Case Report

Primary small cell carcinoma of oesophagus with syndrome of inappropriate antidiuretic hormone secretion in a young child - a case report with review of literature

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Abstract

Gastrointestinal malignancies are in general, infrequent among children and oesophageal carcinomas in particular are extremely rare among the paediatric age group. Small Cell Carcinoma of Oesophagus (SCC) is a highly progressive tumour and is associated with a poor prognosis and prone to early dissemination. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) occurs often (10%) as a paraneoplastic syndrome in small cell carcinoma of lung, its occurrence in SCC of oesophagus is very rare even in adults. We report a seven year old boy who had small cell carcinoma of oesophagus who also had SIADH.

Key words: Small Cell Carcinoma of Oesophagus, children, SIADH

Introduction

Small Cell Carcinoma of Oesophagus (SCC) is a highly progressive tumour and is associated with a poor prognosis and prone to early dissemination. Extensive review of literature revealed only very few case reports on small cell carcinoma of the oesophagus in children probably because these malignancies have a long latent period of carcinogenesis. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) occurs often (10%) as a paraneoplastic syndrome in small cell carcinoma of lung, its occurrence in SCC of oesophagus is very rare even in adults [1].

Case Report

A 7 years old male child presented with complaints of cough, breathing difficulty and severe fatigue of 20 days duration. There was no history of pain during deglutition, weight loss, nausea, vomiting, diarrhoea or constipation and chest pain. His parents also denied history of fever, chills, jaundice, hematemesis, melena or hematochezia. There was no history of accidental consumption of any corrosive substance. He did not have any family history of oesophageal disorders, gastrointestinal malignancies and other familial or genetic disorders. Antenatal, natal and post natal history were non-contributory and he was immunized appropriately for age. Physical examination revealed a palpable right supraclavicular lymph node of size 2x3cm. Laboratory investigations revealed low serum sodium (112 mEq/L), elevated urinary sodium concentration (81 mEq/L), elevated urine osmolality (380 mOsm/L) and elevated serum ADH levels (13 pg/mL). Chest

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X-ray showed widening of the mediastinum. (Figure 1a). Axial and sagittal contrast enhanced computed tomographic sections at the level of upper mediastinum showed circumferential wall thickening of the oesophagus extending from C6 to T5 level, with multiple enlarged lymph nodes in the mediastinum - paratracheal and subcarinal region (Figure 1b).

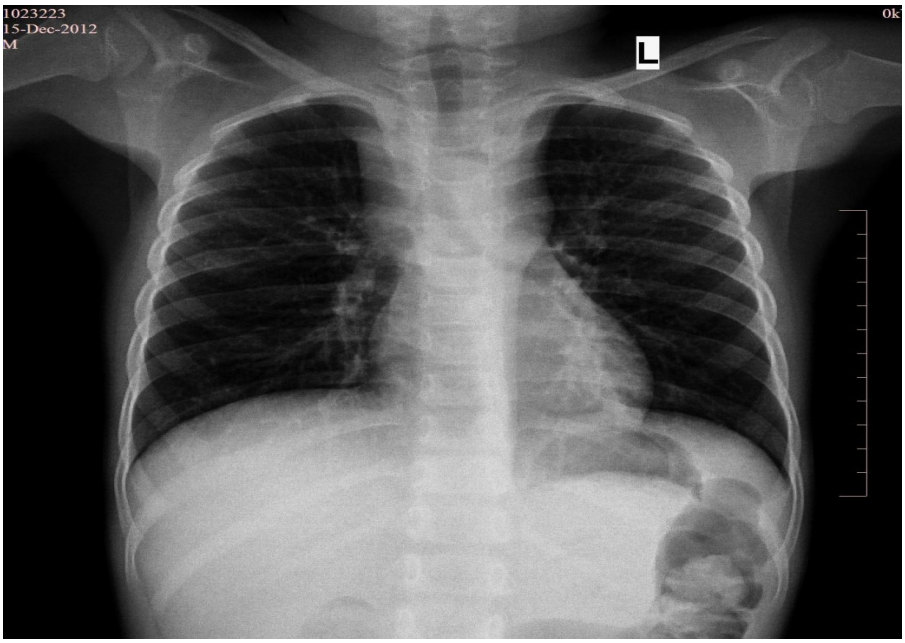

Figure 1a.: Chest x-ray [PA view] shows widening of the superior mediastinum, silhouetting the margins of the arch of aorta - Suggestive of an anterior, middle mediastinal mass probably enlarged lymph nodes.

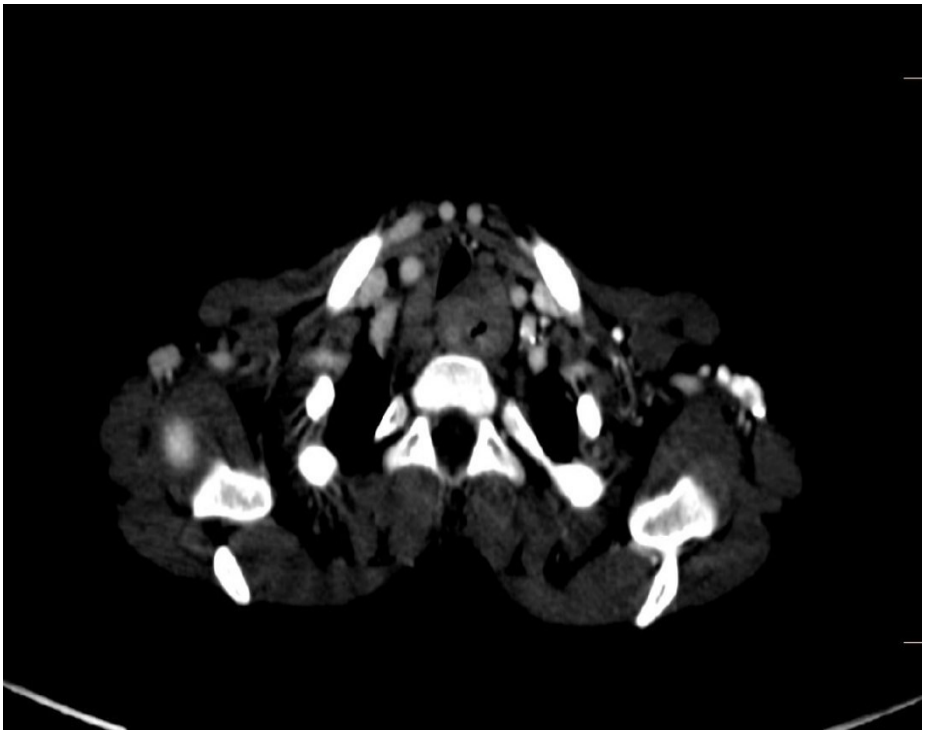

Figure 1b.: axial and sagittal contrast computed tomographic sections at the level of upper mediastinum shows long segment [8 cm] circumferential wall thickening of the proximal esophagus with multiple lymph nodes in the mediastinum (paratracheal and subcarinal region).

Upper GI scopy showed ulceroproliferative growth involving 2/3rd lumen of thoracic oesophagus. Oesophageal biopsy showed acute esophagitis.

Right supraclavicular lymph node biopsy revealed multiple islands of small cell tumor separated by wide bands of loose fibrous tissue (figure 2a). The small spindle cells showed scanty cytoplasm, large nuclei with stippled chromatin and increased mitosis. Some foci showed thin fibrillary cytoplasm around these cells. Immunohistochemistry showed strong positivity for vimentin, EMA, chromogranin, synaptophysin, while P63, CD 99, Myogenin, Desmin, S100, CD45, CD3, CD20, CD10 were negative which confirmed the diagnosis to be Small Cell Carcinoma (SCC), poorly differentiated neuroendocrine carcinoma (Fig 2b).

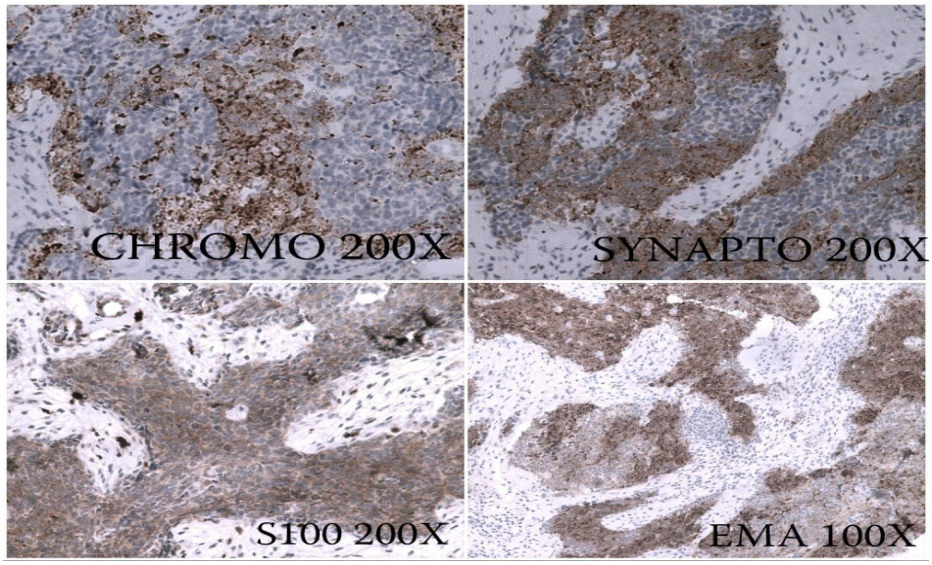

Fig-2a: Lymphnode with partially effaced architecture with Nests of tumor cells seen surrounded by sclerotic stroma, cells are showing severe pleomorphism and increased mitosis 12/10 hpf and several apoptosis.

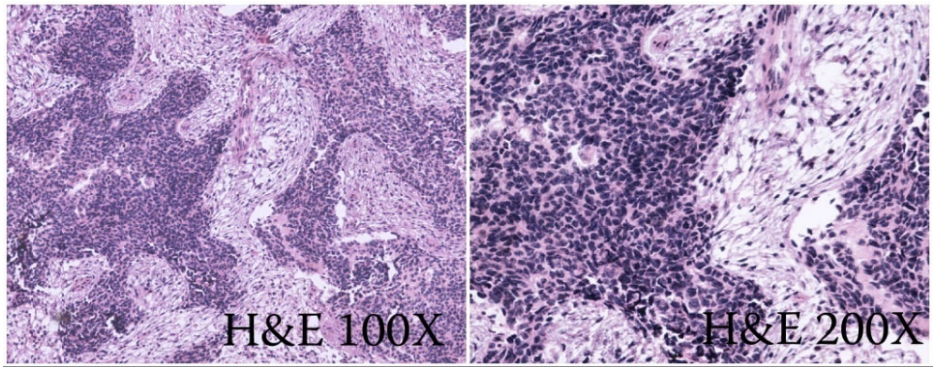

Fig-2b: by IHC tumor cells were positive for synaptophysin, chromogranin, S100 and EMA.
Histology and IHC are in the favor of small cell carcinoma (poorly differentiated neuro endocrine tumor).

USG Abdomen, CT abdomen and 24 hr urinary VMA was normal. Bone marrow biopsy, bone scan and MIBG were all also found to be insignificant. With diagnosis of SCC of oesophagus the child received 4 cycles of cisplatin and etoposide, followed by radiotherapy with 50 Gy in 28 fractions. Post radiotherapy he was followed up with 2 more cycles of cisplatin and etoposide. PET scan done 6 weeks after the last chemotherapy was normal.

During follow up- 3 months after completion of treatment, child presented with same symptoms and found to have relapse. The family opted for alternative medicine and the child reportedly succumbed to the disease, three months from the relapse.

Discussion

Gastrointestinal malignancies are in general, infrequent among children and esophageal carcinomas in particular are extremely rare among the pediatric age group. Small cell carcinoma (SCC) occurs more commonly in the lung. The incidence of SCC in esophagus is rarely reported accounting for only 0.8-2.4% of all esophageal cancers in adults [2].

Primary SCC of the esophagus was first reported in 1952 by Mckeown in an adult patient [3,4]. SCC usually occurs in the sixth or seventh decade of life but ranges from 29-88 years (mean 64years). SCC of the esophagus is a highly progressive tumour and is associated with a poor prognosis. These tend not to occur in children probably because these malignancies have a long latent period of carcinogenesis.

The etiologies of esophageal cancer are usually attributed to the habit of cigarette smoking and high alcoholic beverage consumption. The premalignant condition reported is Barett's esophagus. Factors associated with low risk of esophageal cancer are high intake of fruit and vegetables. Folate, fibre, β-carotene, vitamin C, vitamin D and B6 were inversely associated with risk of SCC of oesophagus whereas dietary cholesterol, vitamin B12 and animal protein were positively associated with SCC of oesophagus [5]. Salivary glands, pharynx, larynx, esophagus, stomach, pancreas, colon, rectum, skin and cervix are the most common extrapulmonary sites of SCC [6].

There are two histological origin of SCC. They either originate from the neuroendocrine cells of the submucosal gland or stratum basal or from the multi potential stem cells of the endoderm.

Immunohistochemical staining of the biopsied cells is vital to determine the carcinoma. In this case, there was positive staining for the neuroendocrine markers, synaptophysin and chromogranin A. SCC has been found to be of mixed type 63% of the time, demonstrating coexisting adenocarcinomatous and squamous cell histological characteristics.

Many patients are asymptomatic while some other present with dysphagia and weight loss as a common presenting symptom. Other symptoms include dyspepsia, chest pain, hematemesis and rarely syndrome of inappropriate antidiuretic hormone (SIADH) [7].

SIADH is thought to be due to ADH producing tumor cells which is seen predominantly after recurrence [8].

SCC of the esophagus is being treated with various treatment modalities which include surgical resection, chemotherapy, radiotherapy and combinations of therapy.

While there is currently no formal treatment of esophageal SCC due to the paucity of cases, chemotherapy appears to be the most effective treatment.

Historically in adults the 5 year survival rates were <10% with surgery or radiotherapy alone due to early dissemination of the disease and up to 25% when chemotherapy and radiotherapy were combined [9]. Later other combination used were cisplatin, etoposide, alternating with cyclophosphamide, doxorubicin and vincristine[10]. Other chemotherapy agents tried with success paclitaxel, irinotecan, oxaliplatin, and vinorelbine [11].

Conclusion

Small cell carcinoma of esophagus is a clinically challenging and very rare tumor in children with a poor prognosis. Accurate diagnosis with immune-histochemistry coupled with multimodality treatment is the basis of management of this tumour. Multicentre studies for this kind of tumors and shared protocols will help in future to develop standard treatment guidelines for this tumor.

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