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Metastatic Carcinoma Ex Pleomorphic Adenoma of Parotid Gland

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Abstract : Pleomorphic adenoma is a mixed tumour commonly involving major salivary glands. 25 of pleomorphic adenomas can undergo malignant transformation if untreated, even though they are benign tumors. There are three distinct entities in the spectrum of malignancy in pleomorphic adenomas which include Carcinoma ex pleomorphic adenoma, carcinosarcoma and benign metastasising pleomorphic adenoma. CXPA is defined as the carcinomatous transformation within a benign mixed tumour in which the initial benign elements are still identifiable .They develop from epithelial components of pleomorphic adenoma which display aggressive behaviour. Distant metastases have been reported to occur in as many as 44 of patients with CXPA which include the lungs (the most common site), pleura, pharynx, kidney, ocular choroid, liver, bone, brain, and spinal cord. None of the published literature has reported synchronous brain and lung metastasis at presentation.We report an interesting case of CXPA with upfront multiple brain and lung metastasis and review the literature of this aggressive tumor.

Keyword : Salivary glands, Pleomorphic adenoma, mixed tumour, Malignancy

Case Report

A 30-year-old lady without comorbid illnesses complained of an insidious onset swelling in the right parotid region for 3 months duration,which was gradually increasing in size (Pic 1). Physical examination revealed firm to hard swelling measuring a 4x5cm in the right parotid region, predominantly involving the lower pole and extending on to the retro mandibular region. The swelling was associated with a left facial nerve paralysis. There was no significant cervical lymphadenopathy and examinations of the other systems were within normal limits. Her haematological and biochemical parameters were within normal limits. A chest x-ray however showed bilateral multiple opacities suggestive of lung metastasis (Pic 2). A CT scan of the head and neck region showed highly vascular multi lobulated lesion in the right upper cervical region and jugular fossa with involvement of superficial and deep lobes of arotid gland and infiltrating the pterygoid muscles (Pic 3). .

In addition multiple small ring enhancing lesions were seen in the cerebellum, temporal, parietal and occipital region suggestive of brain metastasis (Pic 4). An ultrasound guided biopsy from the swelling showed linear cores of salivary gland tissue with necrotic and chondromyxoid areas. Additionally few clusters lined by cells with pleomorphic hyper chromatic nuclei were also seen. The histological picture was suggestive of a carcinoma ex pleomorphic adenoma high grade(Pic 5). The patient was planned for palliative external beam radiotherapy to thetumor bed of the right parotid and to the whole brain followed by Capecitabine. The patient had good pain relief with morphine and opted to take the palliative treatment at her local place

Fig 1

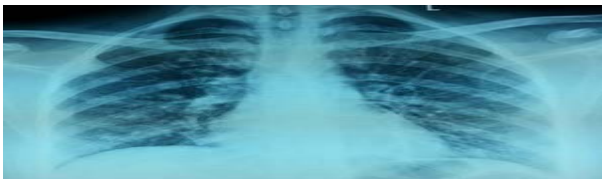

Fig 2

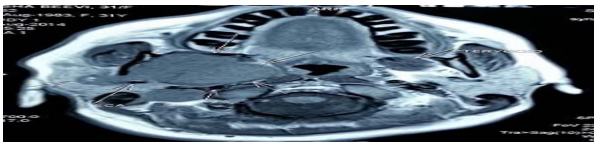

Fig 3

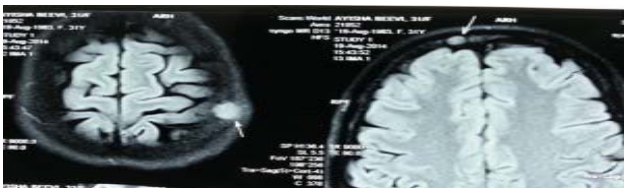

Fig 4

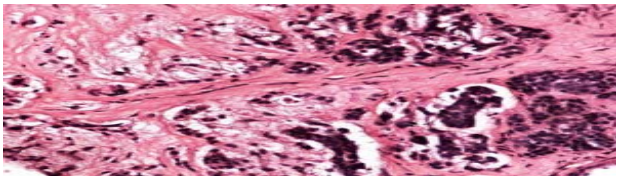

Fig 5

Discussion

25% of pleomorphic adenomas can undergo malignant transformation if untreated,even though they are benign tumor. [1].CXPA is defined as the carcinomatous transformation within a benign mixed tumour in which the initial benign elements are still identifiable .They develop from epithelial components of pleomorphic adenoma which display aggressive behaviour [2]. The typical history of the patient with CXPA is that they have a long standing swelling of the parotid region and they suddenly experiences increase in size, pain or facial nerve involvement. The CXPA typically occurs in 6th to 8th decade of life,and it's more poorly circumscribed than the benign pleomorphic adenoma .CXPA most likely to involve major salivary glands [3]. Contrary to the published literature our patient presented in the third decade.

CXPA displays an aggressive behaviour and majority develops from epithelial component [2]. Based on the presence and extent of invasion of the carcinomatous component outside the fibrous capsule, CXPA can be divided into non-invasive, minimally invasive or invasive. All 14 patients with non-invasive CXPA reported by Lewis et al., LiVolsi et al. and Brandwein et al. had tumors that behaved in a benign manner [4, 5, 6].CXPA with extracapsular invasion can be subdivided into minimally invasive or invasive, Olsen and Lewis noted that the extent of invasion beyond the fibrous capsule ranged

from 2 to 100 mm, with a mean of 24 mm, and that patients with invasion <5 mm had a benign clinical course [7].Tortoledo et al. observed that all patients with >8 mm of invasion died from their disease, whereas none with <8 mm of invasion died [8].Brandwein et al. found no recurrence in patients with tumor invasion of <1.5 mm [6]. The current WHO classification considers 1.5 mm as the cut -off for minimally invasive CXPA [9].

CXPA spreads through a direct loco-regional extension or lymphatic spread (typically to the cervical lymph nodes), and rarely hematogenously.It is reported that CXPA involves regional nodes with a frequency nearly equal to the distant metastatic rate. Olsen and Lewis reported that metastasis occurred regionally in 37 [56%] and distantly in 29 [44%] of 66 patients [10].

Gnepp et al. found that 5-year survival ranged from 25% to 65% and that the detection of metastases is considered pre-terminal [11]. Distant metastases have been reported to occur in as many as 44% ofpatients with CXPA [7]. Previously reported sites of hematogeneousmetastases include the lungs (the most commonsite), pleura, pharynx, kidney, ocular choroid, liver,bone, brain, and spinal cord [10- 12,13,14,15].None of the published literature reported synchronous brain and lung metastasis at presentation as in our case.

Thetreatment of CXPA in salivary gland is controversial since in iew of its rarity and lack of randomized evidence based guidelines. The therapy of choice for a CXPA in the parotidgland is surgery.Since the incidence of positive margins, perineural invasion, facial nerve involvement and lymph node metastasis is higher than other malignancies of parotid gland; post-operative adjuvant radiation is recommended to eradicate the residual deposits of microscopic disease. Neck dissection has both diagnostic and a therapeutic value, butstill for very small carcinomas at a clinically N0 neck, the procedure might be dispensable. At present, radical surgery with and without post-operative adjuvant radiation therapy is the recommended standard of care. [16, 2] The response of major salivary gland neoplasm to chemotherapy is poor, and adjuvant chemotherapy is currently indicated only for palliation. Doxorubicin- and platinum-based agents are most commonly used. The platinum-based agents induce apoptosis versus the doxorubicin-based drugs that promote cell arrest.Capecitabine is a pro-drug, that is enzymatically converted to 5 - fluorouracil (5-FU) in the bodyand has increased activity against malignant cells and while having fewer GI side effects. It has shown to be efficacious against malignant salivary cancers and to potentiate the effects of radiotherapy by increasing apoptosis. Recent data indicate that HER2/neu expression is relatively commonin CXPA, occurring in 30-46% of cases. Various targeted biologic agents such as trastuzumab, imatinib and cetuximab are currently being investigated. [17]

Conclusion

Even though pleomorphic adenomas are classified as benign tumours it should not overshadow the wide range of biological behaviourassociated with these neoplasms and our casedemonstrates an aggressivetransformation of a pleomorphic adenoma. It is extremely crucial for early diagnosis and treatment of malignant mixed tumours of the salivary gland as recurrence and distant metastasis are associated with an extremely dismal outcomes.

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