Case Report

Small cell neuroendocrine carcinoma of frontal sinus-A rare case report

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Introduction: Neuroendocrine neoplasms arise from specialized body cells called neuroendocrine cells and have traits of both nerve cells and hormone-producing cells. They can arise in almost every organ of the body that contain endocrine cells, although they are most commonly found in the gastrointestinal tract and respiratory system and occasionally develop in the head and neck region. The present case is of a small cell neuroendocrine carcinoma of frontal sinus which was diagnosed using immunohistochemistry after ruling it out the closest differential diagnosis of olfactory neuroblastoma. **Case Report:** A 40-year-old female presented with gradual onset of swelling over forehead of size 5x5.5 cm size with an ulcer over it. Histomorphology and immunohistochemistry features supported the diagnosis of small cell neuroendocrine carcinoma of frontal sinus. Chemoradiotherapy was started but after a brief resolution, tumor again started to increase in size. **Discussion:** Very few small cell neuroendocrine carcinomas of the nasal cavities and paranasal sinuses have been reported. Extra pulmonary small cell neuroendocrine carcinomas are thought to arise from a multi-potential stem cell. Metastasis to the lungs, liver, and bone is fairly common. The treatment is Surgery with radiochemotherapy. **Conclusion:** Although rare, the possibility of small cell neuroendocrine carcinomas should be considered for any nasal cavity or sinus mass and early diagnosis can have a significant impact on the outcome and prognosis of patient.

KEY WORDS: Neuroendocrine neoplasms, sino-nasal undifferentiated carcinoma, Ki 67, multi-potential stem cell

INTRODUCTION

Paranasal sinuses (PNS) carcinoma accounts for approximately 0.3% of all cancers.[1] Among which small cell neuroendocrine carcinoma of sinonasal tract (SNT) is rare and distinctive tumor with aggressive clinical behavior.

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Neuroendocrine neoplasms are defined as epithelial neoplasms with predominant neuroendocrine differentiation. These neoplasms arise from specialized body cells called neuroendocrine cells. These cells have traits of both nerve cells and hormone-producing cells, and liberate hormones into the blood in response to signals from the nervous system. They can arise in almost every organ of the body that contain endocrine cells, although they are most commonly found in the gastrointestinal tract - small intestine and respiratory system.

They occasionally develop in the head and neck region, either as a primary tumor or, more commonly, as a metastasis. It can be non-cancerous (benign) or cancerous (malignant). They are usually slow growing, increasing over many years, but there are fast-growing forms present too.

SNT tumors are considered as tumors that occur in the nasal cavity or PNS. These SNT tumors have diversity of malignant tumors; this is because of the anatomic complexity and tissue variability. Among all types of tumors, squamous cell carcinoma is the most common, followed by adenocarcinoma, malignant lymphoma, sinonasal undifferentiated carcinoma, malignant melanoma, and olfactory neuroblastoma.

Patients with sinonasal tumors present with vague complaints such as nasal obstruction, nasal congestion and discharge, headache and/or swelling and facial pain. Diagnosis is done by a thorough clinical history and physical examination. Computed tomography or magnetic resonance imaging (CT or MRI) scans are usually done to stage the tumor locally and to check for the presence of metastasis. Biopsy of the tumor is necessary to make a final diagnosis.

Small cell neuroendocrine carcinoma can be classified by grade as well differentiated carcinoid tumor, moderately differentiated atypical carcinoid tumor and poorly differentiated tumors (small and large cell types), by type as typical, atypical, small cell, or neuroendocrine, and by biochemical activity as typical or atypical, based on the production of vasoactive substances such as serotonin. Being a rare neoplasm, there are no specific guidelines pertaining to its management however treatment options are generally concluded from its similarity found with tumors of pulmonary origin.

The present case is of a small cell neuroendocrine carcinoma of frontal sinus which was diagnosed using immunohistochemistry after ruling it out the closest differential diagnosis of olfactory neuroblastoma. Rarely of its occurrence in paranasal sinus makes the case interesting and lack of proper guidelines for the treatment of this tumor in the paranasal sinus region makes it challenging.

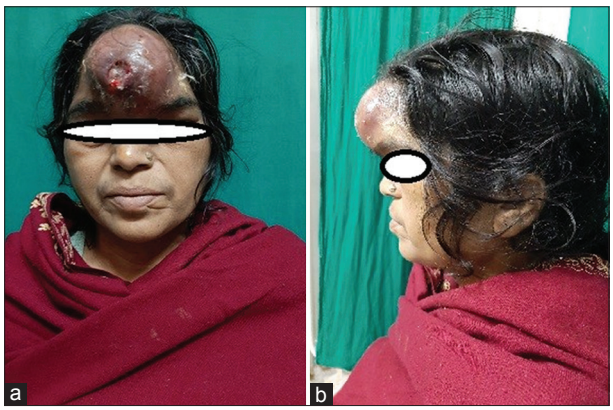

Figure 1: Figure of the patient showing the swelling with ulcer over it. (a) Frontal view; (b) lateral view

CASE REPORT

A 40-year-old female patient presented in the OPD with gradual onset of swelling over forehead for 5 months which was associated with pain and an ulcer over it since 3 months which developed spontaneously after the rupture of the swelling. Physical examination showed firm tender, globular forehead swelling of 5x5.5cm size with an ulcer over it [Figure 1a and b]. The single oval ulcer measured 2 × 1.5 cm in size, edges were inflamed with undermined margins, and floor was full of granulation tissue with purulent discharge with thickened surrounding skin.

Contrast enhanced CT (CECT) scan of Paranasal sinus showed an ill-defined heterogeneously enhancing soft tissue density centered at bilateral frontal sinus, extending to forehead in subcutaneous plane, superior part of nasal cavity, medial canthus of both eyeballs and to frontal bone and causing permeative destruction of its outer table [Figure 2a and b].

Histological examination of biopsy sample stained section showed features suggestive of undifferentiated carcinoma. In Immunohistochemistry cells were positive for synaptophysin, Ki 67 and diffusely positive for TTF. These histomorphology and immunohistochemistry features supported the diagnosis of small cell neuroendocrine carcinoma of frontal sinus [Figure 3].

The patient was started with chemoradiotherapy. After 1 month of treatment, the patient started responding: ulcer healed and swelling decreased and pain resolved [Figure 4a and b].

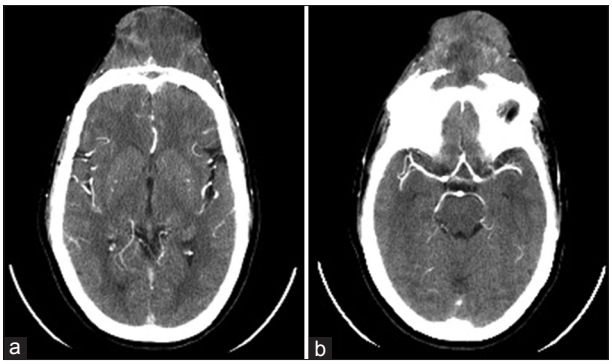

Figure 2: Contrast enhanced CT plates; (a) uppermost part of tumor at the level of beginning of frontal sinus, (b) breach in the anterior wall of frontal sinus

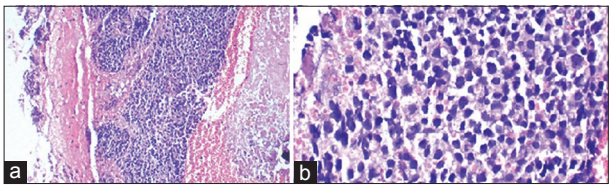

Figure 3: Hispathological examination: (a) Section show sheets of tumors with areas of Hemorrhage and necrosis; ×100 magnification (H and E) (b) Section show round to polygonal tumor cell with irregular nuclear membrane, hyperchromatic to vesicular nuclei and moderate amount of eosiniphilic cytoplasm; ×400 magnification (H and E)

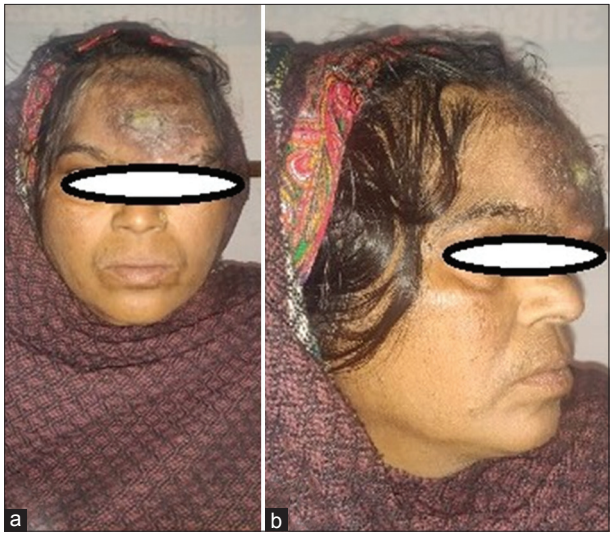

Figure 4: After 1 month of treatment, (a) Frontal view; (b) Lateral view

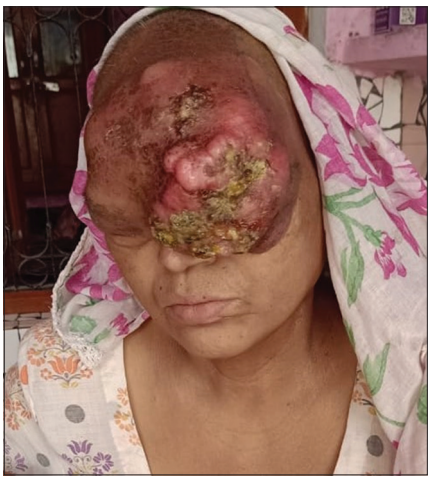

Figure 5: Photograph after 3 months of treatment suggestive of no response to chemotherapy

After 2 months, it was noticed that swelling has again began to increase with severe pain with multiple lobules over the swelling thereby suggestive of no response to chemotherapy. At the end of 3 months, swelling grown to the extent that it obliterated both eyes completely [Figure 5].

DISCUSSION

Small cell neuroendocrine carcinomas commonly seen in gastrointestinal system and lungs while extrapulmonary small cell neuroendocrine carcinomas amount to only 4%.[2] Among these, very few small cell neuroendocrine carcinomas of the nasal cavities and PNS have been reported. Extra pulmonary small cell neuroendocrine carcinomas are thought to arise from a multi-potential stem cell. However, there is recent molecular evidence that small cell elements may arise as a late-stage phenomenon in the genetic progression of more organ-typical carcinomas. They are often asymptomatic and found incidentally. When symptoms do occur, they are vague and nonspecific, which can lead to long delays in diagnosis.

Review of literature shows equal sex predilection for small cell neuroendocrine carcinomas. The mean age of presentation in small cell neuroendocrine carcinoma patient, in the study by Su *et al*.[3] was 49 years. Patient usually presents at advanced stage of disease at this stage there is rapid onset of symptoms and poor prognosis. Predictors of poor outcomes were patient with orbital involvement and tumor originating outside the nasal cavity.[4]

Small cell neuroendocrine carcinomas are a high-grade carcinoma consisting of small to intermediate sized cells with scanty cytoplasm. These tumors are composed of sheets, nests, and trabeculae with extensive areas of necrosis and hemorrhages. While Necrosis, frequent mitotic figures and lack of neurofibrillary stroma are microscopic hallmarks of this tumor. On Immunohistochemistry, it is either positive for one or both synaptophysin and chromogranin. There are high chances of recurrence and distant metastasis post treatment. Metastasis to the lungs, liver, and bone is fairly common. Paraneoplastic syndromes due to ectopic hormone production can also occur, however, clinical evidence of endocrine overactivity in the head and neck cancers is rarely detected. Treatment is based on the location of the primary tumor and guided by whether or not metastasis has occurred. Options include surgery plus radiotherapy, radiotherapy alone, and concurrent chemotherapy.[5]

CONCLUSION

Despite of rare incidence, the possibility of Small cell neuroendocrine carcinomas should be considered for any nasal cavity or sinus mass because a high clinical suspicion is necessary to diagnose this disease with such nonspecific symptoms. Therefore, early and accurate diagnosis of this rare tumor can have a significant impact on the outcome and prognosis of patient.

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