in the head and neck region and usually originate from the larynx but still accounts for just 0.5-1% of all tumors occurring here.[4]They mostly occur in the major salivary glands, parotid being the most common one. There are very few cases of primary neuroendocrine tumors of the parotid mentioned in the literature and they mostly are small cell carcinomas and others are large cell and well differentiated types.

Neuroendocrine tumors are malignant tumors from cells derived from the neural crest with neuroendocrine differentiation. Although they differ in nomenclature, primary location, functional status and biological origin, they have common ultrastructural and immunohisto chemical features.[3]Recently WHO has graded neuroendocrine tumors according to their proliferation index. Proliferation index <2% -grade I which were equated with carcinoid tumor, proliferation index 2-20%- grade II consists of well differentiated neuroendocrine tumors and proliferation index >20%- grade III consist of large cell or small cell type.[2] Using this system our case would be classified as grade 2 neuroendocrine tumor. Peak incidence of neuroendocrine tumors is in the 7-8th decade and is most common in males but the case we presented was a female of 48 years.

The histomorphological features of neuroendocrine tumor is arrangement of tumor cells in organoid pattern, cytoplasm shows neurosecretory granules and fine granular chromatin without keratinization.[5]It is very important to differentiate the tumor as "Well differentiated or Poorly differentiated" to predict the clinical behaviour of the tumor. Accurate diagnosis is based on histopathology and immunohistochemistry. Due to the rarity of this tumor in this location a complete workup is necessary to differentiate these tumors from much more common squamous cell carcinoma and metastasis from other sites due to completely different therapeutic approaches and prognosis[3]The tumor cells are positive with a broadspectrum cytokeratin and usually show punctate paranuclear dot staining.[6]Neuroendocrine tumors stain positively for atleast one of the known neuroendocrine markers such as synaptophysin and chromogranin and also CD56, CD57 and neuron specific enolase (NSE).[3]

Clinical examination and radiologic imaging with CECT, PET/CT and octreoscan along with the immunohistological study contribute to rule out an alternative primary tumor.[7] The treatment mainly given varies according to the histological type and disease stage. Surgical resection is the mainstay of treatment. Many along with surgical resection of tumor also perform elective neck dissection but whether neck dissection should be done in all cases is still not clear. Along with surgical approach to neuroendocrine tumors, chemoradiotherapy is the treatment of choice to poorly differentiated neuroendocrine carcinomas.[3]

CONCLUSION

It is very important to accurately identify these tumors microscopically with the help of immunohistochemistry and not to misinterpret them as other malignant tumors or as metastasis since the treatment and prognosis of the patient is not the same. Likewise, it is also important to subclassify them as well differentiated or poorly differentiated. Early diagnosis and treatment can improve the outcome of the patient.

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