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Metastatic Adenoid Cystic Carcinoma of Salivary Gland: A Case Report and Review of Literature

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Abstract- Adenoid cystic carcinoma (ACC) is rare neoplasia of salivary glands, constitutes 7-10% of salivary gland neoplasms. It occurs in both major and minor salivary glands however found in other sites like head and neck, lung, breast, female genital tract, prostate and skin. It is a slow-growing tumour with gradual evolution, quite aggressive locally with perineural spread, tendency towards local recurrence and distant metastasis. This is a case report and review analysis of adenoid cystic carcinoma of salivary gland and other sites. Hereby we report a 53-year-old female, post-operative case of adenoid cystic carcinoma of submandibular gland remained asymptomatic for 6 years after treatment with radiotherapy alone, now developed metastases to lung. Performance status is 2 therefore metastasis was challenged with Adriamycin based chemotherapy. After four cycles of chemotherapy desired response was not achieved hence palliative radiotherapy to lung lesion was planned.

Keywords:- *Adenoid Cystic Carcinoma, Cribriform Pattern, Submandibular Gland.*

I. INTRODUCTION

Adenoid cystic carcinoma (ACC) which is also referred to as cylindromatous carcinoma is a slow growing, but aggressive neoplasm with a remarkable capacity for recurrence (1). It forms about 1% of all malignant tumours of the oral and maxillofacial region and 21.9% of all salivary gland malignancies (2).

It can arise in any salivary gland site, but approximately 50–60% develops within the minor salivary glands. Although it presents in a widespread age distribution, peak incidence occurs predominantly among women, between the 5th and 6th decades of life. ACC has three histopathologic patterns, viz., tubular, cribriform and solid (1).

A high affinity for perineural invasion is common. With the haematological spread, adenoid cystic carcinoma (ACC) can metastatize to lungs, bones and liver (3). On the other hand, primary ACC of lung is a rare tumour, and accounts for 0.04–0.2% of all primary pulmonary tumours (4).

The treatment of ACC is chiefly surgical, although in some cases it has been successfully coupled along with the radiation therapy (4). Majorly salivary gland tumours have good prognosis, but if associated with positive margins and perineural spread, a poor prognosis can be asserted. However, lung metastasis does not affect the prognosis (1).

II. CASE REPORT

A 53 years old female known case of ACC of salivary gland presented for regular follow up with the complaints of generalized weakness and weight loss for past 4 months. The patient had no history of consumption of tobacco, alcohol or smoking. History of hypothyroidism, on medications since 7 years. General physical examination showed patient was well oriented to time, place and person. Performance status was 2. There was a scar mark on lower part of left cheek of previous excision of local tumour mass. On palpation a single cervical lymph node was palpable on the left side measuring 1.2*1.0 cms, firm, non-tender and mobile. On auscultation, vesicular breath sounds heard except on right side in the lower lobe were diminished. Rest of the systemic examination was within normal limits.

III. INVESTIGATIONS

In 2014, MRI- Neck and Face showed a well-defined area of altered signal intensity seen on left side of floor of mouth having a cystic component which was hyperintense on T2 weighted image as well as STIR measured 5.0*2.6 cms in maximum axial dimensions. Subcentimetric lymph nodes were visualized in the bilateral level I, II and V locations.

A FNAC, of a neck swelling suggestive of Adenoid cystic carcinoma of salivary gland (submandibular gland).

Patient underwent excision of mass with left supra omohyoid neck dissection. Histopathology showed non-capsulated tumour arranged mainly in cribriform pattern. All margins were involved by tumour. Level 2A lymph nodes were involved in metastasis.

Post-surgery patient received adjuvant external beam radiotherapy 66Gy in 2 Gy per fraction in 6.3 weeks duration.

Thereafter patient was kept on regular follow up. Initially monthly for three months and then 6 monthly. Biyearly PET-CT whole body was advised for reviewing disease status.

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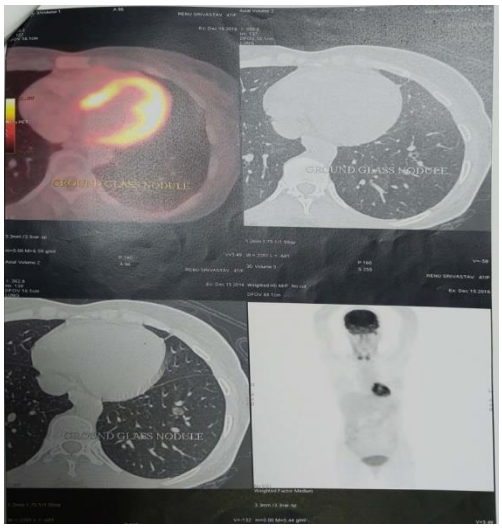

Fig 1: PET-CT scan showing a ground glass nodule in left lung

A PET-CT done 4 years back, the findings were non-FDG avid multiple, subpleural soft tissue nodules, predominantly in upper lobe in both the lungs, likely to be infective or metastatic with no evidence of significant cervical lymphadenopathy. As compared to previous PET-CT, the bilateral lung nodules were new; meanwhile, the patient was asymptomatic. No further treatment was started and patient was kept on follow up.

In between there was loss to follow up. Patient came after 2 years. Another PET-CT, showed an abnormal FDG uptake at the post-operative site which suggested any residual or recurrent disease. Also, multiple, non-FDG avid, randomly distributed parenchymal and subpleural nodules were found in both the lungs, largest in right upper lobe measuring 1.3*1.4 cms along with no significant mediastinal/hilar lymphadenopathy suggesting an increase in size and number of nodules without any metabolic activity in contrary to the previous one.

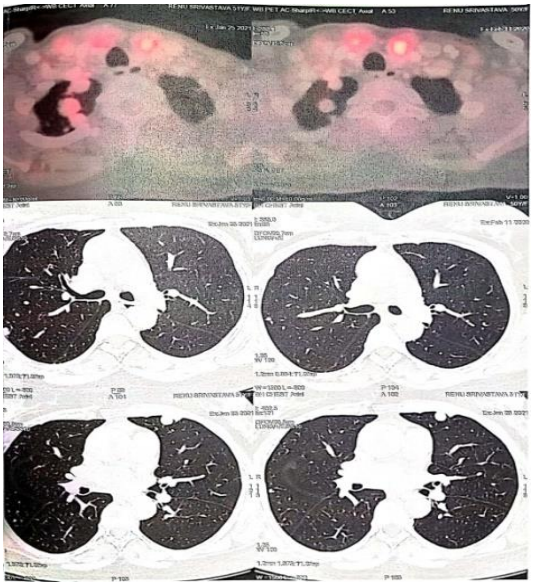

Fig 2: PET-CT revealing metabolically inactive nodules in bilateral lung fields

On the next follow-up, PET-CT scan done this year, the findings were FDG avid multiple pleural and pulmonary nodules in both the lungs with FDG avid enlarged right hilar nodes. In contrast with the previous one, an increase in size from 1.7*1.5 cms to 2.4*1.6 cms, also in number and metabolism is noted in pulmonary nodules likely to be a progressive disease. It was also associated with mild productive cough and mild difficulty in breathing.

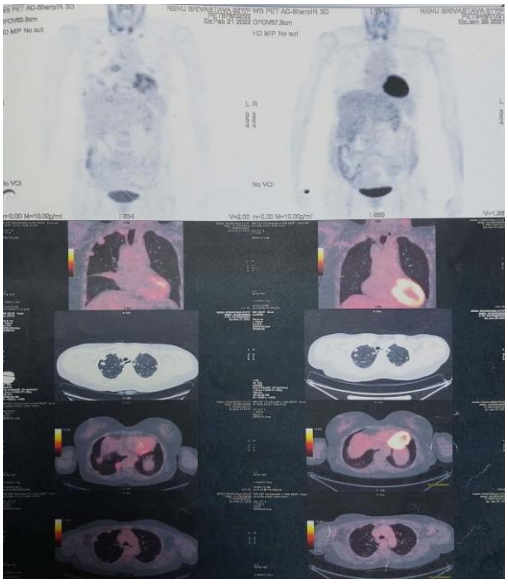

Fig 3: PET-CT scan depicting FDG avid multiple pleural and pulmonary nodules in both lungs

Thereafter, a bronchoalveolar lavage was done and the fluid was sent out for cytology report which showed few atypical cell groups consistent with salivary gland epithelium neoplasm suggestive of progressive disease, whereas the chest fluid cytology showed smears to be predominantly haemorrhagic along with degenerating epithelial cells and occasional macrophages with no evidence of atypical cells. Thus a bronchial biopsy was done revealing involvement by adenoid cystic carcinoma.

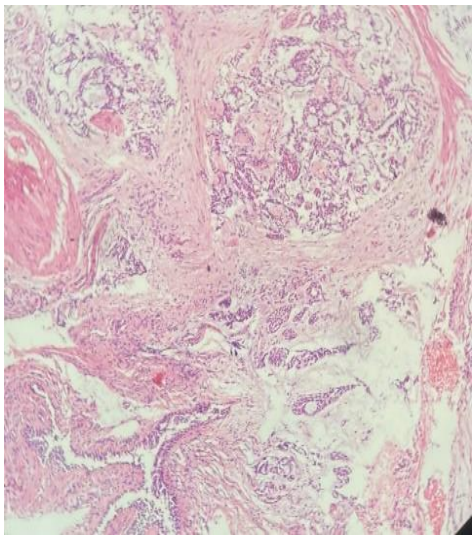

Fig 4: Photomicrograph revealing tumour cells arranged in cribriform pattern (H&E stain) at 10X

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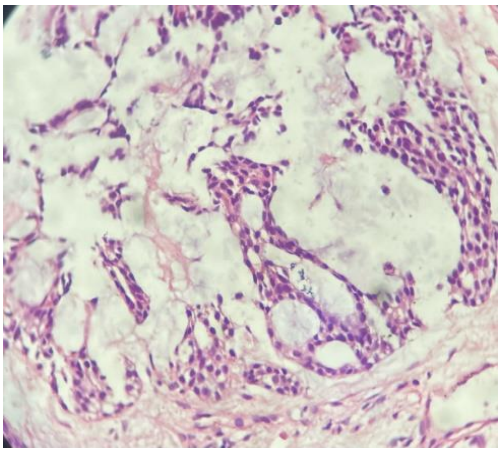

Fig 5: Photomicrograph revealing tumour cells arranged in cribriform pattern (H&E stain) at 40X

As there was multiple lesions in the lung surgery was not feasible, so the patient was started with chemotherapy, patient received three weekly, four courses with Cyclophosphamide, Cisplatin and Doxorubicin.

For response assessment a contrast enhanced CT (CECT) scan of chest was done which showed multiple well-defined homogenously enhancing soft tissue nodules with lobulated margin scattered throughout in bilateral lung fields suggesting of metastasis. As patient showed no response to chemotherapy, palliative radiotherapy 30 Gy in 10 fractions in two weeks was planned to hemi-thorax. Patient is now kept on monthly follow ups. Patient is symptomatically doing better. Repeat CECT is advised at 3 months.

IV. DISCUSSION

ACC is a rare epithelial tumour with an indolent but persistent growth pattern. ACC occurs predominantly in fourth to sixth decade of life with a slight female predilection (5). In our case, a 53-year-old female was affected. ACC clinically is characterized as a slow-growing mass with a propensity to invade peripheral nerves with a high recurrence rate and metastasis to other organs. Pain is usually a common and important associated symptom, occasionally occurring before clinical evidence of the disease (6). Neoplastic cells shows neurotropism causing pain, which was not evident in our case, suggesting of no invasion of tumour cells into adjacent peripheral nerves.

In a following study, Bosch et al. (7) demonstrated that there was a higher incidence of neck metastases in ACC of the submandibular gland in comparison with the parotid gland and it was due to direct extension of the tumour from the gland to the adjacent nodes rather than by a classic embolic metastasis. In our case, the lymph nodes at level I, II, V were positive attributing to the direct involvement. Another study done by Jacqueline E van der Wal et al. (8) studied 51 ACC patients out of which 28 showed distant metastasis. In 12 of the 28 patients with distant metastases (42.8%), only the lungs were involved, whereas in 5 of the 28 patients (17.8%), the distant metastases occurred in other organs like bones and brain coinciding with the most common organ to be the lungs as same is true with the case subject.

A study conducted by Verena Ruhlmann et al. (9) described the sensitivity of PET-CT and MRI was 96% and accuracy 94% for detection of local ACC tumours. Additionally, PET-CT revealed lymph node metastases in one patient and distant metastases in 9 out of 36 patients. In three patients second primaries were found. A correlation between the clinical behaviour of ACC and their histological patterns has been suggested. The solid histological pattern has been associated with a more aggressive clinical course and early distant metastases, in contrast to the cribriform type which shows a more benign behaviour (10). However in our case, the cribriform subtype-predominant pattern showed a very aggressive clinical course that is quite unusual for such tumours.

The most common treatment for ACC is complete surgical resection irrespective of the site, with or without post-operative radiotherapy (PORT), while conventional photon and/or electron radiotherapy alone and chemotherapy are commonly used in unresectable or metastatic disease (11). While for ACC of the tracheobronchial tree, when the radical resection (R0) is over risky or may cause mortal complication, the R1 resection (close margins) with adjunctive therapy or a combined approach of chemotherapy with radiotherapy is acceptable for patients to obtain a promising prognosis (12).

Bhattasali et al. (13) presented a small series of 9 patients with unresectable head and neck ACC receiving definitive proton RT and concurrent cisplatin and concluded that this treatment is a good option for these patients. The complete listing of clinical trials of single agents and combination chemotherapies were recently reviewed by Laurie et al. (14) the studies of chemotherapy for ACC range in size from 10 to 32 patients. The objective tumour response rate to single or multiple drug regimens ranges from 0% to 29%, with a single-institution outlier that reported 7 responding to cisplatin in 10 patients. Due to its complicated clinical course and vague etiology, medical therapy is not standardized for ACC, yet radical excision and postop-radiation is mainly utilized for loco regional control for early stage disease. Specifically, there are no National Comprehensive Cancer Network recommendations regarding specific chemotherapy regimens (15). In advanced stage, conventional chemotherapy regimens are still utilized as first-line therapy. Cisplatin and 5-FU or CAP (cisplatin, doxorubicin, and cyclophosphamide) regimens can be used for combination chemotherapy (16). In one study, patients with advanced salivary gland malignancy treated with the CAP regimen achieved partial response or stable disease rates of 67% (8 out of 12 patients) (17).

A study conducted by Luana Guimaraes de Sousa et al. (18) depicted that molecular drivers, such as NOTCH1, have emerged as potential therapeutic targets for ACC and are being explored in clinical trials. Despite its biological heterogeneity, treatment for ACC also involves various cytotoxic agents and VEGFR inhibitors, which produce

modest responses but significant toxicity. It is recommended by Bradley P.J. (19) that all patients who have a malignant salivary gland tumour treated; be it of any histology, should be followed up and clinically assessed at least once every year for lifetime.

V. CONCLUSION

ACC has an aggressive clinical course with recurrence, perineural invasion and metastasis. A regular follow-up along with effective treatment to prevent an indolent ACC from evolving into recurrent metastatic disease remains a challenge. Newer diagnostic as well as therapeutic models need to be researched for better outcomes.

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