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A huge esophageal Schwannoma occurring in a Caucasian young male: a case report

M.V. MATTEO[1], C. SASSOROSSI[1], F. LOCOCO[1], R. RICCI[2], S. MARGARITORA[1], A. GASBARRINI[1], L. ZILERI DAL VERME[1]

[1]Dipartimento di Scienze Mediche e Chirurgiche, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy
[2]Dipartimento di Scienze della Salute della Donna, del Bambino e di Sanità Pubblica, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

Abstract. – OBJECTIVE: Gastrointestinal schwannomas are rare benign mesenchymal tumors originating from Schwann cells, the nerve sheath belonging to the Auerbach's plexus or, less frequently, to Meisser's plexus. The esophagus is the least common site accounting for less than 2% of all esophageal tumors, and the upper to mid portion is usually involved. Esophageal schwannomas affect more frequently middle-aged Asian women. The most common symptom is dysphagia. Diagnosis requires histological and immunohistochemical studies and the standard of care is surgical resection.

CASE REPORT: We present the case of a 22-year-old Caucasian male who was admitted to our hospital for progressive dysphagia and acute chest pain. An EGDS showed an elongated bulging of the lower esophagus with signs of a subcentimetric mucosal erosion. A CT-scan showed a lower esophageal ectasia and a huge postero-lateral wall mass measuring 37x28x70 mm. An endoscopic ultrasonography showed a hypoechoic heterogeneous mass with multiple anechoic areas and a fine needle biopsy was performed. Histological examination showed tissue made up of spindle cells with mild eosinophilic cytoplasm and rare nuclear atypia, which were intensively and diffusely positive for the S100 protein on immunohistochemical studies thus allowing pre-operative diagnosis of "ancient" schwannoma. after a multidisciplinary discussion, the patient underwent a surgical resection. Since the tumor had a transmural extension, a subtotal esophagectomy was performed to achieve complete resection with negative margins.

CONCLUSIONS: This is the first case of a young Caucasian male patient with an "ancient" schwannoma of the lower esophagus, a benign but locally advanced lesion treated by subtotal esophagectomy.

Key Words:
Schwannoma, Esophagus, Ancient Schwannoma, Surgery, Histology, Case report.

Introduction

Gastrointestinal schwannomas are slow-growing benign mesenchymal tumors originating from Schwann cells, the nerve sheath belonging to Auerbach's plexus or less frequently to Meissner's plexus[1]. Esophageal schwannomas represent less than 2% of all esophageal tumors and present with similar characteristics of the esophageal leiomyoma, that is the most common benign tumor of this gastrointestinal tract[2]. Esophageal schwannomas have usually been described in Asiatic patients, with a certain predominant in the female gender and middle age (about 50-60 years)[3]. Most patients are asymptomatic, and the diagnosis is incidental during the work-out examination for other diseases. Unlikely, in symptomatic patients a moderate up to severe dysphagia may be referred followed by dyspnea or chest pain[4].

Considering the lack of specific symptoms and its rarity, the diagnosis of esophageal schwannoma is very challenging. Imaging may have only a limited diagnostic utility with computed tomography (CT) and magnetic resonance imaging (MRI) showing esophageal lesion/mass with non-infiltrative characteristics (as like as esophageal leiomyoma)[5].

Thus, a final diagnosis may be done on surgical specimen and more rarely on fine-needle-aspiration (FNA) biopsy guided by EUS[6]. Surgical treatment is usually preferred, especially in symptomatic patients. While tumor enucleation is preferred in esophageal schwannomas with no infiltrative attitude, esophagectomy is very rarely required to achieve a complete resection of the tumor[4].

Herein, we report a challenging case of a large esophageal schwannomas occurring in a 22-years old Caucasian male patient.

Corresponding Author: Maria Valeria Matteo, MD; e-mail: mariavaleria31191@gmail.com

Case Report

A 22-years old Caucasian male was admitted to the Emergency Department of our hospital complaining of progressive dysphagia to both solids and liquids and acute onset of chest pain. He referred a 3-months history of mild but progressive dysphagia and the onset in the last 12 hours. He had an unremarkable medical and familiar history, except for sporadic episodes of gastroesophageal reflux-like symptoms and smoking habitude. His vital signs and physical examination were normal. His weight and height were 55 kg and 1.73 cm, respectively, (Body Mass Index 18.4 kg/m^2) and he denied weight loss. Blood analysis revealed only mild leukocytosis (WBC 10.710/mm^3) with predominant neutrophils (70%) with normal hematocrit and platelet count. Serum C-reactive protein was increased at 6.9 mg/L (normal range < 5 mg/L) and erythrocyte sedimentation rate was normal. The blood biochemistries, as well as urine analysis, were normal except for a mild hypercalcemia (10.4 mg/dl). A CT-scan (Figure 1B) ruled out an aortic dissection and revealed a lower esophageal ectasia associated with a postero-lateral wall mass measuring 37 x 28 mm (transvers diameter) with a craniocaudal extension of 70 mm. An esophagogastroduodenoscopy (EGD) (Figure 1A) revealed an elongated "bulging" of the distal esophageal wall (34 to 41 cm from incisors) covered by normal mucosa with signs of subcentimetric superficial erosion.

An endoscopic ultrasound (EUS) examination demonstrated a hypoechoic heterogeneous mass lesion with multiple anechoic areas located in the mid-lower esophagus. The mass had no doppler signals. EUS-guided fine needle biopsy (FNB) was then performed. The histological examination showed fragments of tissue made up of spindle cells with mild eosinophilic cytoplasm, rare nuclear atypia, without mitosis or necrosis. Immunohistochemical studies revealed the cells to be intensively and diffusely positive for the S100 protein, indicating nerve sheath origin; the tumor was negative for CD117 (c-kit), DOG1, desmin, caldesmon, AE1/AE3, melanA and HMB45. These findings were consistent with an "ancient" schwannoma, a rare variant of schwannoma, characterized by increased cellularity and atypia. After a multidisciplinary discussion, a surgical resection was indicated and planned. In detail, as first step, the mobilization of the stomach in the thorax and its tubulization was performed *via* a small upper midline laparotomy. Then, a muscle sparing lateral thoracotomy was performed at the level of the 6th right intercostal space. At exploration of the pleural cavity neither sign of pulmonary nor pleural abnormalities were observed. The tumor was located at the level of the third inferior thoracic esophagus involving the esophageal mucosa. No enlarged lymph nodes were found in the mediastinum. Thus, a subtotal esophagectomy was performed for achieving an adequate completeness of resection. An Ivor Lewis esophagectomy with intrathoracic termino-terminal anastomosis was performed by using a 24Fr circular stapler. Two chest drains and one abdominal drain were left at the end of the surgery. No intra-operative and post-operative complication occurred, and the patient was discharged in good clinical condition 7 days after surgery. Gross examination of the resected esophagus and stomach revealed an intramural mass of 75 mm extended from lu-

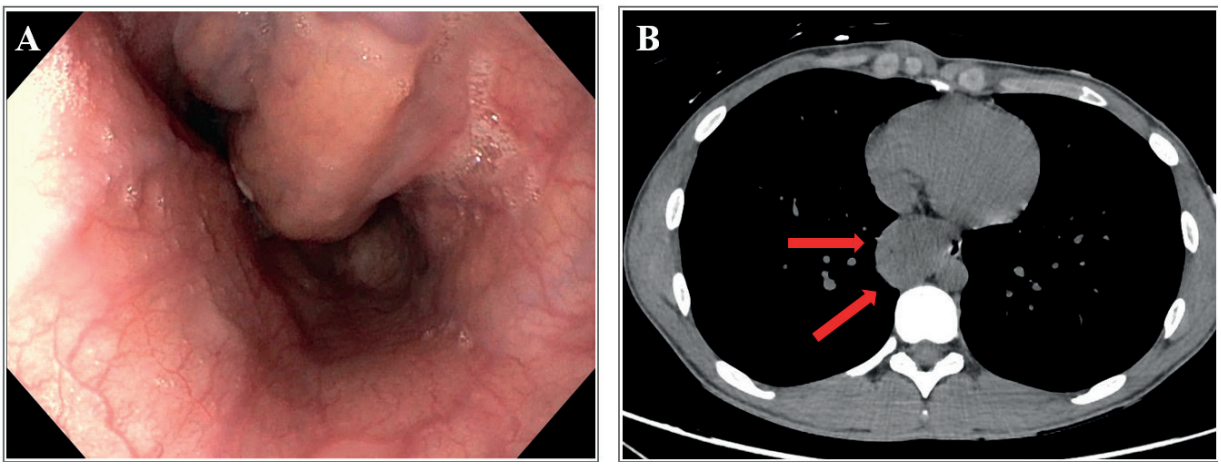

Figure 1. Endoscopic and imaging appearance of the tumor. **A,** Upper gastrointestinal endoscopy showing an elongated bulging at the lower tract of the esophagus; **B**, CT scan showing a postero-lateral esophageal wall mass.

minal surface, that was ulcerated, to perivisceral tissue. The specimen was fixed in 4% buffered formalin, processed in the usual manner, and paraffin embedded. The sections were stained with hematoxylin and eosin. The following antibodies were employed utilizing the EnVision™ FLEX+ detection system (DAKO, Glostrup, Denmark) according to manufacturer protocol: CD117 and S100 (rabbit polyclonal, 1:400 and 1:800 respectively), EMA, desmin, HMB-45 and Melan-A (1:500, 1:50, 1:50 and 1:50, respectively) (DAKO, Glostrup, Denmark); DOG1 (rabbit polyclonal, 1:100) (Spring Bioscience, Pleasanton, CA, USA). The Benchmark ULTRA autostainer (Roche, Basel, Switzerland) was employed using the UltraView DAB universal detection kit (Roche, Basel, Switzerland) according to manufacturer protocol for the antibodies to synaptophysin and neurofilaments (prediluted) (Ventana Medical Systems, Oro Valley, AZ, USA).

On histological examination, the lesion showed a plexiform architecture and made up of spindle cells with pronounced nuclear atypia and some drafts of palisade architecture and/or Verocay body (Figure 2A). A subcentimetric erosion of the mucosa was observed at this level (Figure 2B) an indirect sign of an infiltrative attitude of the tumor. At macroscopic view (Figure 2C) no mitotic activity was observed. The neoplastic cells were reactive with S100 protein (Figure 2D) and negative for desmin, DOG1, CD117, EMA, HMB45, MelanA, synaptophysin and neurofilaments. The histopathologic and immunohistochemical features were consistent with a plexiform "ancient" schwannoma.

Discussion

Gastrointestinal schwannomas are benign mesenchymal tumors that originate from Schwann cells localized in the myelin sheath around nerves of the myenteric plexus (i.e., Auerbach's plexus) or, less often, of the submucosal plexus (Meisser's plexus)[1]. The esophagus is the least frequent location of GI schwannomas that represent less than 2% of all esophageal tumors[1]. According to the available literature, esophageal schwannomas affect more frequently the female gender with a predominance of the 5th-6th decade of life. Further,

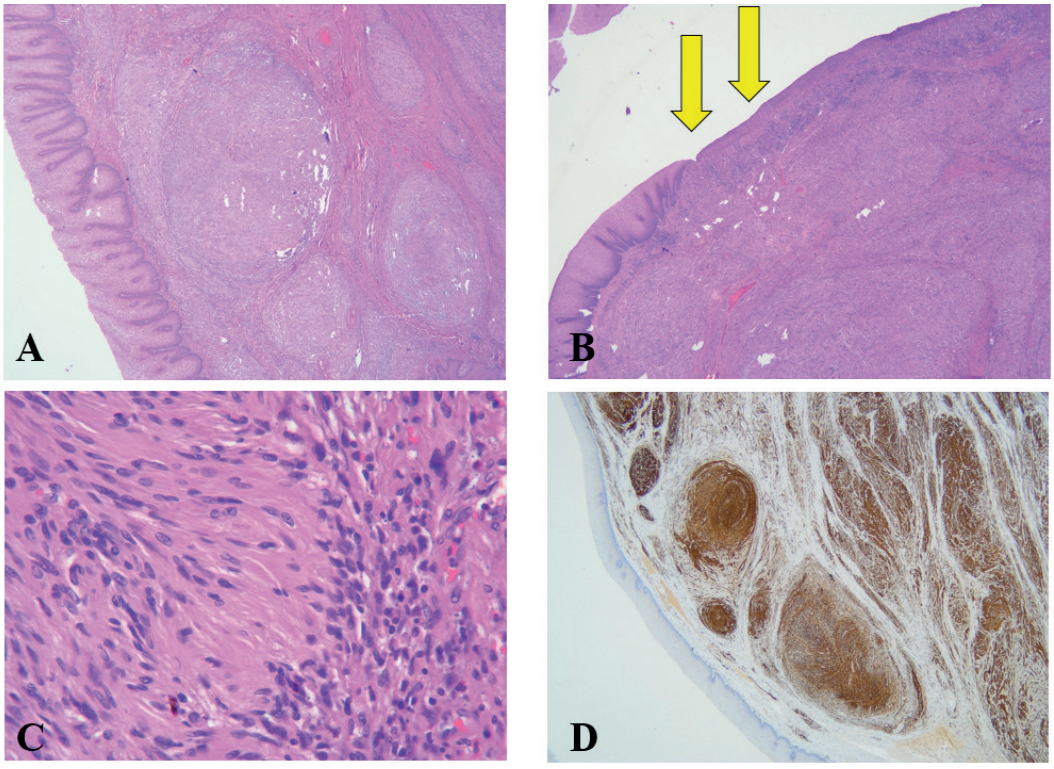

Figure 2. Pathological features of the tumor. **A,** At H&E stains, the oesophageal tumour revealed a plexiform architecture (x20); **B,** the luminal surface was ulcerated (see yellow arrows); **C,** the tumor was composed of elongated spindle cells with tapered nuclei, featuring nuclear palisading a plexiform architecture (x20); **D**, S100 was intensely and diffusely positive (x20).

they seem to be predominant in Asian ethnicity[1,7] with only anecdotical cases reported in Caucasian population. The present case had several peculiarities: first of all ethnicity (Caucasian) but also the age and gender (22-years old male). Furthermore, esophageal schwannomas only rarely present with infiltrative characteristics as in the present case where the mucosa was involved by the neoplasm. Finally, the tumor is more frequently located in the upper thoracic segment[1], while in this case involved the lower esophagus.

Most of these neoplasms are clinically asymptomatic and found incidentally. When present, symptoms are usually related to lesion size and position. The mean size of esophageal schwannomas reported in literature is 5.6 cm, with a range of 0.5 to 10 cm[1]. The case we present is a mass measuring about 7 cm in greatest dimension (cranio-caudal).

Moderate to severe dysphagia is the most common symptom of these tumors, but other clinical manifestations like dyspnea, cough, chest pain or epigastric pain may also be referred. Our patient had a 3-months history of progressive dysphagia, such as other reported cases. However, he had also a history of long standing but mild reflux-like symptoms that could be ascribed to an impairment of esophagogastric junction as a consequence of a very slow but progressive tumoral growth. Furthermore, he referred also an episode of acute chest pain and an endoscopic finding of a pulsating mass, so the diagnosis of aortic dissection had to be ruled out.

A definitive preoperative diagnosis of esophageal schwannomas can often be challenging since they have no peculiar characteristics on CT or MRI. Moreover, mucosal biopsies obtained during a standard endoscopy may not be useful since these lesions usually involve the submucosa and the muscularis propria. Currently, endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-guided FNAB) is the diagnostic tool of choice for submucosal tumors allowing more adequate samples[6]. In fact, a conclusive diagnosis requires histopathological and immunohistochemical studies.

Schwannomas can show one or two histological patterns: "Antoni A" characterized by compact areas of spindles cells arranged in palisades, and "Antoni B" showing fewer cells and myxoid change. An even more rare variant is the "ancient" schwannoma characterized by degenerative changes, such as areas of hypocellular tissues, nuclear pleomorphism and hyperchromasia[8]. Moreover, "ancient" schwannomas are usually large tumors[9]. The term "ancient" was coined in 1951 by Ackerman and Taylor[9] because both the large dimensions and the degenerative histological findings were suggestive of a long-standing growth and an "ageing" of the tumor[8-11]. However, despite these degenerative characteristics, "ancient" schwannomas have a benign behavior and the absence of mitoses and invasive pattern allows a correct differential diagnosis with malignant neoplasms[9,11].

The immunohistochemical Schwannoma's hallmark is the strong reactivity to S100. In particular, immunohistochemistry is crucial to distinguish schwannomas from other mesenchymal lesions such as leiomyoma, which is the most common benign esophageal tumor and is positive for smooth muscle markers, and GIST, which overexpress CD117 (c-kit) and is important to rule out because of its malignant potential. None of these markers are expressed by schwannomas.

The standard of care for esophageal schwannoma is surgical enucleation or esophagectomy. The surgical planning must take into account the tumor site, its dimensions, local extension and patient's condition. An endoscopic therapeutic approach could be considered when pre-operative EUS study shows a well-demarcated submucosal mass with no signs of deep muscular invasion. So far, the published cases of esophageal schwannoma endoscopically resected were all peri-centimetric superficial lesion and the endoscopic technique used was mucosal resection (EMR)[12-14]. Endoscopic submucosal dissection (ESD) can provide an en-bloc resection for larger lesions ensuring a radical mass excision and an accurate pathology study. However, this is a complex technique that requires high levels of endoscopic expertise and it's not always feasible due to tumor site and local extension[1].

The case we present was not a good candidate for endoscopic resection because of its size and intramural extension as shown by pre-operative imaging so, after a multidisciplinary discussion, he underwent surgical resection.

A subtotal esophagectomy was performed to achieve complete resection with negative margins since the tumor was extended from the ulcerated luminal surface to perivisceral tissue. Despite the Ivor-Lewis esophagectomy is more invasive than simple tumor removal, this approach was preferred to achieve a radical resection of a mass with an uncertain biological attitude.

Conclusions

We reported the first case of a young Caucasian male patient affected by a huge "ancient" esophageal schwannoma of the lower esophagus. This case is reported for its rarity and peculiarities, such as patient's age and ethnicity, tumor site and histological features. To our knowledge, "ancient" esophageal has a benign biological behavior and, even our patient had a locally extended lesion, the radical surgical approach should provide a long disease-free survival.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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