CASE REPORT

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NODULAR HIDRADENOCARCINOMA OVER THE PAROTID GLAND: A PATHOLOGIC PRESENTATION

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Abstract: Background. Nodular hidradenocarcinoma (NHAC), an eccrine carcinoma, has been reported in the dermatology and pathology literature, but few references have been made in the otolaryngology literature even though the head and neck is a common site of occurrence.

Methods. A case report of a 37-year-old Hispanic man with a right-sided neck mass diagnosed preoperatively as a parotid mass by imaging and fine-needle aspiration is presented. After presentation at our multidisciplinary tumor board, excision of the mass was undertaken.

Results. Final pathology revealed a NHAC, which is presented in our report.

Conclusion. NHAC is an aggressive malignant tumor that is often misdiagnosed preoperatively and that must be treated with aggressive multimodality therapy for increased survival.

Keywords: nodular hidradenocarcinoma; eccrine tumor; malignant skin tumor; skin cancer

Nodular hidradenocarcinoma (NHAC) is a malignant cell eccrine tumor, often with clear cell morphology, which has been reported less than 60 times in the literature. It has been rarely reported in the otolaryngology literature, though the head and neck is a common site of occurrence. The tumor has been identified in the literature under many names including clear-cell hidradenocarcinoma, malignant clear-cell hidradenoma, solid-cystic adenocarcinoma, malignant acrosiroma, malignant clear-cell myoepithelioma, and clear-cell eccrine carcinoma.1 NHAC tumors usually develop as malignant tumors, though there have been reports of malignant degeneration of the benign counterpart, hidradenomas.2 We present the case of a patient with what was believed to be a parotid neoplasm by preoperative clinical examination that turned out to be a hidradenocarcinoma.

CASE REPORT

A 37-year-old otherwise healthy Hispanic man presented to our tertiary care hospital complaining of a painless right neck mass that the patient said had been present for approximately 3 months. On physical examination the patient had a 4 cm × 2 cm right parotid mass that appeared to be connected to the skin though there were no skin changes. Facial nerve function was House Brackmann I/VI bilaterally. The patient was sent for fine-needle aspiration of the neck mass, which showed cellular clusters and sheets of monomorphic epithelial cells with low nuclear:cytoplasmic ratio. The mass was removed surgically and final pathology showed a NHAC.
ratio, round to oval bland nuclei with fine chromatin and small indistinct nucleoli (see Figure 1). The cytoplasm ranged from finely granular and eosinophilic to clear. Focal basement membrane-like deposits were noted. The rendered diagnosis was low-grade salivary neoplasm with a wide differential diagnosis including monomorphic adenoma, pleomorphic adenoma, polymorphous low-grade neoplasm, and adenoid cystic carcinoma. CT scan of the neck showed a 3.3 cm × 2.1 cm × 4.0 cm heterogeneously enhancing mass in the right parotid gland without associated cervical lymphadenopathy (Figure 2A). MRI of the neck showed a 3.8 cm × 2.2 cm mass within the superficial lobe of the parotid gland. The mass showed heterogeneity on the T2-weighted and post-contrast enhanced images (Figure 2B). After presentation to our multimodality head and neck tumor board, the patient was taken to the operating room for a planned superficial parotidectomy with facial nerve preservation and skin excision. Intraoperatively the lesion was seen splaying the upper and lower divisions of the facial nerve and extending to but not invading the mandible (see Figure 3). Initial frozen section diagnosis was consistent with neoplasm. Because of concern for possible high-grade neoplasm, a right neck level I-IV dissection was performed. Final pathology showed a malignant NHAC with a positive deep margin but no lymph node involvement. Gross examination revealed a well-circumscribed solid mass measuring 4.3 cm in greatest dimension with a prominent multinodular solid growth pattern with focal small cystic areas. Microscopic findings demonstrated solid nodular proliferation of rather uniform round to ovoid polygonal epithelial cells with distinct cell borders and scant to moderate clear to eosinophilic cytoplasm (see Figure 4). The nuclei were round or spindled with slightly irregular membranes, mild hyperchromasia, and small indistinct nucleoli. No increased mitotic activity or necrosis was noted. At the periphery of some nodules, a peculiar nuclear palisading was noted.
The interstitial space between tumor nodules consisted of hyalinized fibrous tissue with hemosiderin deposits and focal myxoid degeneration. Despite the pushing gross appearance of the tumor border, the latter displayed at least focally a definitive infiltrative growth pattern with destructive invasion of the adjacent deep soft tissue associated with desmoplasia. Focal primitive ductules associated with squamoid differentiation (cuticles) were seen, in keeping with the eccrine nature. Despite extensive sampling, there was no angiolymphatic or perineural invasion by the tumor.

No basaloid, sebaceous, or trichilemmal differentiation are noted. A periodic acid-Schiff (PAS) stain demonstrated high glycogen contents of the clear cytoplasm (Figure 4F). No PAS diastase-resistant reactivity was noted.

The patient was represented to our multidisciplinary tumor board with recommendation for postoperative radiation. Thirteen months postoperatively the patient is without evidence of recurrence.

**DISCUSSION**

NHAC was first reported in the literature as a clear cell eccrine carcinoma by Keasby and Hadley in 1954. Malignant eccrine tumors appear in 1:13,000 dermatopathology biopsies, and NHAC accounts for approximately 6% of these tumors. Malignant sweat gland tumors occur on average...
in the sixth decade of life with an equal male:female distribution. Approximately 1/3 of both malignant and benign primary sweat gland tumors arise in the head and neck. They most often present as asymptomatic solitary intradermal masses or nodules measuring 1 to 5 cm with or without central ulceration that slowly grow over the course of a year. Diagnosis is very difficult, and often the preoperative diagnosis is incorrect, as in our patient. In a review of 35 cases of eccrine adenocarcinoma, Mehregan et al showed that none were diagnosed correctly preoperatively, and specifically, the 2 cases of NHAC were misdiagnosed.

The histologic features of hidradenocarcinoma characteristically entail a prominent nodular (lobular) pattern similar to that noted in its benign counterpart. Although the cytology is typically that of a low-grade neoplasm, the tumor may display increased mitotic activity with focal areas of necrosis. While these features help distinguishing malignant from benign nodular hidradenoma, the infiltrative borders, presence of perineural or vascular invasion, and documented lymph node metastases remain the most reliable criteria for establishing malignancy.

The neoplastic cells in NHAC are usually positive for PAS but negative for PASD (PAS with diastase digestion), indicating glycogen content rather than mucin. Immunophenotypically, NHAC shows reactivity for cytokeratin (AE1/AE3, CAM 5.2, CK5/6, etc.). They are usually positive for EMA, CEA, and S100 protein. They are characteristically negative for androgen receptor and myoepithelial markers (SMA, calponin, etc.).

The histopathologic differential diagnosis of hidradenocarcinoma generally includes other tumors with clear cell change such as sebaceous carcinoma, trichilemmal carcinoma, clear cell changes in squamous cell carcinoma, balloon cell melanoma, basal cell carcinoma, porocarcinoma, and metastatic renal cell clear cell carcinoma. In addition, given the presentation of the current case, salivary gland neoplasms, particularly, low-grade epithelial tumors with clear and oncocytic differentiation such as mucoepidermoid carcinoma, acinic cell carcinoma, epithelial myoepithelial carcinoma, hyalinizing clear cell carcinoma (HCCC), and oncocytoma should be included in the differential diagnosis.

Sebaceous cell carcinoma and trichilemmal carcinoma, which may have the most overlapping features with NHAC, both lack true cuticles and show at least focally microvesicular cytoplasm and indented nuclei in sebaceous cell carcinoma and trichilemmal-type keratinization in trichilemmal carcinoma. Furthermore, the majority of sebaceous cell carcinoma shows immunoreactivity for androgen receptor markers, which are not expressed in NHAC.

Basal cell carcinoma, clear cell changes in squamous cell carcinoma, and porocarcinoma generally have an intraepidermal component, and they also lack cuticular differentiation. Balloon cell melanoma does not demonstrate squamous or cuticular differentiation, and the tumor cells are always cytokeratin negative and usually S100 and HMB45 positive. While metastatic renal cell carcinoma to the skin may be nodular and composed of clear and eosinophilic epithelial cells, the presence of rich sinusoidal vascular network and often the existing history of primary renal neoplasm should help in establishing the correct diagnosis.

The histopathologic differentiation of NHAC from primary salivary gland neoplasms is usually not difficult, probably with the exception of low-grade mucoepidermoid carcinoma with predominant clear cells. The presence of neutral mucin (as demonstrated by mucicarmine and PAS with diastase) in the neoplastic cells is particularly helpful in this regard. Acinic cell carcinoma may show clear and oncocytic cell change. The tumor cells are typically PASD positive and show immunoreactivity for alpha anti-chemotrypsin. Oncocytoma and epithelial myoepithelial carcinoma are characterized by the presence of anti-mitochondria and calponin (myoepithelial) immunoreactivity, respectively. Finally, HCCC is typically a tumor of minor salivary glands and rarely affects the parotid gland. Also, in contrast to NHAC, the neoplastic cells in HCCC are negative for S100 protein, EMA, and CEA.

The preoperative cytologic diagnosis of malignant or even benign clear cell hidradenoma is very difficult due to the wide differential diagnosis of low-grade epithelial neoplasms with clear cell features. Such diagnosis is even more difficult in the parotid region due to the presence of many low-grade tumors of salivary gland origin with clear cell differentiation, such as clear cell oncocytoma, hyalinized clear cell carcinoma, mucoepidermoid carcinoma, epithelial-myoepithelial carcinoma, and acinic cell carcinoma with clear cell features. In a limited cytologic sample, most low-grade salivary gland tumors enter the differential diagnosis (polymorphous low-grade adenocarcinoma, pleomorphic adenoma, and adenoid cystic carcinoma).
Most of these neoplasms may show foci of squamous, clear, and oncocytic differentiation.

In our case, the preoperative FNA demonstrated a basal lamina-like material, suggesting the diagnosis of adenoid cystic carcinoma or other matrix-forming salivary gland neoplasms (such as pleomorphic adenoma). On the other hand, no definitive cuticle-like formations were noted, thus, making the appropriate diagnosis of primary eccrine neoplasm rather elusive.

In essence, due to the rarity of hidradenocarcinoma, such diagnosis can be only made on surgical excisional specimens. Features that may help in discerning eccrine nature in cytologic material includes the presence of cuticle-like formations, the complete lack of acinar cells, and the lack of myoepithelial cells (especially plasmacytoid and spindle types), noting that all of these features are not definitive nor pathognomonic for eccrine neoplasms. Furthermore, even when an eccrine neoplasm is cytologically suspected, malignancy can only be determined in the excisional specimen as earlier illustrated.

Prognosis for hidradenocarcinoma is generally poor. The tumor has up to a 50% local recurrence rate and a 60% metastatic rate within the first 2 years. Metastases favor the regional lymph nodes followed by the lung and bone. Disease-free 5-year survival has been reported at less than 30%.

Most authors support wide local excision as the treatment of choice. The need for lymph node dissection has not been definitively determined owing to the rarity of the tumor, though several authors have advocated lymphadenectomy based on the high rate of lymphatic invasion.

The role of radiation therapy in the treatment of these tumors was addressed by Harari et al in 1990 in an article on the role of radiotherapy in the treatment of malignant sweat gland neoplasms. They reported on 3 patients undergoing postoperative radiation therapy for NHAC. Two of the patients had positive surgical margins but no evidence of metastasis and were disease free 27 and 35 months postoperatively. The third patient was treated after cervical metastatic disease had occurred and died of disease 3 weeks after radiation therapy.

In conclusion, NHAC is an aggressive malignant tumor that is often misdiagnosed preoperatively and that must be treated with aggressive multimodality therapy for increased survival.

REFERENCES