Basaloid Squamous Cell Carcinoma of the Larynx: Report of Two Cases
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Aim. To present two patients with basaloid squamous cell carcinoma of the larynx, a rare, highly aggressive variant of the squamous cell carcinoma.

Methods. Surgical excision of the polypoid tumor of the anterior comissure of the larynx was performed in a 62 year-old male, and in the second case, total laryngectomy with radical dissection of the neck was performed in a 66 year-old male with supraglottic tumor of the larynx and enlarged lymph nodes of the neck. Histopathological analysis of biopsy specimens was performed on routine hematoxylin-eosin stained sections and on sections stained with antibodies to cytokeratin, epithelial membrane antigen, S-100 protein, neuron-specific enolase, and chromogranin.

Results. In both cases, the tumors were composed of moderately pleomorphic basaloid cells forming nests, cords, and cribriform patterns with foci of necrosis, squamous differentiation, and small cystic spaces containing mucin-like material. Surface mucosa showed squamous dysplasia. Cytokeratin and epithelial membrane antigen were positive. After surgery, both patients received radiotherapy and had no signs of tumor recurrence or metastases 12 and 15 months later, respectively.

Conclusion. Basaloid squamous cell carcinoma has a potential for diagnostic confusion because of its basaloid and squamous component. It should be distinguished from adenoid cystic carcinoma that is much less aggressive.

Key words: carcinoma, basal cell; carcinoma, baseosquamous; carcinoma, squamous cell; larynx

Basaloid squamous cell carcinoma is a histologically distinctive, rare, highly aggressive variant of squamous cell carcinoma (1,2). It shows predominantly basaloid pattern intimately associated with squamous cell carcinoma, dysplasia or focal squamous differentiation (1,3). The tumor mainly affects men in the sixth and seventh decades of life and usually presents as high stage disease with widespread metastases. It arises in a variety of anatomic sites, most frequently in the upper aerodigestive tract with strong predilection for the base of the tongue, supraglottic larynx and hypopharynx, but is also found in the anus, thymus and uterine cervix (4-6). Less than 30 cases related to the larynx have so far been reported (1-3,6-8). We report two cases of basaloid squamous cell carcinoma, both located in the larynx, presented as stage I and stage IV disease.

Case Reports
Case One
A 62 year-old man presented with hoarseness that lasted for two months. He had a long history of cigarette and alcohol abuse. Due to colorectal carcinoma he underwent surgery 5 years before. Clinical examination revealed polypoid tumor of the anterior comissure, extending to the laryngeal side of the epiglottis, 1 cm in the greatest diameter, with preserved vocal cords mobility. Ultrasound examination of the neck was unremarkable. Only excision of the tumor was performed.

Case Two
A 66 year-old male complained of hoarseness, dysphagia, and dyspnea for the last three months. He also had a long history of cigarette and alcohol abuse. Clinical examination and computerized tomography revealed a supraglottic tumor of the larynx extending to the epiglottis, and enlarged lymph nodes of the neck. A total laryngectomy with radical dissection of the neck was performed. The surgical specimen was a partially ulcerated tumor of the larynx and epiglottis, 4 cm in the greatest diameter, infiltrating underlying cartilage and with no extension to the vocal cords.

Figure 1: Basaloid squamous cell carcinoma of the larynx in Case 1 (H-E, x40). [view this figure]
Figure 2: Basaloid squamous cell carcinoma with peripheral palisading and central comedo-type necrosis in Case 1 (H-E, x100). [view this figure]

Pathohistological Findings
In both cases, the microscopic examination showed tumors predominantly composed of moderately...
pleomorphic basaloid cells forming nests, cords, and cribriform patterns with nuclear palisading at the periphery (Figs. 1 and 2). Foci of comedo-type necrosis and squamous differentiation, stromal hyalinezation, as well as small cystic spaces containing mucin-like material, were also observed. The major part of the tumors was covered with intact mucosa that focally showed squamous dysplasia. Nine out of 21 lymph nodes taken out during the neck dissection in the case 2 were positive for metastatic carcinoma. Metastases manifested both basaloid and squamous components. Immunohistochemistry showed positive reaction for cytokeratin and epithelial membrane antigen, while S-100 protein, neuron-specific enolase, and chromogranin reactions were negative in both cases.

Following surgery, both patients were treated by radiotherapy (the first patient received 62 Gy and the second 64 Gy). Twelve and 15 months after the diagnosis, respectively, the patients showed no signs of the disease.

Discussion
Basaloid squamous cell carcinoma is a newly recognized entity first described by Wain et al (1) who presented a series of ten cases. Basaloid squamous cell carcinoma is a rare variant of the squamous carcinoma.

Histologically, basaloid squamous cell carcinoma is defined by basaloid component, including moderately pleomorphic basaloid cells with hypercromatic nuclei and scant cytoplasm (although increased amount of cytoplasm and vesicular nuclei and scattered nucleoli may be present), that form cords and nests with nuclear palisading at the periphery. Comedo-type necrosis, cribriform pattern, and small cystic spaces containing mucin-like material are frequently present. Stromal hyalinezation is usually prominent. Mitotic figures, including atypical forms, are often numerous (1,2).

The second major characteristic of the basaloid squamous cell carcinoma is the presence of squamous component that includes at least one of following features: adjacent foci of conventional squamous cell carcinoma, dysplasia or carcinoma in situ of the overlying mucosa, or focal squamous differentiation within basaloid component. Focal squamous differentiation is recognized by abundant eosinophilic cytoplasm of cells arranged in pavementing or mosaic pattern, by intercellular bridging, individual cell keratinization or collections of keratinized cells within the nests of basaloid cells. Some squamous clusters may form keratin pearls. The junction between the squamous cells and the adjacent basaloid cells is often abrupt with no or little transition (1,2).

In many cases, the tumor appeared to arise from the surface epithelium, while in others mucosal ulceration obscured the connection with the surface epithelium (2,3). Metastases may manifest both components or only one of the components, regardless of the predominant component of the primary tumor (7).

Although histologically distinctive, basaloid squamous cell carcinoma has a potential for diagnostic confusion due to its basaloid and squamous components. Because of the differences in the clinical behavior, this tumor should be distinguished from the solid adenoid cystic carcinoma, neuroendocrine carcinoma, adenosquamous carcinoma, mucoepidermoid carcinoma, and conventional squamous cell carcinoma (1-3). The presence of both components differentiates this carcinoma from the solid adenoid cystic carcinoma, high-grade mucoepidermoid carcinoma, and neuroendocrine carcinoma. Furthermore, stromal hyalinezation is not a feature of conventional squamous cell carcinoma and the absence of involvement of ducts and acini of mucous glands distinguishes basaloid squamous cell carcinoma from the adenosquamous carcinoma.

Basaloid squamous cell carcinoma can be diagnosed on routine hematoxylin and eosin-stained sections, or in rare cases, with the aid of immuno-histochemical methods (2,7). Immunohistochemical studies performed by Banks et al (2) and Tsang et al (7) showed cytokeratin positivity in the areas with squamous differentiation. Carcinoembyronic antigen was positive in approximately half of the studied cases, and was observed in the cells with squamous differentiation. Epithelial membrane antigen was positive in more than two thirds of the cases. S-100 protein was positive in less than 30%. Basaloid squamous cell carcinoma lacked immuno-reactivity for chromogranin, synaptophysin, muscle-specific actin, and glial fibrillary acidic protein. Immuno-histochemical findings in our two cases confirm the previously reported observations.

As can be seen from the previous case reports, basaloid squamous cell carcinoma presents as high-stage disease with frequent local and widespread metastases. Most of the patients were male in the sixth or seventh decades of life. Tobacco and alcohol abuse appear to be strong risk factors for the development of basaloid squamous cell carcinoma (1-3,6). Both of our patients had a long history of smoking and alcohol abuse. Our first patient with basaloid squamous cell carcinoma presented with a stage I disease, probably due to the glottic location of tumor that produced early symptoms. Only a few patients with stage I or II of basaloid squamous cell carcinoma were reported, whereas the majority presented as stage III or IV (1-3), as was observed in our second patient. Although the
supraglottic location of the tumor is common, there are no reports on basaloid squamous cell carcinoma related to the glottic region of the larynx.

A few reported cases of basaloid squamous cell carcinoma were associated with synchronous carcinomas of the upper gastrointestinal tract or larynx, and a few patients had a history of previous primary malignancies, including chronic lymphocytic leukemia and adenocarcinomas of the prostate gland and colon (1-3,6-8). The first patient had an adenocarcinoma of the colon five years before the initial presentation.

Basaloid squamous cell carcinoma is considered to be a poorly differentiated variant of the squamous carcinoma and thus more aggressive and with a lower survival rate than the conventional squamous cell carcinoma (1,2,7). However, in some reports, when the anatomic site, treatment, and clinical stage were matched, survival and the incidence of cervical lymph node metastases were parallel with those of conventional squamous cell carcinoma (3). Additional cases of basaloid squamous cell carcinoma should be reported and careful follow-up is required to confirm these observations.

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References

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