Small Cell Carcinoma of the Esophagus

Sir,

A 72-year-old man presented with progressive dysphagia and abdominal distension of two months' duration. An endoscopy was done, which revealed a circumferential, infiltrative tumor involving the mid-esophagus region. Multiple biopsies were taken from the esophagus, which showed a tumor composed of small, round or elongated, dark cells with hyperchromatic nuclei and scanty cytoplasm arranged in sheets, nests, ribbons, and in a peritheliomatous pattern. It was diagnosed as a primary small cell carcinoma (SCC) of the esophagus [Figure 1].

A Computed tomography scan of the abdomen, showed hepatomegaly with enhancing multiple focal lesions in both lobes of the liver. Fine needle aspiration cytology (FNAC) of these lesions showed heavy cellularity comprising of necrosis in the background with abundant sheets, clusters, and discrete populations of malignant cells. Individual cells were either round or spindle-shaped, with a high nuclear-cytoplasmic ratio and scanty-to-no cytoplasm. The nuclei were round or spindle-shaped with powdery nuclear chromatin.

Immunohistochemical studies showed patchy moderate positivity for cytokeratin [Figure 2], neuron-specific enolase and synaptophysin and patchy weak positivity for chromogranin. Due to the advanced nature of the disease, the patient was offered only symptomatic palliative treatment.

The incidence of esophageal SCC is reported to be 0.4-7.6% of all malignancies in different esophageal sites.[1] The cellular origins of esophageal SCC have been the subject of intense speculation and debate - it was initially thought to arise from the argyrophilic Kulchitsky cells in esophageal mucosal.[2] These cells have the ability to synthesize and store amines and to decarboxylate some amino acids - a feat that gave rise to the term, "amine precursor uptake, decarboxylation (APUD) cells." It would now appear that esophageal SCC is of endodermal origin derived from pluripotential basal epithelial cells, which serve as the common precursor for adenocarcinoma, squamous cell carcinoma, and SCC.[3] The small cells retain their potential for further differentiation into either mucin-producing or keratin-forming cells, which explains the coexistence of small cells, squamous, and glandular elements in the same lesion. Recent studies have shown that microsatellite instability (MSI) may be a more frequent cause in SCC than in squamous-cell carcinoma of the esophagus for the development of esophageal cancer.[4]

Grossly, esophageal SCC cannot be distinguished from esophageal squamous carcinoma. Esophageal SCC might present as an ulcerating, hard tumor mass on the mucosal surface of the esophagus or as a polypoid infiltrative process growing in the submucosal layer without any obvious ulceration of the mucosal surface. Microscopically, in all of the cases, the tumor is described as having a histological appearance of SCLC consisting of round to spindle-shaped cells with scanty cytoplasm, granular nuclei, inconspicuous nucleoli, along with ultrastructural and immunohistochemical evidence of neuroendocrine differentiation.[5]

Both esophageal SCCs and squamous cell carcinomas are similar with regard to the mean age of patients at the time of presentation, the location of the carcinomas and the presenting symptoms. However, esophageal SCC is a more aggressive tumor associated with rapid growth, and patients

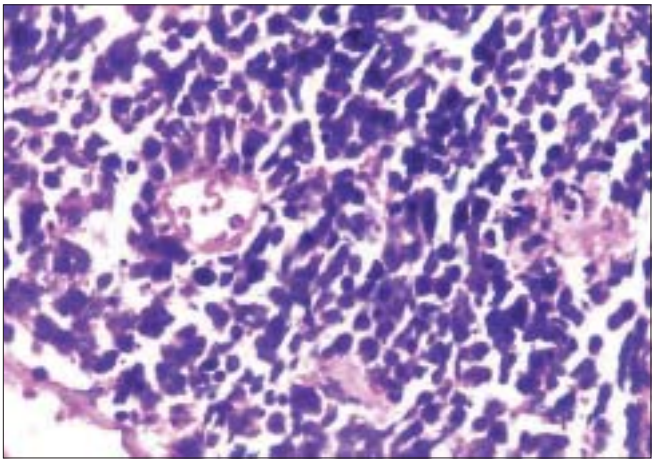

Figure 1: Esophageal biopsy shows small round or elongated cells with hyperchromatic nuclei and scanty cytoplasm arranged in sheets, nests, ribbons, and in a peritheliomatous pattern (H and E, ×500)

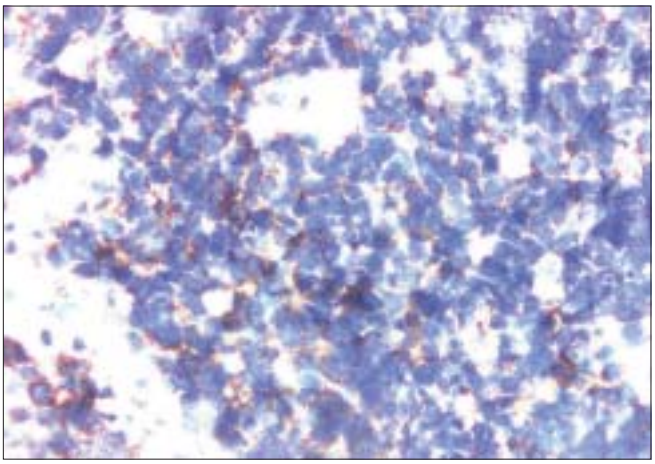

Figure 2: Immunohistochemical studies (×500) showed moderate positivity for Cytokeratin

usually present with widespread metastasis. Prospective randomized trials of therapy for esophageal SCC are unlikely due to the rarity of the disease.

ACKNOWLEDGEMENT

We would like to acknowledge Dr. Fouzia Ziad, MD (Path) for performing the histopathologic and cytologic analysis.

Sanjeev S. Chatni, Hiran K. Ravindran[1], Anantha Narayanan, Vallath Balakrishnan

Departments of Gastroenterology and [1]Pathology, Amrita Institute of Medical Sciences and Research Center, Amrita Lane, Elamakkara P.O., Cochin - 682 026, Kerala, India.
E-mail: sanjeevchatni@aims.amrita.edu

REFERENCES

1. Takubo K, Nakamura K, Sawabe M, Arai T, Esaki Y, Miyashita M, *et al*. Primary undifferentiated small cell carcinoma of the esophagus. Hum Pathol 1999;30:216-21.
2. Craig SR, Carey FA, Walker WS, Cameron EW. Primary small cell cancer of the esophagus. J Thorac Cardiovasc Surg 1995;109:284-8.
3. Ugras S, Akpolat N, Yalcynkaya I, Karaayvaz M. Primary composite tumour with bipartite differentiation of the esophagus. Acta Chir Belg 2000;100:39-43.
4. Gonzalez LM, Sanz-Esponera J, Saez C, Alvarez T, Sierra E, Sanz-Ortega J. Case report: esophageal collision tumor (oat cell carcinoma and adenocarcinoma) in Barrett's esophagus: Immunohistochemical, electron microscopy and LOH analysis. Histol Histopathol 2003;18:1-5.
5. Noguchi T, Takeno S, Kato T, Wada S, Noguchi T, Uchida Y, *et al*. Small cell carcinoma of the esophagus: Clinicopathological and immunohistochemical analysis of six cases. Dis Esophagus 2003;16:252-8.