**Case 6: A Real Pain In The Neck**

A 63-year-old man noticed a pruritic mass on the back of his central/right neck, prompting a dermatologic biopsy revealing lymphoepithelioma-like carcinoma and subsequent wide local excision (8 cm × 4 cm) by otolaryngology, with negative margins. Postoperative management involved quarterly follow-up, with no adjuvant therapies recommended.

Five months postoperatively the patient was lost to follow-up; 10 months later the patient noticed a palpable, nontender left lower neck mass. Neck ultrasound revealed a 2.3 × 2.1 × 1.5 cm mass with microcalcifications and multiple adjacent small lymph nodes. Computed tomography scans of the chest and head and neck (Fig. 1) revealed the mass in level 5B of the left neck and no distant disease. Otolaryngology subsequently performed selective left neck dissection of levels 4 and 5, revealing lymphoepithelioma-like carcinoma involving 1 of 11 lymph nodes with marked extracapsular extension into the surrounding soft tissue and occupying 3.7 cm. The patient was referred for radiation oncology consultation.

Fig. 1: Preoperative axial neck computed tomography image after tumor recurrence.

**Expert 1: Rare Tumor, Common Approach**

Lymphoepithelioma-like carcinoma of the skin is a rare entity. Histologically, it is described as an undifferentiated nonkeratinizing squamous cell carcinoma with lymphocytic infiltration, similar to lymphoepithelioma of the nasopharynx. Consequently, it has an improved prognosis compared with other poorly differentiated carcinomas and is exquisitely radiosensitive. Other reviews of the literature for lymphoepithelioma-like carcinoma of the skin have indicated favorable prognosis with only a 12% rate of spread to the lymph nodes. Basic principles of treatment for lymphoepithelioma-like carcinoma can be extrapolated from other more common head and neck diseases.

Although excision alone for localized involvement is typically sufficient, the biology of the disease in the presented case has displayed aggressive behavior with nodal recurrence in the contralateral neck developing rapidly after initial treatment. Therefore, adjuvant radiation treatment is warranted. Based on the anatomic pathway of nodal spread along the cervical lymph node chain, there is a high likelihood that microscopic disease remains in multiple regions, including the portions of the left neck that were undissected and the primary site and ipsilateral right neck. Given the short time interval to disease recurrence and its unusual spatial pattern, we recommend a comprehensive approach with treatment volumes encompassing the primary operative bed and bilateral cervical neck to nodal levels II to V, with consideration of higher doses to the primary site and areas of extracapsular extension. Standard of care need not include adjuvant chemotherapy because of the risk of added morbidity and the potential for excellent control with surgery and radiation alone.

**Expert 2: Regaud, Rare Skin Cancer, and Radiotherapy**

Pioneering radiation biologist and oncologist Claudius Regaud (1870-1940) described a radiosensitive neoplasm of the nasopharynx now known as “lymphoepithelioma” in 1921. Lymphoepitheliomas and lymphoepithelioma-like carcinomas originate in a variety of subsites of the head and neck including the skin, mucosa, and salivary glands, but are rare.

Our approach to this situation would be to first confirm this is truly a primary tumor of the skin. The pattern of disease spread is more consistent with nasopharynx cancer (ie, bilateral involvement of the neck, involvement of the low neck) than skin cancer (ie, recurrence in contralateral lymphatics after excision of well-lateralized primary cutaneous tumor). Imaging alone would not sufficiently rule out the possibility of nasopharynx cancer. Additional clinical, histopathologic, and molecular information might help establish an accurate diagnosis, which is of paramount importance.

After excluding the possibility of a nonskin cancer, we would offer the patient adjuvant radiation therapy acknowledging this is a rare variant of cutaneous squamous cell carcinoma without clear evidence to guide management. We would target the neck bilaterally, including levels 2 to 5B and the right postauricular lymphatics. We would deliver total doses in the table below in

30 fractions according recently published guidelines by the Head and Neck Cancer International Group: total dose 60 Gy for left 5B and primary tumor site on right neck; total dose 56.1 Gy for left 4-5B; total dose 54 Gy for right 2-3 and postauricular, left 2-5B.

Finally, we would encourage the patient to consult with an expert head and neck medical oncologist to discuss adjuvant chemotherapy.

**Expert 3: Return to First Principles**

Primary lymphoepithelioma-like carcinomas of the skin (LELCS) are rare, indolent tumors that develop in sun-exposed skin. LELCS are regarded as a variant of cutaneous squamous cell carcinoma with low metastatic risk. Lymphovascular space invasion is associated with a more aggressive phenotype; for this case, histologic comparison of the primary skin tumor and the excised neck lymph node is important, along with identification of high-risk features. A subset of lymphoepithelioma-like carcinomas arise from the nasopharynx and are Epistein Barr Virus positive; although the computed tomography revealed no metastases, we recommend fluorodeoxyglucose whole-body positron emission tomography-computed tomography and assessment of the nasopharynx for an occult primary.

The evidence base for the management of LELCS is not strong; for this unusual case we recommend returning to first principles. Adjuvant radiation therapy to the operated neck is indicated to achieve local control, and a potential dose-fractionation schedule is 65 Gy in 30 daily fractions to level 5b and 60 Gy in 30 daily fractions to the remainder of the operated neck. There is no role for concurrent chemotherapy. The argument for adjuvant radiation therapy to the primary excision site is less strong owing to the time elapsed. There is a significant risk that the cancer will relapse either in an at-risk nodal basin or distantly. The morbidity associated with radiation therapy to the contralateral neck is unjustified, as is the role of prophylactic radiation therapy to the remainder of the at-risk nodal basins−the bilateral axillae.

The two years after neck dissection is the highest period of relapse; the patient should undergo regular clinical and imaging surveillance throughout this interval.

ChatGPT’s initial recommendation

**Expert 4: Adjuvant Radiation Therapy and Concurrent Chemotherapy**

The patient has experienced a regional recurrence of lymphoepithelioma-like carcinoma in the neck, with extracapsular extension of the tumor in the dissected lymph nodes. In this case, our most favored therapeutic approach would be a combination of adjuvant radiation therapy and concurrent chemotherapy, considering the high risk of additional microscopic disease and potential for further recurrence.

* Adjuvant radiation therapy would be recommended due to the presence of extracapsular extension, which is a known risk factor for local and regional recurrence. The radiation treatment would target the neck, specifically focusing on the areas of dissection (levels 4 and 5) and the surrounding region to address potential microscopic residual disease. The radiation dose would typically be in the range of 60-66 Gy, delivered in 2 Gy fractions over 6-7 weeks.
* Concurrent chemotherapy would be advised to enhance the effect of radiation and improve locoregional control. Cisplatin-based chemotherapy is a standard option for head and neck cancers, and I would recommend a regimen of high-dose cisplatin (100 mg/m²) administered every three weeks for a total of three cycles during the course of radiation therapy.

This combined modality approach (chemoradiation) is supported by clinical evidence showing improved survival and locoregional control compared to radiation therapy alone, particularly in patients with high-risk factors like extracapsular extension.

It is important to closely monitor the patient's response to treatment, as well as manage any side effects that may arise from the chemoradiation. In addition, the patient should be advised to attend regular follow-up appointments to assess for any signs of recurrence or potential complications.

ChatGPT’s revised recommendation after seeing other human experts’ recommendations

**Expert 5: Rare Cutaneous Carcinoma, Comprehensive Approach**

In this rare case of lymphoepithelioma-like carcinoma of the skin, it is crucial to first confirm the primary tumor origin and exclude the possibility of nasopharynx cancer through additional clinical, histopathologic, and molecular evaluations.

Upon confirmation of primary cutaneous squamous cell carcinoma, adjuvant radiation therapy should be administered, targeting the bilateral neck (levels 2 to 5B) and right postauricular lymphatics. Careful radiation planning according to the patient's specific anatomy and risk factors is essential to achieve optimal treatment outcomes. The following dose guidelines are recommended for the radiation therapy:

1. Left neck level 5B (area of extracapsular extension): 60 Gy in 30 fractions
2. Left neck levels 2 to 4: 56.1 Gy in 30 fractions
3. Primary area (right posterior neck skin scar): 60 Gy in 30 fractions
4. Right uninvolved neck levels 2 to 5: 54 Gy in 30 fractions

In parallel, consultation with a medical oncologist is recommended to discuss the potential benefits of concurrent chemotherapy, such as cisplatin-based chemotherapy, to enhance the effect of radiation and improve locoregional control.

Regular follow-up appointments and close monitoring of the patient's response to treatment, as well as management of any side effects that may arise from the chemoradiation, are essential to ensure the best possible outcome for the patient