Justyna Szumiło[1], Andrzej Dąbrowski[2], Krzysztof Zinkiewicz[2], Monika Chyżyńska[1], Elżbieta Korobowicz[1]

Sarcomatoid Carcinoma of the Esophagus

[1]Department of Clinical Pathomorphology, Prof. Feliks Skubiszewski Medical University, Lublin,
[2]2nd Department of General Surgery, Prof. Feliks Skubiszewski Medical University, Lublin

The authors present two rare cases of sarcomatoid carcinoma of the lower thoracic esophagus in a 73-year-old woman and a 42-year-old man. The histogenesis, clinicopathological features and differential diagnosis of this unusual tumor are also discussed.

Introduction

Virchow was the first who described in 1864 a biphasic tumor composed of both carcinomatous and sarcomatous components and called it carcinosarcoma [16]. This unusual neoplasm was reported in many locations including the oral cavity, respiratory tract, kidneys, pancreas or skin, however the lack of consensus regarding its origin especially of the sarcomatous component led to chaos in nomenclature, as a result of which many terms were used to describe it, e.g., sarcomatoid carcinoma, pseudosarcomatous carcinoma, carcinoma with sarcomatoid change, carcinoma with pseudosarcomatous stroma, metaplastic carcinoma, polypoid carcinoma, carcinosarcoma, so-called carcinosarcoma and pseudosarcoma [1, 2, 10]. The results of many immunohistochemical and ultrastructural studies support the epithelial origin of both components of the tumor and therefore the term "sarcomatoid carcinoma" as refers to the histogenesis and typical microscopic pattern seems to be the most appropriate and is now more frequently used [1, 2, 7, 10]. Esophageal sarcomatoid carcinomas (SCs) are very rare and represent approximately 0.5–2.8% of all tumors of this organ [5].

This paper presents two cases of esophageal sarcomatoid carcinoma diagnosed on the basis of morphological, immunohistochemical and ultrastructural features.

Case Descriptions

Case 1

A 73-year-old woman with congestive heart failure has suffered from solid food dysphagia for about 2 months. Barium esophagogram and esophagoscopy demonstrated large polypoid tumor located at 31 cm from the incisor teeth. Biopsy specimens revealed squamous cell carcinoma. Chest radiographic examination, abdominal ultrasonography and chest and abdominal computed tomography showed no evidence of distant metastases. Transhiatal subtotal esophagectomy with posterior mediastinal gastric interposition and cervical esophagogastrostomy were performed. The patient died of respiratory failure 14 days after surgery.

Case 2

A 42-year-old man was admitted to hospital with a 3-month history of solid food dysphagia, vomiting, malaise and loss of body weight of about 12 kg. The patient was a heavy smoker and drinker. He suffered from liver cirrhosis. Barium esophagogram and esophagoscopy revealed a polypoid and ulcerated tumor located at 33 cm from the incisor teeth. Biopsy specimens contained mainly necrotic tissues with a few atypical cells. Abdominal ultrasonography and computed tomography demonstrated an enlargement of upper abdominal lymph nodes. Transthoracic subtotal esophagectomy with wide regional lymph nodes dissection, retrosternal gastric interposition and cervical esophagogastrostomy were performed. The postoperative course was uneventful. The patient died of liver failure 20 months after surgery.

Pathological findings

General pathological data on both esophageal SCs are summarized in the Table 1. The tumors were grossly polypoid

and superficially ulcerated (Fig. 1). Microscopic examination revealed co-existence of two components. The carcinomatous component, located deeply at the base of the tumors, was composed of moderately differentiated squamous cell carcinoma (Case 1) (Fig. 2a), and poorly differentiated squamous cell carcinoma with focal glandular differentiation (Fig. 2b) confirmed by positive mucicarmine staining (Case 2). In both tumors the sarcomatous component was hypercellular and consisted of spindle-shaped cells with marked, especially in Case 1, nuclear pleomorphism, as well as bizarre multinucleated giant cells (Figs. 2a and 2b). There was no differentiation towards heterologous elements. This predominant component was located superficially. Moreover, in Case 1, single, 1-cm-in-diameter esophageal intramural metastasis located 2.5 cm proximally to the primary tumor and composed exclusively of sarcomatous component was also found.

Carcinomatous components revealed strong positive immunostaining exclusively for cytokeratins (clones: MNF-116, AE1/AE3, 34βE12) and epithelial membrane antigen (EMA). Sarcomatous components were positive for vimentin, α-smooth muscle actin, and the minority of cells were also cytokeratin-positive with all the antibodies applied (Fig. 3). Both components of each tumor showed positive p53 immunostaining (clone DO7; all antibodies from DakoCytomation).

Ultrastructural examination of the sarcomatous component of the tumor in Case 1 revealed spindle cells and bizarre giant cells with multilobated nuclei and well-developed rough endoplasmic reticulum and abundant extracellular collagen fibers. The sarcomatous component in Case 2 was composed of spindle cells with fibroblastic and myofibroblastic features i.e. well-developed rough endoplasmic reticulum and microfilaments with dense bodies, admixed with cells with the evidence of epithelial differentiation i.e. desmosomes and tonofilaments (Fig. 4a). Single cells with both microfilaments with dense bodies and desmosomes were also found (Fig. 4b).

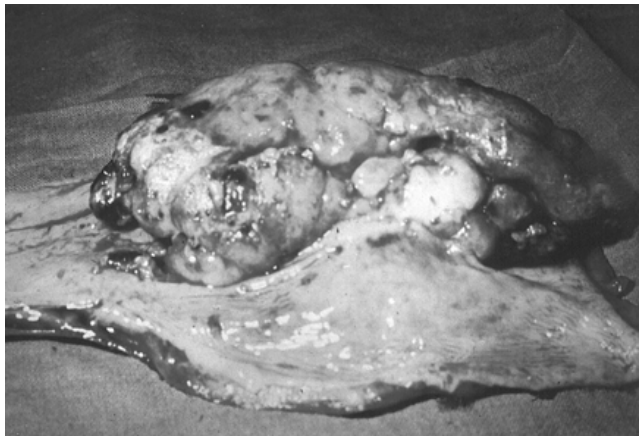

Fig. 1. Gross appearance of esophageal sarcomatoid carcinoma (before fixation) (Case 1).

Discussion

Sarcomatoid carcinoma is a very rare esophageal tumor, and to the best of our knowledge the presented cases are the only well-documented ones in Polish literature.

Tumors consisting of both carcinomatous and sarcomatous components are controversial neoplasms. The matter of controversy is either the histogenesis, or classification of these tumors. It was suggested that both components originate from a single totipotential stem cell (divergence hypothesis) or from two or more stem cells (convergence hypothesis). It was also speculated that the spindle cell component represent a non-neoplastic reactive change to developing carcinoma [2]. However, many recent findings advocate the first hypothesis and epithelial origin of the sarcomatous component *via* metaplasia [1–3, 7, 9]. The re-

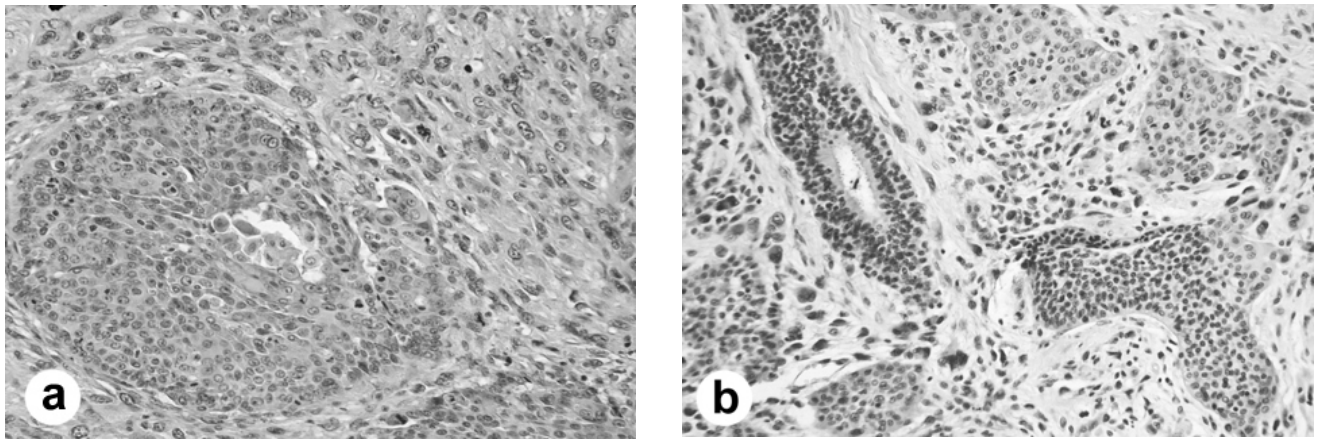

Fig. 2. Microscopic appearance of esophageal sarcomatoid carcinomas: (a) squamous cell carcinoma mixed with pleomorphic spindle-shaped cells exhibiting high mitotic activity (Case 1), and (b) squamous cell carcinoma with glandular differentiation intermingled with spindle-shaped and multinucleated giant cells (Case 2). HE. Magn. 200×.

TABLE 1
General pathological data on two esophageal sarcomatoid carcinomas

Feature	Case 1	Case 2
Gross pattern	polypoid	polypoid
Tumor size (cm)	7.0x4.0x3.0	2.5x2.0x1.5
pT†	pT2	pT2
pN†/components	pN1a/Sa	pN1b/Ca&Sa
pM†	M0	M0
Stage†	IIb	IIb
Resectability	R0	R0
Intramural metastasis/ location/components	(+) / esophagus / Sa	(-)
Intraepithelial spread	(+)	(+)

† – according to TNM classification [4]; Sa – sarcomatous component, Ca –carcinomatous component; R0 – complete resection

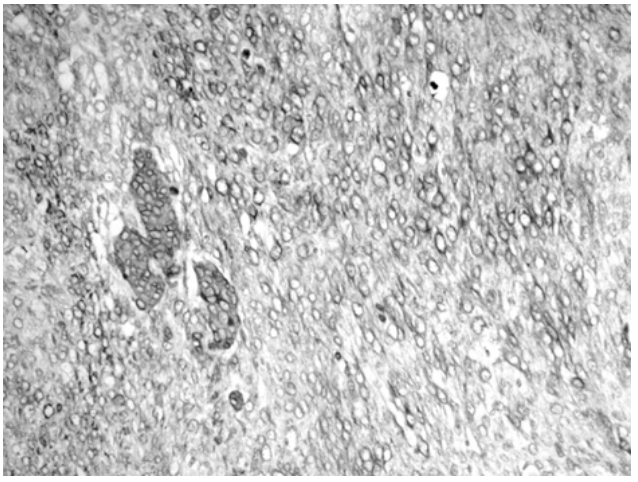

Fig. 3. Positive immunostaining for cytokeratin in both components of esophageal sarcomatoid carcinoma (Case 1). LSAB2/HRP, CK-AE1/AE3. Magn. 200×.

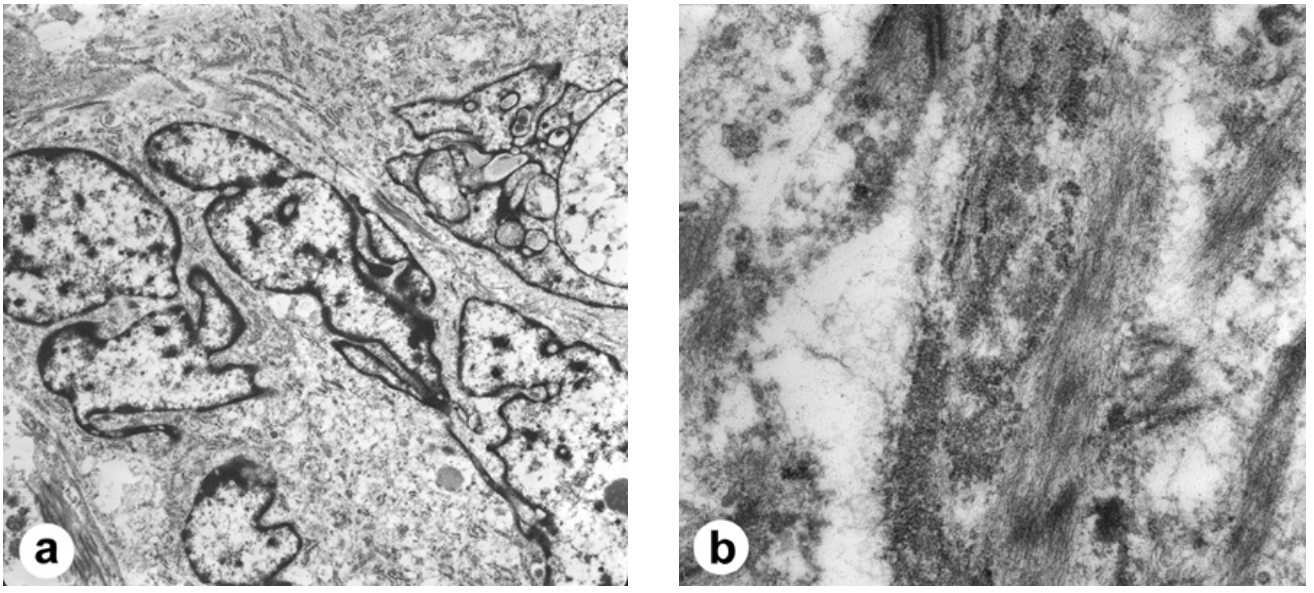

Fig. 4. Electron micrograph of the sarcomatous component (Case 2): (a) malignant spindle cells with multilobated nuclei, well-developed rough endoplasmic reticulum and tonofilaments (magn. 4,400 ×), and (b) cell containing both microfilaments with dense bodies (asterisk) and desmosome (arrowhead) (magn. 20,000 ×).

sults of our study seem to support the last concept. The presence of cells exhibiting two-directional differentiation (myofibroblastic and epithelial) in the sarcomatous component of one tumor and concordant positive pattern of p53 immunostaining in both components of tumors suggest a common origin of both components. Since, positive p53-immunoreactivity is not always associated with gene mutations, therefore only a molecular analysis of the gene status in both tumoral components can provide irrefutable evidence concerning their clonality.

Esophageal SCs occur usually in middle-aged and elderly men frequently with a history of smoking and/or alcohol abuse. They are mostly polypoid, and located in the middle and lower esophagus [2, 3, 5–10, 12, 14, 15]. The majority of tumors are single lesions; however the multiple primary ones have also been described [10]. Esophageal SCs are thought to be associated with better prognosis than typical squamous cell carcinomas, which probably is a consequence of relatively superficial infiltration as the frequency of nodal or distant metastases is similar [10]. The microscopic picture of esophageal SCs is complex. The carcinomatous component may exhibit distinct lines of differentiation i.e. squamous frequently with intraepithelial spread as well as glandular or neuroendocrine ones. In most cases, the sarcomatous component does not show any specific features, however the differentiation toward chondrosarcoma, osteosarcoma, and rhabdomyo-

sarcoma was also noted [2, 3, 6–10, 12, 14, 15]. Regardless of the heterogeneous histological pattern, SCs are characterized by similar clinical and behavioral features, and represent probably the same entity on the various directions and levels of differentiation [5].

The diagnosis of SCs may be difficult especially from biopsy samples or frozen sections due to inadequate quality and/or quantity of the specimens. The biopsy samples may contain necrotic debris or may be partly crashed at taking of the tissue. Furthermore, both biopsy specimens and frozen sections allow investigation of relatively small parts of the tumor. Therefore, in such heterogeneous tumors like SCs, in which proportions of carcinomatous and sarcomatous components vary considerably, one of the components could be overlooked at diagnosis. It should be mentioned that in cases presented here, the correct initial diagnosis was not possible for both reasons.

The differential diagnosis of esophageal SCs includes first of all pure sarcomas e.g. leiomyosarcoma as well as gastrointestinal stromal tumor (GIST), and malignant melanoma [8, 10, 13]. However, radiation-induced stromal atypia after therapy of conventional squamous cell carcinoma and extremely rare, esophageal pleomorphic giant cell carcinoma should be excluded [1, 11]. Invasion of the esophageal wall by pleomorphic neoplasms from adjacent organs e.g. lung has to be also taken under consideration. It should be stressed however, that careful searching for typical carcinomatous component is the basis for diagnosis, although immunohistochemistry and electron microscopy are also very helpful.

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Address for correspondence and reprint requests to:
Justyna Szumiło M.D.
Department of Clinical Pathomorphology
Prof. Feliks Skubiszewski Medical University of Lublin
Jaczewskiego 8, 20-950 Lublin
Phone/fax: (081) 747 57 17
E-mail: jszumilo@wp.pl