Concurrent Squamous-Cell Carcinoma Esophagus and Atypical Carcinoid Tumor: A Rare Case Report and Review of Literature

Sir,

Carcinoma esophagus is very common malignancy which is usually managed with chemoradiation or chemoradiation plus surgery and squamous cell and adenocarcinoma are the two most common types. Very rarely, we can have neuroendocrine carcinoma or tumor of the esophagus. Here, we are presenting a very rare, probably first such case of concurrent squamous-cell carcinoma of the esophagus along with atypical carcinoid tumor which was incidentally detected in residual node postchemoradiation and surgery.

A 52 year-old nonsmoker, alcoholic male patient with spinocerebellar ataxia as comorbidity, presented in November 2016, with a complaint of progressive dysphagia of 2 months duration. Upper gastrointestinal endoscopy showed circumferential growth in lower-third of the esophagus with luminal narrowing. Computed tomography (CT) of thorax showed 13-mm thick circumferential mural thickening involving long segment of the lower esophagus causing marked luminal narrowing [Figure 1]. There was 3.5 cm × 2.5 cm mass in the subcarinal region, compressing esophageal lumen along with the few perigastric nodes [Figure 2]. Positron-emission tomography (PET)-CT showed intense fluorodeoxyglucose (FDG) avid thickening in the lower third of esophagus with FDG avid lower parastrachal, subcarinal, and perigastric nodes. Biopsy from the esophagus was done which was suggestive of moderately differentiated squamous-cell carcinoma [Figure 3]. The patient received neoadjuvant chemoradiation with 41.4Gy/23#/5 weeks by 3D-conformal radiation therapy technique along with five cycles of chemotherapy with injection paclitaxel 60 mg/m²

Histopathology showed minimal residual squamous-cell carcinoma [Figure 4]. The patient underwent thorascopic esophagectomy with gastric pull with feeding jejunostomy in February 2017. Histopathology showed minimal residual squamous-cell carcinoma of the esophagus with subcarinal node showing features of neuroendocrine tumor [Figure 4]. Subsequently, immunohistochemistry (IHC) was done to confirm the histopathological findings. IHC in esophageal blocks showed strong positivity for CK 5/6 [Figure 5], P63 [Figure 6], and epithelial membrane antigen [Figure 7] in tumor and surface epithelium with Ki67-30% [Figure 8], suggestive of residual small focus of squamous-cell carcinoma. IHC on subcarinal node was negative for CK5/6 and P63, strongly positive for synaptophysin [Figure 9] plus chromogranin [Figure 10], and weekly positive for CK7 [Figure 11], CK20 [Figure 12], and CDX2 [Figure 13]. Ki67 index was 4% [Figure 14], overall suggestive of atypical carcinoid tumor. There was no symptom related to endocrine overactivity or carcinoid syndrome. Follow-up PET-CT was normal, and hence the patient was kept on close follow-up, but at the time of writing the paper, the patient was untraceable.

Carcinoma esophagus with neuroendocrine carcinoma is a very rare entity. There are two types of mixed tumors, namely, collision and composite. Collision tumor is composed of two independent tumors growing very closely, which subsequently collide with each other, ultimately forming a single mass. The cells of origin are different, and histopathology too shows clear demarcation between the two tumors.[1] The second type is composite tumors in which one neoplastic clone diverges into different cell lineages. The origin is from one single pluripotent stem cell.[2] Histopathology, IHC analysis, microsatellite instability testing, and electron microscopy can help distinguish between these two tumor types.[2] Although some degree of focal neuroendocrine differentiation is common in squamous-cell carcinomas, its clinical relevance is not very clear. The neuroendocrine tumors are graded from Grade 1-3. Grade 1 is <2 mitosis/10 high-power fields (HPF) or Ki67 ≤2%. Grade 2 is 2–20 mitosis/HPF or Ki67 2-20%. Grade 3 is >20 mitosis/HPF or Ki 67 >20%. Grade 1 and 2 are called neuroendocrine tumors (Grade 1-typical carcinoid and Grade 2-atypical carcinoid). Grade 3 is called neuroendocrine carcinoma, which is further divided into small cell and large cell types.[3] There are no definite guidelines for the treatment of these colliding/composite tumors. But, whenever there is a high-grade neuroendocrine carcinoma then usually small-cell lung cancer guideline is followed. The outcome is generally poor.

Till now, only two cases of colliding tumor of the esophagus are reported. The first case by Dias et al. showed squamous cell and neuroendocrine carcinoma collision.[4] The second case by Wilson et al. showed the collision of large-cell neuroendocrine carcinoma with papillary carcinoma arising in Barrett’s esophagus.[5] Till now, only seven cases of composite tumor of the esophagus are reported, and out of seven cases, five are in the squamous cell and neuroendocrine carcinoma combination.[6-12] Our case is different because we could not find any neuroendocrine component in the primary, that is, in esophageal biopsy as well as surgical specimen. We could find atypical carcinoid in subcarinal nodes only. The possible explanation could be because of neoadjuvant chemoradiation, which resolved carcinoid part along with minimal residual squamous component only left. Another explanation could be neuroendocrine primary from pancreato-biliary or colonic origin, in view of week positivity for CK7, CK20, and
CDX2. However, distant metastasis from atypical carcinoid is very rare phenomenon, especially in the absence of obvious primary. Subsequent scans as well as colonoscopy could not find anything in the abdomen. Moreover, all cases
reported so far are of high-grade neuroendocrine carcinoma with other histological types. However, our case showed morphologically as well as by IHC, features of atypical carcinoid (Ki67-4%) along with squamous-cell carcinoma.
There is one-case report showing squamous-cell carcinoma converting to neuroendocrine carcinoma, on relapse after chemoradiation. The combination of squamous-cell carcinoma and atypical carcinoid has been reported in the floor of the mouth by Yamagata et al., in the larynx by Davies-Husband et al., and in the lung by Okazaki et al. Hence, to the best of our knowledge, this is the first such case of a combination of squamous-cell carcinoma esophagus with Grade 2 neuroendocrine tumor (atypical carcinoid).

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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Submitted: 08-Feb-2018
Accepted in Revised Form: 29-Nov-2018
Published: 04-Dec-2019

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