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An Unusual Cause of Clubbing: The Esophageal Carcinoma

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Abstract

Clubbing is a sign that is usually found in association chronic respiratory diseases or cyanotic cardiac conditions. Few reports have demonstrated an association with gastrointestinal malignancies. We report a rare case of clubbing associated with advanced esophageal adenocarcinoma. The association is rare but it can trigger a revisit to some pathogenesis concepts such the neutrally mediated hypothesis and possible further understanding better approach to targeted therapy for this rare subtype of malignancy.

Keywords: Adenocarcinoma; Clubbing; Esophageal

Introduction

The access to developed health care system has contributed to increased life expectancy. As a result, more chronic diseases and unusual forms of malignancies are seen with variety of associations. Patients with esophageal carcinoma usually present late in its course. The presentation varies demonstrating different clinical manifestations [1]. Such manifestations could be pure gastrointestinal such as; dysphagia, hematemesis, melena or weight loss. Extra- gastrointestinal manifestations such as skeletal manifestations including in its rare form digital clubbing [1]. Digital clubbing is known to be associated with pulmonary diseases commonly primary lung cancer, bronchiectasis, or cystic fibrosis and in some cardiac and liver conditions [2]. The association between esophageal carcinoma and clubbing is not clear, therefore, we report a case demonstrating such rarity.

Case Report

A 71 years old male who is not known to have any medical illnesses, presented to our institute complaining of progressive dysphagia for 3 months duration. Initially to solids progressing to liquids. He also gave history of weight loss of 6 kilograms in the last 6 months. There were no other symptoms. He is an active smoker for more than 35 years (1 pack per day). The rest of his medical and surgical histories as well as his review of systems were unremarkable. On examination the patient was conscious, oriented and alert. His vital signs were normal. Systemic examinations were all normal except for digital clubbing in both hands. Genitourinary examination showed absent right testis. Routine laboratory investigations revealed: White blood cells 8.2 $\times 10^9$ /L, hemoglobin 13.7g/dL, hematocrit 40.9% and platelets 212 $\times 10^9$ /L. Liver Function Test (LFT) and Renal Function Test (RFT) were within normal limits. His coagulation profile was within normal limit. The liver infection serology panel were all negative. His hormonal profile; Follicular-Stimulating Hormone (FSH) was high 25,3 unit (N 0.95- 11.95), Growth Hormone (GH) 0.136 (N 0-3), Thyroid Stimulating Hormone (TSH) 1.624 (N 0.35-4.94), rheumatoid factor all were normal. Chest x-ray showed retro cardiac shadow most likely the dilated esophagus (Figure 1). The hand x-ray did not show any bone lesion or pathology. Computed Tomography (CT) scan showed lower esophageal tumor, with no evidence of metastasis namely to the lung or liver (Figure 2). Right undescended testis was found intra-abdominally with no suspicious features of malignancy. Contrast study, Barium meal, showed dilated esophagus till its lower end and stricture length was about 2.5 cm. His pulmonary function test and echocardiography were unremarkable. Upper gastrointestinal endoscopy showed tight stricture seen at 33cm. multiple biopsies were taken, and the histopathology came consistent with invasive poorly differentiated esophageal adenocarcinoma. The patient was discussed in tumor board meeting and was decided to start a palliative course due to poor fitness to surgical resection and tolerance to chemotherapy. An esophageal stent was inserted and obstructive symptoms relieved.

The patient lost follow up after discharge.

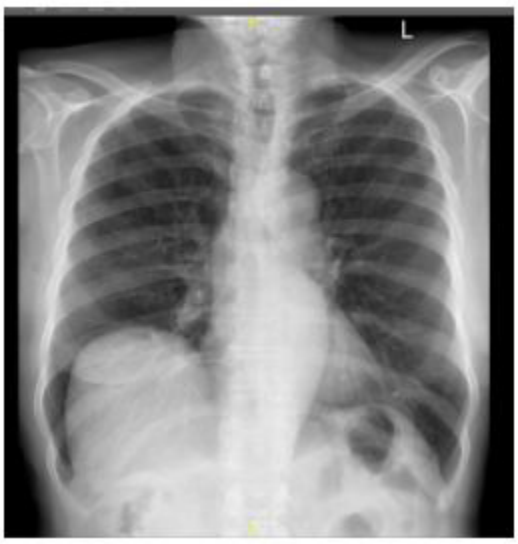

Figure 1: CXR, AP view.

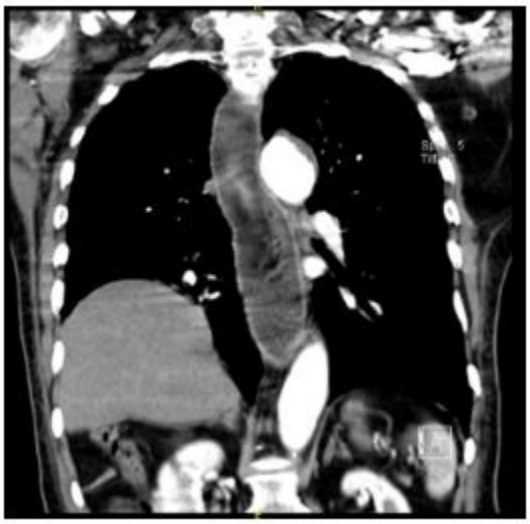

Figure 2: CT scan of the chest, coronal view shows lower esophageal Ca.

Discussion

The Pathophysiology of digital clubbing remains unclear, but there are some hypotheses suggested its formation. Hypoxia which leads to opening of deep arteriovenous fistulae to increase the blood supply of the digits causing them to hypertrophy [2]. This explains clubbing in cases of cyanotic heart diseases or chronic respiratory diseases. Another hypothesis suggests that megakaryocyte lodged in the peripheral vessels of the digits, releasing vascular endothelial growth factor (VEGF) which cause dilatation of vessels and lead to increase vascularity, permeability, and connective tissue changes [2]. This explains the clubbing in respiratory cases like bronchogenic carcinoma. The neurally mediated hypothesis further suggested a relationship between clubbing and vagus nerve [3], since clubbing occur in organs supplied by vagus nerve, and reversal of clubbing after vagotomyis seen. This explains clubbing in case of esophagus cancer as in our case. Esophageal adenocarcinoma is infrequently reported as a cause of digital clubbing. We found few case reports demonstration the relation between esophageal cancer and clubbing (Table 1).

	Author	Age	Sex	Pathology of esophagus
1	K. B. Carroll et al.	78	female	Esophageal adenocarcinoma
2	M. I. Polkey et al.	71	female	Esophageal adenocarcinoma
3	R. J. WILSON et al.	69	female	Squamous cell carcinoma

Table 1: Case reports demonstration the relation between esophageal cancer and clubbing.

From the table, we can see that all patients were elderly females. Adenocarcinoma was the predominant pathology. Our case was male. In some cases, the onset of clubbing was parallel to the growth of the esophageal tumor [4]. Interestingly, symptoms and radiological changes of clubbing get relieved following the operation and surgical resection [5]. In our case, the patient was an active smoker for more than 35 years, the CT scan showed emphysematous changes in the lungs, however emphysema alone does not usually associate with clubbing unless there is an underlying lung malignancy [6]. Upon investigation, there was no evidence of lung malignancy which was ruled out as cause of clubbing. Moreover, there was no evidence to suggest that undescended testis or high Follicular Stimulating Hormone (FSH) could cause clubbing, so this concludes that esophageal adenocarcinoma is the cause of clubbing in our patient. In conclusion, clubbing and hypertrophic osteoarthropathy have many causes, but very rare to be associated with esophageal cancer as in our case. The basis of such association could not be explained, this might open room for further investigation and revisit the neutrally mediated hypothesis. The presence of clubbing can be a strong indicator for aggressive growth of the tumor. Considering the VEGF hypothesis too, the genetic buildup of such tumors can respond to targeted therapy addressing such point.

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