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True carcinosarcoma of the larynx

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Abstract
A case of carcinosarcoma of the larynx and pyriform sinus with sarcomatous and epithelial malignant components is described in a 68-year-old male. The primary site was composed of spindle-shaped malignant mesenchymal cells with osteosarcomatous and chondrosarcomatous differentiation intermingled with areas of well differentiated squamous cell carcinoma, tubular and papillary adenocarcinoma, and trabecular neuroendocrine carcinoma. The metastatic lymph node showed squamous cell carcinoma and chondrosarcoma. Immunohistochemical studies showed that keratin was present in epithelial cells and negative in sarcoma, whereas vimentin and S-100 protein were present in sarcoma, but negative in carcinoma. Neuron-specific enolase was present in the neuroendocrine part of the tumour.

Introduction

Carcinosarcomas, tumours of mixed malignant mesenchymal and epithelial origin are very rare. They are known to occur in the uterus, bladder (Holtz *et al.*, 1972), breast (Wargotz and Norris, 1989), lung (Bergmann *et al.*, 1951; Berean *et al.*, 1988), cervix (Rotmensch *et al.*, 1983) and rarely in other sites. The larynx appears to be a highly unusual site, as only three cases having been described to date (Minckler *et al.*, 1970; Bat-

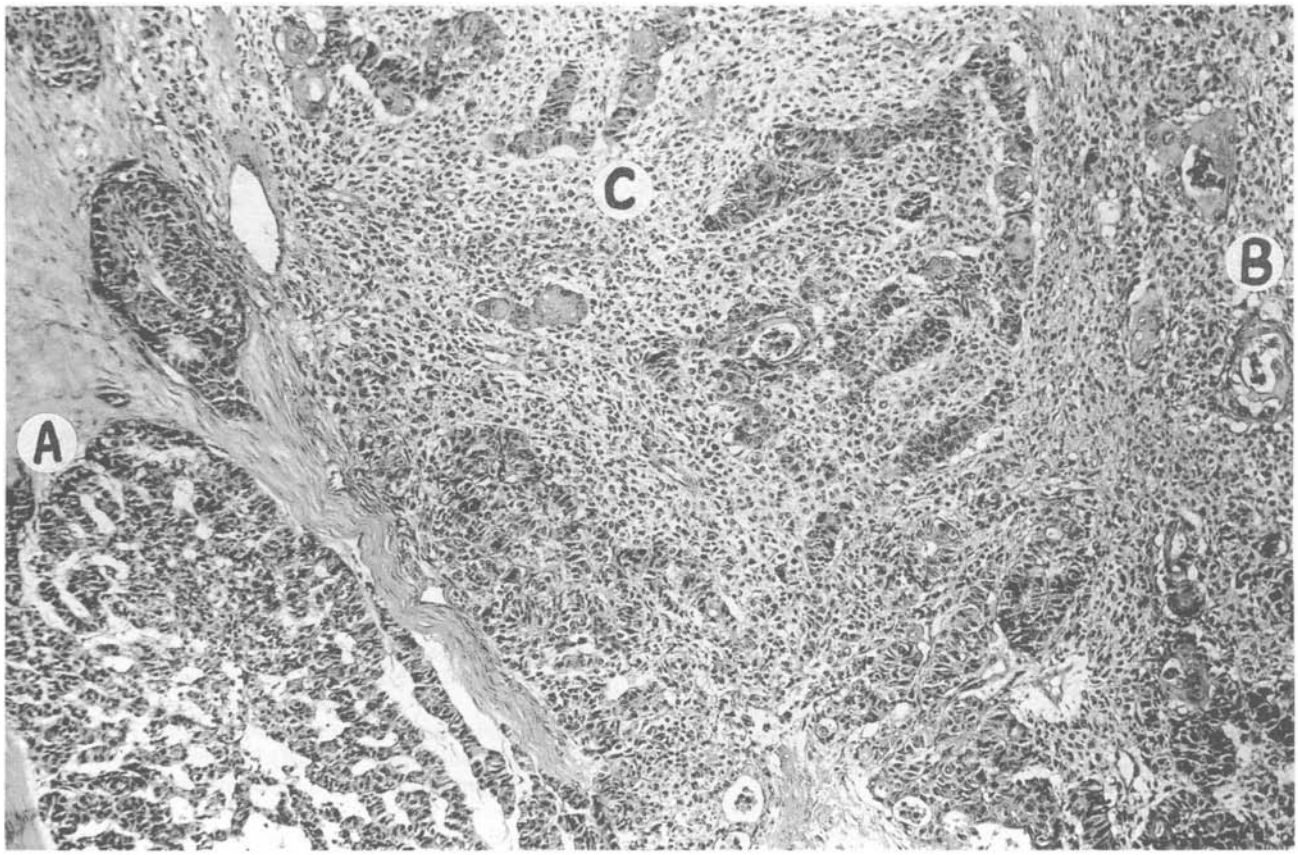

FIG. 1
Carcinosarcoma of the larynx. Adenocarcinomatous component of the tumour (A) adjacent to squamous cell carcinoma with keratin pearls (B) intermixed with spindle-shaped cell sarcoma (C). (Haematoxylin-eosin ×60).

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sakis, 1974; Srinivasan and Talvalkar, 1979). We report here another case of true carcinosarcoma of the larynx, showing squamous-cell, adenocarcinomatous, neuroendocrine, chondrosarcomatous and osteosarcomatous malignant components in the primary site, and squamous cell and chondrosarcomatous differentiation in the metastatic lymph-node.

Case report

A 68-year-old white male with a long history of heavy smoking, was admitted to the Institut Gustave-Roussy in January 1974 for evaluation of a tumour situated in the right epiglottis and right pyriform sinus. Physical examination performed at admission only revealed a firm homolateral (3 × 6 cm) cervical lymph node (T_3 N_3 M_0) (Hermanek and Sobin, 1988). The biopsy of the primary showed well differentiated squamous cell carcinoma. The patient was irradiated (30Gy) and total pharyngolaryngectomy and right cervical lymph-node node resection followed by irradiation (25 Gy) were performed. The resection margins were judged to be free of tumour. The cut surface of surgical specimen revealed a 3 × 4.5 × 3.5 cm multichromatic and partially necrotic tumour involving the right epiglottis, pharyngo-laryngeal wall and right pyriform sinus.

The patient was lost to follow-up 16 months later with no evidence of disease.

Histological features

Multiple sections of the total pharyngolaryngectomy specimen were reviewed. The pyriform fossa mucosa and lateral epiglottis showed multifocal *in situ* and invasive squamous cell carcinoma. It merged and blended into areas of tubulo-papillary adenocarcinoma, and areas of high-grade malignant spindle-cell sarcoma with foci of chondro- and osteoformation (Fig. 1). The cytoplasm of the mesenchymal cells was abundant and slightly eosinophilic. Some multinucleated and pleomorphic giant cells were present in rare sites.

The metastatic lymph node showed foci of chondrosarcoma and typical squamous cell carcinoma (Fig. 2). Peroxidase-anti-peroxidase methods demonstrated the presence of vimentin and S-100 protein in the cytoplasm of sarcomatous cells, whereas keratin was present in squamous cell carcinoma, adenocarcinoma and neuroendocrine carcinoma; neuron-specific enolase was present in trabecular neuroendocrine carcinoma, and desmin was always negative. The adenocarcinomatous component of the tumour showed Alcian-blue positive intracellular vacuoles.

Discussion

Carcinosarcoma is a malignant tumour with both malignant epithelial and mesenchymal components. To prove the existence of such lesions, it is necessary to demonstrate that both components are able to metastasize.

Primary sarcoma represent 0.3–1 per cent of all laryngeal malignancies (Barnes, 1985). Most of them occur spontaneously, but some are radiation-induced (Donaldson, 1978). Chondrosarcoma is by far the most common sarcoma of the larynx, accounting for 48 per cent of all cases (Barnes, 1985). However, one example of malignant mesenchymoma has been reported in the larynx (Tobey *et al.*, 1979). This tumour was thought to be a liposarcoma on light microscopy, but ultrastructurally, it was composed of a variety cells which were also compatible with fibroblasts, skeletal and smooth muscle cells. Nevertheless, true carcinosarcomas may occur in the larynx. Batsakis (1974) mentions one case of true carcinosarcoma with a mixture of rhabdomyosarcoma and squamous cell carcinoma. Another authentic case has been reported by Minckler *et al.* (1970). They described a lesion which metastasized both as carcinoma and as sarcoma and resulted in the death of the

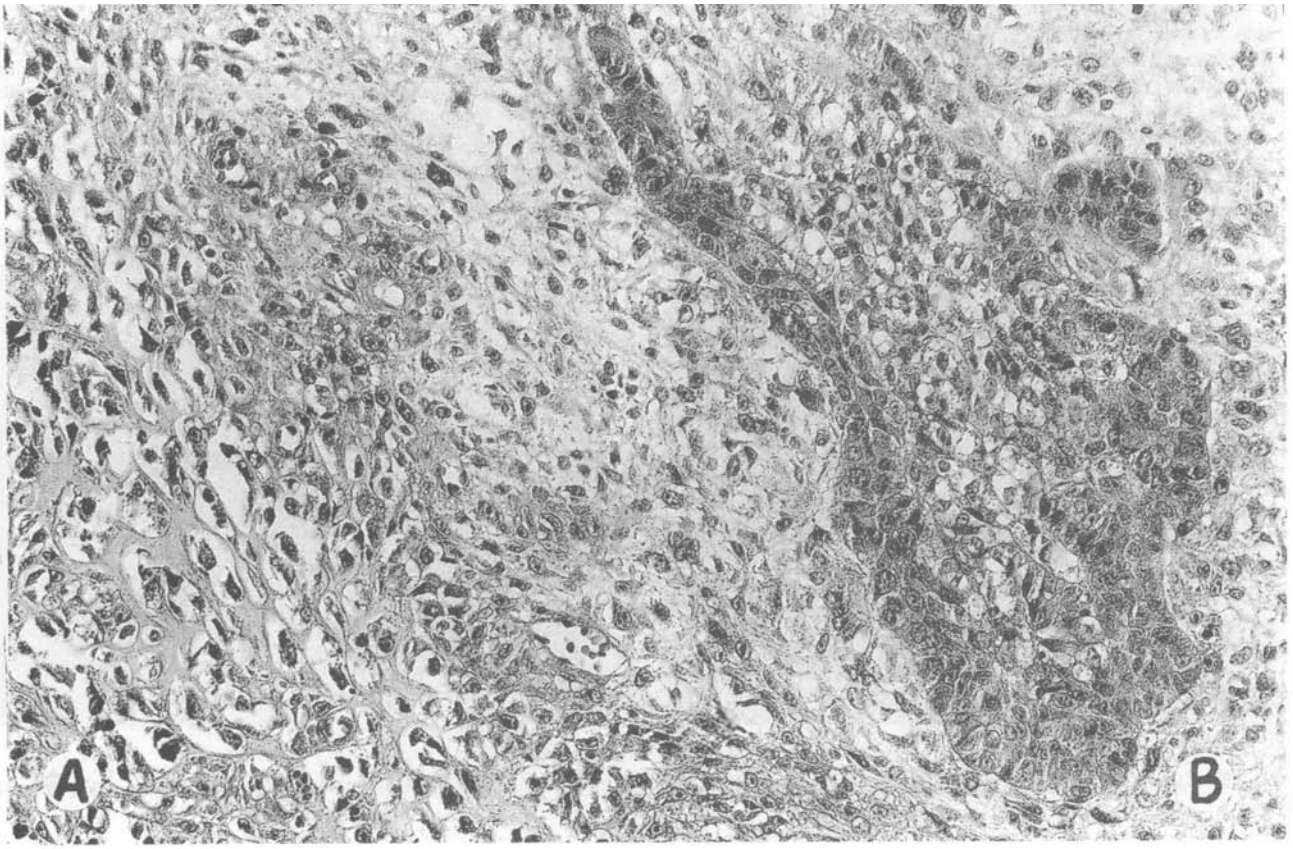

FIG. 2

Carcinosarcoma. Metastatic lymph node. Chondrosarcoma (A) adjacent to irregular thin cord of squamous cell carcinoma (B). (Haematoxylin-eosin ×250).

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patient 15 months after recession. The third and last case of true carcinosarcoma is that reported by Srinivasan and Talvalkan (1979) of a tumour composed of well differentiated squamous cell carcinoma and rhabdomyosarcoma. On the other hand, many 'carcinosarcomas' of different sites have been consistently reported in the literature (Hutter *et al.*, 1966; Zarbo *et al.*, 1986), but their sarcomatous component has never been conclusively studied by immunohistochemistry. These reports described carcinosarcomas of the larynx which metastasized as sarcoma, but the sarcomatous component always seemed to be compatible with dedifferentiated spindle-shaped carcinomatous elements (Zarbo *et al.*, 1986). Spindle-shaped carcinoma should be differentiated from true carcinosarcoma, in which mesenchymal and stromal elements show typical features of malignancy. Features in favour of sarcoma include sharp demarcation from the obvious epithelial elements and immunohistochemical reactivity for mesenchymal antigens. However, it must be emphasized, that intermediate filaments are not perfectly reliable markers for this distinction, because occasional typical carcinomas may stain for vimentin and S-100 protein (Weidner, 1987). In our case, the spindle-shaped elements showed typical features of malignancy with characteristic high mitotic index and nuclear pleomorphism, whereas spindle-shaped squamous cell carcinomas may produce bone or cartilage without atypia. In head and neck pathology, recent immunohistochemical and electron microscopic (Hyams *et al.*, 1988) investigations have supported the opinion that spindle-shaped cells represent an anaplastic dedifferentiation of epithelial squamous cells. The rare findings of benign osseous or cartilaginous tissue is a product of simple, direct stromal metaplasia of the fibroblasts. In the AFIP Atlas of Tumors of the Upper Respiratory Tract (Hyams *et al.*, 1988), reference is made to the fact that only carcinomatous elements of laryngeal 'carcinosarcoma' metastasize. In our opinion, this term of 'carcinosarcoma' is inappropriate to describe all spindle-shaped cell tumours intermingled with carcinoma.

The histogenesis of true carcinosarcoma is not clear. It seems that a primitive blastic mesenchymal cell may mature and produce tumours of multiple differentiation. Currently, the most popular theory is that the pleomorphic spindle-shaped cell is derived from sarcomatous dedifferentiation of the malignant epithelial cell (Zarbo *et al.*, 1986). The simultaneous development (collision tumours) of epithelial and stromal malignancies seems less likely than differentiation of a primitive totipotent cell into two or more divergent pathways.

In order to correctly establish the diagnosis of carcinosarcoma, the histology must reveal carcinoma (glandular or squamous) together with sarcoma (rhabdomyo-, osteo-, chondro-/or fibrosarcoma) both in the primary and the secondary site. Histological grade, mitotic index and the type of sarcomatous tumour composition have not been studied as prognostic factors in laryngeal carcinosarcomas. We therefore believe that the term carcinosarcoma appropriately describes tumours showing both carcinomatous and sarcomatous differentiation, especially when malignant bone, cartilage and skeletal muscle cells are demonstrated. The cases of sarcomatoid squamous cell carcinoma have a different histogenesis and should not be confused with carcinosarcoma.

Key words: Laryngeal neoplasms; Carcinosarcoma

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