CASE STUDY

Lymphoepithelial Carcinoma: A Case of a Rare Parotid Gland Tumor

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Abstract

A 29-year-old woman presented from another hospital with a 10-month history of an enlarging left-sided facial mass. Computed tomographic scan revealed a mass in the superficial lobe of the left parotid gland with left-sided cervical lymphadenopathy. The patient received a total left parotidectomy and a selective neck dissection. Histopathologic slides revealed lymphoepithelial carcinoma (LEC) that stained positive for cytokeratin, as well as Epstein-Barr virus (EBV). An LEC of the parotid is a rare salivary gland tumor accounting for less than 1% of all salivary gland tumors. As reaffirmed in our case, LEC is more common in women, occurs primarily in the parotid gland, and has an ethnic predilection. Histologic analysis reveals an infiltrative, poorly differentiated tumor nestled in a lymphoid stroma, with near 100% positivity for EBV in endemic areas. Complete resection of this poorly differentiated carcinoma followed by postoperative radiation is essential for local control.

Case Report

A 29-year-old woman referred from an outside hospital presented to our clinic with a 10-month history of an enlarging left-sided facial mass. At that time, the patient had no pain, and her facial nerve was intact, with House-Brackmann grade I. Fine-needle aspiration (FNA) biopsy was done at the referring facility and showed cells suggestive of a poorly differentiated neoplasm with spindle cell and epithelioid features. However, additional biopsy material was needed for a definitive classification. A computed tomographic (CT) scan obtained at that time showed a 4.1 × 2.9 × 3.7-cm mass in the superficial lobe of the left parotid gland with left-sided cervical lymphadenopathy (Figures 1 and 2).

The patient was seen at our facility 9 days after the initial FNA and CT scan were performed. Because pathologic results may have altered surgical planning, a core needle biopsy was completed to rule out lymphoma. Core needle biopsy revealed tumor cells that stained negative for CD20, C3, CD45, synaptophysin, and CD30, and confirmed the FNA results of a poorly differentiated carcinoma.

Six days after the core needle biopsy, the patient received a total left parotidectomy and a selective neck dissection involving the level 2 nodes only. A complete neck dissection was not performed because results of a frozen section of level 2 nodes were negative for carcinoma. A specimen was sent for pathologic analysis and revealed an intraparotid lymph node adjacent to the mass with a lymphoplasmacytic cell infiltrate surrounding nests of tumor cells. An adjacent lymph node appeared reactive with a “starry sky” pattern (Figure 3). A brown cytokeratin stain (CK 5/7), an immunoperoxidase stain, revealed cells staining positive for cytokeratin in the mass as well as in an intraparotid lymph node (Figure 4). All other lymph nodes had negative test results. Epstein-Barr encoded RNA (EBER) stain showed Epstein-Barr virus (EBV) positivity in the mass as well as in an intraparotid lymph node (Figure 5). A high-power view of the specimen demonstrated classic lymphoplasmacytic cell infiltrate among nests of poorly differentiated cells (Figure 6).

The diagnosis was lymphoepithelial carcinoma (LEC).

Figure 1. Computed tomography scan reveals a left-sided parotid mass in the coronal plane. White circle marks the site of the tumor.

Figure 2. Computed tomography scan reveals a left-sided parotid mass in the axial plane. White circle marks the site of the tumor.

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Postoperatively, the patient was referred for radiation therapy to the primary site and neck basins.

Discussion

Lymphoepithelial carcinoma accounts for 0.4% of malignant salivary gland tumors and is a variant of anaplastic carcinoma with a dense lymphoid stroma.1 Although Schminke2 first described lymphoepithelial carcinoma in the nasopharynx in 1921, it was not until 1952 that Godwin3 described the first case series of benign lymphoepithelial lesions of the salivary gland in 11 patients.

Epidemiologically, LEC accounts for less than 1% of all salivary gland tumors and has a unique ethnic predilection for Arctic region natives (particularly Eskimos and Inuits), southeastern Chinese, and Japanese. Hamilton-Dutoit et al4 first published the association between EBV and undifferentiated carcinomas of the salivary gland among the Eskimo population. They showed that the EBV genomes were detected in cases of undifferentiated carcinoma of the Eskimo population, but not in similar tumors of non-Eskimo ancestry.4 The current theory is that when the EBV incorporates into the DNA of certain susceptible populations, it has a predilection for tumorigenesis (i.e., turning off tumor suppressor genes such as p53). The most common site of occurrence is the parotid gland, and LEC has a nearly 100% association with EBV in endemic areas.5 Patients usually present with a mass swelling with or without facial nerve paralysis and pain. There is a high frequency (10% to 40%) of concurrent cervical lymphadenopathy.6

The patient in our case had all these clinical risk factors, as she was of southeastern Chinese/Asian descent, had disease in the parotid gland, and histologic specimens stained positive for EBER (Figure 5). The patient did present with facial swelling but did not have any facial nerve paralysis or any pain. She did not have any cervical lymph node involvement, and pathologic specimens of level 2a nodes showed 19 negative lymph nodes. The patient did have one lymph node involved that was directly adjacent to the tumor (Figure 3), but no regional metastases.

Figure 3. Intraparotid lymph node adjacent to tumor. Lympho-plasmacytic cell infiltrate surrounding nests of tumor cells suggests lymphoepithelial carcinoma. Adjacent lymph node appears reactive with a starry-sky pattern.

Figure 4. Brown cytokeratin stain (CD 5/7), an immunoperoxidase stain, reveals tumor cells staining positive for cytokeratin. However, tumor cells are also seen in the lymph node suggestive of intraparotid spread. All other lymph nodes were negative.

Figure 5. Epstein-Barr encoded RNA (EBER) stain shows Epstein-Barr virus positivity in tumor cells. Tumor cells scattered in lymph nodes also stain positive for EBER.

Figure 6. High-power view of specimen reveals classic lympho-plasmacytic cell infiltrate among nests of poorly differentiated tumor cells.
The tumor was classified as a stage II, T2N0M0, grade 3, poorly differentiated LEC, according to the American Joint Committee on Cancer staging system because the tumor was greater than 2 cm and less than 4 cm and did not appear to have any lymph node or distant metastases. The patient did not have any perineural invasion, and all margins were clear. Postoperatively she had a facial nerve palsy with incomplete eye closure, a House-Brackmann grade IV, and she recovered to baseline grade I within a month. There were 3 primary reasons why a total parotidectomy was performed instead of a superficial parotidectomy. The patient had a deep lobe tumor, the FNA showed a high-grade malignant tumor, and the tumor was relatively large (roughly 4 cm). At our institution, the senior author tends to perform total parotidectomies on all high-grade malignancies. Sometimes superficial parotidectomies may be sufficient for small, low-grade malignancies.

Regarding the decision to perform only a selective level 2a neck dissection, the patient had abnormal-appearing lymph nodes on CT that measured 2.1 × 1.2 cm and 1.7 × 1.1 cm in level 2a. These tumors are very radiosensitive, and the patient was scheduled to have postoperative radiation therapy locally to the tumor bed of the parotid. It was decided that the abnormal-appearing lymph nodes would be removed and sampled as frozen sections to rule out regional metastases. Because the patient would be receiving postoperative radiation to the local tumor bed if the nodes were negative, she would receive radiation to the cervical lymph node basins instead of an elective neck dissection. If the lymph nodes were positive for cancer on the frozen section, a selective neck dissection would be performed.

Histologically, specimens of LEC normally are characterized by a rich nonneoplastic lymphoplasmacytic cell infiltrate present between and around tumor nests (Figures 3 and 6). Abundant histiocytes may be present, demonstrating a starry-sky appearance. Immunohistochemical analysis shows neoplastic cells that stain positive for cytokeratin (Figure 4) and epithelial membrane antigen, with variable expression of EBER. Lymphoid cells are reactive for both CD20 and CD3 markers suggestive of B-cell and T-cell presence, respectively.

With current treatment modalities, the recurrence rate of high-grade salivary gland tumors has decreased, and survival rates have increased. According to a 30-year review of the Mayo Clinic’s surgical experience with 1360 primary tumors of the parotid gland, nearly 17% (228) of those tumors were malignant. Of the 228 malignant tumors, 11 (<5%) were undifferentiated. The recurrence rate decreased from 83% in the 1940s to 40% in the 1960s.

Current treatment recommendations involve completely excising the primary lesion, with a selective neck dissection followed by postoperative radiotherapy to the local site as well as to the neck if there was positive lymph node involvement. Because most LECs of the parotid gland are radiosensitive, combination therapy with surgery and radiation therapy is desirable to control the disease. Our patient received a total parotidectomy on the affected side with selective lymph node sampling. Because the lymph nodes were negative on the frozen section intraoperatively, a complete neck dissection was not performed. Postoperatively, the patient was referred for radiation therapy to the primary site and neck basins.

There have been reports of LECs in several other sites in the head and neck region, including the floor of the mouth, tonsil, thymus, larynx, and sinonasal tract. Histologically, LECs of the parotid are identical to nasopharyngeal lymphoepitheliomas. Similar to lymphoepithelioma of the nasopharynx, LECs of the parotid are very sensitive to radiation. Any high-grade malignant tumor of the parotid usually is treated with radiation therapy because it may be difficult to obtain clear margins.

In conclusion, LEC of the parotid is a rare parotid tumor that requires surgical excision and postoperative radiotherapy. The workup of any parotid mass should begin with an FNA of the mass. Once a pathologic diagnosis of the parotid mass is obtained, surgical excision can be discussed depending on the pathologic results. An elderly patient with multiple medical comorbidities may not need to have a benign pleomorphic adenoma excised. Any malignant neoplasm would require surgical excision, radiation therapy, or both. After the FNA is obtained, imaging with either magnetic resonance imaging or positron emission tomography/CT is appropriate. Magnetic resonance images are preferable for anatomic delineation, whereas positron emission tomography/CT scans allow one to look for regional and distant metastases. In many cases, both types of images can be obtained, especially in cases of high-grade malignancies. Finally, referral to a multidisciplinary head and neck tumor board including head and neck surgeons, a radiation oncologist, and medical oncologists, for evaluation of advanced-stage disease may help facilitate management from a multispecialty approach.

Disclosure Statement
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References