Sarcomatoid Carcinoma of Esophagus

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- Sarcomatoid carcinoma of the esophagus is an uncommon malignancy, representing approximately 2% of esophageal carcinomas. It has also been referred to as carcinosarcoma, pseudosarcoma, pseudosarcomatous squamous cell carcinoma, spindle cell carcinoma, and polypoid carcinoma, reflecting the uncertainty of its pathogenesis. Histologically, carcinosarcomatous and sarcomatous components coexist. The clinical and radiologic findings resemble other esophageal neoplasms. Sarcomatoid carcinoma often presents as a large, intraluminal, polypoid mass on barium esophagogram. Despite its size, however, sarcomatoid carcinoma has a more favorable prognosis than other malignant esophageal neoplasms, likely because of its exophytic growth into the lumen, rather than deep invasion. This article provides a brief overview of the clinicopathologic features and possible pathogenesis of this uncommon tumor. (Arch Pathol Lab Med. 2011;135:945–948)

Virchow first described sarcomatoid carcinoma of the esophagus in 1865, and today it represents approximately 2% of esophageal carcinomas. This tumor has also been referred to as carcinosarcoma, pseudosarcoma, spindle cell carcinoma, and polypoid carcinoma. The various terms in use reflect the uncertain pathogenesis of this tumor, which has a characteristic gross polypoid configuration. Histologically, sarcomatoid carcinomas of the esophagus are biphasic; the epithelial component is usually limited to a few areas, and the bulk of the tumor has a pleomorphic sarcomatoid appearance. The sarcomatoid component is generally considered to result from metaplasia of carcinoma cells. However, some investigators believe that 2 distinct malignancies coexist. Others have suggested that the sarcomatoid component is also of epithelial origin because, in some studies, the spindle cells have been shown to exhibit ultrastructural features of epithelial differentiation (desmosomes and tonofibrils). Immunohistochemically, the sarcomatoid cells may also be focally immunoreactive with cytokeratin, in addition to the epithelial component.

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CLINICAL FEATURES

Patients with this malignancy commonly present with progressive dysphagia, and sometimes with chest pain and weight loss. Duration of symptoms varies from days to months but is usually 3 months or less. Patients often present at an early stage because of the relatively large size and obstructive symptoms. Like other esophageal neoplasms, they are diagnosed with radiography or upper endoscopy. The lumen may be dilated, and the wall stretched. The characteristic radiographic finding is a bulky tumor expanding, but not obstructing, the lumen. Esophageal sarcomatoid carcinomas occur more commonly in men, typically, those aged 60 to 70 years. About 60% of tumors arise in the midesophagus, nearly one-third in the distal esophagus, and less than 10% in the proximal esophagus. A few reports of multiple tumors have been published.

PATHOLOGIC FEATURES

Gross Findings

Grossly, these tumors are polypoid masses that may reach a diameter of 15 cm. The surface may be smooth, intact, or ulcerated. The tumors are commonly attached to the wall by a pedicle, but occasionally, there is no pedicle, and the polypoid tumors are attached to the esophageal mucosa by a broad base. The surrounding mucosa is generally found grossly to be normal. The cut surface is typically white-gray, soft, and fleshy.

Microscopic Findings

Microscopically, these tumors are biphasic, containing a mixture of carcinoma and malignant sarcomatoid elements, with the latter generally forming the bulk of tumor (Figure, A). The epithelial component is usually squamous in nature and ranges from in situ or minimally invasive to infiltrating nests admixed with spindle cells. A few tumors with adenocarcinoma or undifferentiated carcinoma have also been described. The sarcomatous portion is typically composed of undifferentiated, spindle-shaped cells arranged in a fascicular or storiform pattern (Figure, B). These cells are embedded in an undifferentiated matrix that is edematous and contains scattered collagen fibers. Stromal differentiation has been reported with bizarre giant cells and with osseous and cartilaginous differentiation. Foci of rhabdomyoblastic differentiation have also been described.

Sarcomatoid carcinoma of the esophagus can also show heterogenous epithelial components, such as basaloid squamous cell carcinoma. In one report by Ohtaka et al, sarcomatoid carcinoma of the esophagus had squamous...
and basaloid carcinomas that were accompanied by a spindle cell proliferation. Amatya et al also reported an unusual case with a heterogenous carcinomatous component, including a basaloid squamous carcinoma as the major component and an invasive and in situ squamous cell carcinoma as a minor component, with the sarcomatous component showing rhabdomyoblastic differentiation. In that case, the basaloid squamous carcinoma was composed of monotonous cells with a high nuclear to cytoplasmic ratio, round hyperchromatic nuclei, and scant cytoplasm. These basaloid cells were arranged in lobules, nests, and cords. The stroma surrounding these tumor cells contained a basophilic mucoid matrix.

In some other reports, the sarcomatous elements were characterized by specific differentiation toward a true sarcoma, such as malignant histiocytoma, leiomyosarcoma, chondrosarcoma, osteosarcoma, or rhabdomyosarcoma. Kinoshita and coworkers reported a case of sarcomatoid esophageal carcinoma in which the sarcomatous component was composed of dense, interlacing bundles of spindle-shaped cells in the submucosa with transitional features between the 2 components. Later, autopsy

A. Areas of well-differentiated squamous cell carcinoma (upper right) admix with malignant spindle cell component. B. The bulk of the tumor consists of pleomorphic, bizarre spindle cells. C. The epithelial component is immunoreactive with cytokeratin AE1/AE3, whereas the sarcomatoid component is not immunoreactive. D. Strong and diffuse vimentin immunostaining in sarcomatoid component (hematoxylin–eosin, original magnifications ×100).
specimens from the lung, kidney, and iliac bone of that patient showed metastatic osteosarcoma composed of an interlacing pattern of bone and osteoid components. The authors concluded that the sarcomatous elements in the esophagus resulted from sarcomatous transformation of carcinoma cells, and the metastatic lesions showed differentiation of neoplastic cells to osteosarcoma.

**Special Stains and Immunohistochemistry**

Test results show the epithelial component of a sarcomatoid carcinoma is cytokeratin positive (Figure, C), whereas the mesenchymal element exhibits strong immunoreactivity with vimentin (Figure, D) and may occasionally exhibit immunoreactivity with cytokeratin, but when present, it is almost always focal and less intense.\(^{2,10-11}\) The sarcomatoid cells are occasionally immunoreactive with actin and desmin.\(^{12}\) The tumor cells in the transitional zone between the carcinomatous and sarcomatous elements may have the same immunoreactivity as the sarcomatous element.

A study was conducted by Wang and coworkers\(^{13}\) on the immunohistochemical pattern and histogenesis of these tumors. Out of the 20 cases of sarcomatoid carcinomas, they found positive immunoreactivity for cytokeratin AE1/AE3 in carcinomatous areas in all cases. Spindle cell findings in transitional areas were positive for cytokeratin in 9 cases and for vimentin in 5. Two cases demonstrated trace positivity to both cytokeratin and vimentin in the transitional areas. The sarcomatous component showed positivity for vimentin in 10 cases and for desmin in 2. Their findings strongly suggested that neoplastic epithelial cells may show dedifferentiation to transforming spindle cells and to nonepithelial sarcoma, like chondrosarcoma and leiomyosarcoma.

**Ultrastructural Features**

In the few studies where electron microscopy was used, some of the stromal cells had epithelial features, such as tonofilaments and intercellular junctions, similar to squamous epithelial cells. Other studies\(^{14}\) failed to identify ultrastructural features of epithelial differentiation but rather showed features of myofibroblasts or other mesenchymal cells. Ultrastructural examination reveals a transition zone between the carcinoma and the sarcoma at the border between these 2 components.\(^{15}\)

**GENETIC ANALYSIS**

There are no consistent or specific genetic alterations associated with sarcomatoid carcinoma of the esophagus; however, \(TP53\) mutation was analyzed by Amatya et al.\(^{7}\) In their study, they found that basaloid squamous carcinoma, squamous cell carcinoma, and sarcomatous components showed similar point mutations of \(TP53\). Their study concluded that the similar \(TP53\) mutation in the carcinomatous and sarcomatous components suggest these neoplasms are monoclonal. On the other hand, chromosomal analysis by Iwaya and coworkers\(^{11}\) revealed distinct genetic clonalities for each sarcomatous and carcinomatous element, suggesting that the 2 entities are clonally distinct. Suzuki et al.\(^{16}\) studied cyclin \(D1\) amplification using polymerase chain reaction. Out of their 4 cases, 3 (75%) showed amplification in the sarcomatous components, and 1 (25%) showed amplification in the carcinomatous component.

**PATHOGENESIS**

The various terminologies (sarcomatoid carcinoma, carcinosarcoma, pseudosarcoma, pseudosarcomatous squamous cell carcinoma, spindle cell carcinoma, and polypoid carcinoma) reflect the uncertain histogenesis of this tumor. Because of the combination of sarcoma and carcinoma, the debate has centered upon whether the 2 components are independent or the sarcomatous component is derived from metaplasia of the carcinomatous component. The latter idea is supported by some studies.\(^{17}\) The term *pseudosarcoma* was first used by Lane in 1957 to describe neoplasms of the upper digestive tract, which consisted of discrete epithelial and mesenchymal components.\(^{18}\) Lane suggested that the sarcomatous elements were a reactive, fibroblastic proliferation stimulated by the adjacent epithelial malignancy.

Two theories evolved to explain the development of sarcomatoid carcinoma. The "collision tumor" theory suggests that 2 distinct malignancies coexist and then collide and intermingle. The second theory suggests there is a reciprocal, neoplastic induction of the epithelial and stromal elements. A common criticism of both theories is that they do not explain the intermediate immunohistochemical and electron microscopic characteristics of some tumor cells.\(^{19}\) Amatya et al.\(^{7}\) reported a case of esophageal sarcomatoid carcinoma with predominant basaloid squamous carcinoma. In their study, similar \(TP53\) point mutations in squamous cell carcinoma, basaloid squamous carcinoma, and sarcoma suggest these components are clonal, thereby supporting a pluripotential stem cell theory. They also noted the histologically gradual transformation from squamous basal epithelium to basaloid squamous carcinoma as well as a gradual transition from basaloid squamous carcinoma to malignant spindle cells. The positive vimentin immunoreactivity in basaloid squamous carcinoma with an absence of immunoreactivity in squamous cell carcinoma also suggested that the basaloid squamous carcinoma underwent the transition to sarcoma.

Several immunohistochemical studies have found the sarcomatoid cells to be immunoreactive with cytokeratin, suggesting epithelial derivation, and earning the label of sarcomatoid carcinoma. However, other studies report the stromal component to exhibit only vimentin immunoreactivity and failed to exhibit cytokeratin immunoreactivity.

**DIFFERENTIAL DIAGNOSIS**

Because of the exophytic intraluminal growth pattern, the differential diagnosis includes other polypoid esophageal lesions, which include benign lesions, such as squamous papilloma and fibrovascular polyp, or malignant neoplasms, such as squamous cell carcinoma (especially the verrucous variant). Other entities in the differential diagnoses include malignant melanoma and pure sarcomas (such as malignant fibrous histiocytoma). The lack of malignant epithelial elements help in differentiating pure sarcomas from sarcomatoid carcinomas, but the epithelial component might not be sampled in the biopsy specimen. Rarely, biphasic malignant mesotheliomas may spread from the pleura to involve the esophagus, but these may be differentiated by the appropriate clinical history and by the distinctive immunophenotype of mesothelioma (cytokeratin, WT1, and calretinin immunopositivity).\(^{3}\)
TREATMENT AND PROGNOSIS

The prognosis of sarcomatoid carcinoma is much better than that of common squamous cell carcinoma because the sarcomatoid carcinoma tumors tend to grow into the lumen rather than into the wall. Despite their size, these tumors typically invade no deeper than the lamina propria or the submucosa. The depth of invasion determines the risk of metastasis and prognosis: 10% risk when the invasion is confined to the lamina propria, 25% for those reaching the submucosa and muscularis propria, and 75% for those reaching the adventitia.4 McCort29 concluded that carcinosarcoma had a more favorable prognosis than squamous cell carcinoma. His conclusions were based on the carcinomatous component of the tumor usually being at an early stage at the time of diagnosis, and thus, having a lower incidence of lymph node metastasis. In addition, sarcomatoid carcinomas do not invade early in their course and have a lower tendency to metastasize. Finally, because of their exophytic growth, sarcomatoid carcinomas become symptomatic early in the disease course compared with typical squamous cell carcinoma.

These lesions are usually treated surgically with esophagectomy. Early detection and treatment by surgical resection is fundamental to long-term survival. Chemoradiotherapy may be considered before resection for bulky tumors. The metastases may be carcinomatous, sarcomatoid, or mixed. Metastatic sites include the regional lymph nodes, followed by the lungs and pleura.

CONCLUSION

Sarcomatoid carcinoma is an uncommon tumor of the esophagus representing approximately 2% of esophageal malignancies. Despite its large size and cytologic atypia, a sarcomatoid carcinoma tends to have a good prognosis. Its origin and nature are still unclear. Its clinical and radiologic features overlap with those of other esophageal malignancies. Histologically, a biphasic pattern is the key diagnostic feature, but sometimes the carcinomatous element may not be obvious, especially in limited biopsies, and the tumor may be mistaken for a pure sarcoma.

References