CLINICAL VIGNETTE

Metastatic Cutaneous Squamous Cell Carcinoma

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Case

An 81-year-old male with past medical history significant for hypertension and hyperlipidemia presented for evaluation for a palpable right axillary mass. Patient had a long history of cutaneous squamous cell carcinomas and basal cell carcinomas treated with Mohs procedures in the past. His most recent dermatologic intervention was 6 months prior to presentation when he had a Mohs procedure performed of a lesion on his right shoulder with pathology confirming a basal cell carcinoma, nodular type and a separate right forearm lesion with pathology confirming moderate to poorly differentiated squamous cell carcinoma. The patient did not report any pain or discomfort with the mass. He denied any fevers, night sweats, or recent weight loss.

Social History

The patient grew up in Southern California with significant sun exposure history as he used to be an avid surfer. He is married and does not use tabacco or alcohol. Family history was significant for breast cancer in his mother.

Physical Examination included normal vital signs. The right axillary mass was moderately firm but mobile measuring approximately 3 cm in size. No other lymph nodes were palpable.

Laboratory tests included: White Blood Cell Count 7.1 x 10^3/uL, Hemoglobin 12.8 g/dL, Hematocrit 41%, Platelet 385,000. Sodium 139, Potassium 3.3, Bicarbonate 102, CO_2 28, BUN 12, Creatinine 0.9, Glucose 110.

Treatment Course

Ultrasound imaging of the palpable axilla mass measured 3.2 cm x 2.1 cm x 2.2 cm. Subsequent core biopsy confirmed histologic appearance consistent with squamous cell carcinoma. PET-CT scan showed metabolic uptake with SUV 5.6 in the palpable axillary mass. A few nonspecific subcentimeter pulmonary nodules were noted without PET uptake and no other signs of metastatic disease sites were detected.

The patient was sent for surgical and oncologic evaluation. The consensus was that this metastatic malignancy was likely cutaneous in origin based on his long history of skin cancer. After discussion he opted for surgical axillary dissection. He declined targeted immunotherapy. Surgical pathology showed one out of three lymph nodes involved with moderate-poorly differentiated squamous cell carcinoma. No extracapsular extension was noted. Immunostaining pattern included PD-L1 testing which was positive and p16 testing which was negative. Patient recovered from surgery without complications.

Discussion

Cutaneous squamous cell carcinomas (cSCC) have an estimated incidence of over one million[1] cases per year with the lifetime incidence estimated to be 7-11%.[2] The most common risk factors include sun exposure, fair skin, immunosuppression, and age.[3] cSCC are also more common in men than women by a 3:1 ratio.[3] Unfortunately, because these cutaneous squamous cell skin cancers are not required to be reported to cancer registries, reported statistics are likely underestimates of the true prevalence, especially in geographic areas of the country with greater ultraviolet sun exposure.

Metastatic cSCC are generally uncommon. One review reported rates of metastatic cSCC to be approximately 3-9% and typically seen 1-2 years after the initial diagnosis.[4] Nodal metastasis are the most common presentation of metastasis, typically seen in the parotid or cervical lymph nodes.[5] The next common regions include the axillary and groin nodes along with distant metastasis.[5] While most early detected cSCC have high local control and cure rates, metastatic cSCC can carry a much worse prognosis. One study examined patients with regional lymph node metastasis from cutaneous squamous cell carcinoma reported 2 and 5-year survival rates to be 33% and 22%, respectively, with the 5-year disease free survival rate at 34%.[6]

With biopsy proven lymph node metastasis from cSCC, recommended evaluation includes a full body PET/CT scan to rule out distant metastatic disease. With operable disease in the trunk and extremities as in this case, excision of the primary tumor and regional lymph node dissection is recommended with consideration of adjuvant radiation treatment if multiple lymph nodes are involved or if extracapsular extension is noted.[7] Lymph node metastasis specifically in the head and neck region are often treated surgically followed with adjuvant therapy including radiation, systemic therapy, or both based on the number of lymph nodes found as well as the presence or absence of extracapsular extension.[7]

Patients with advanced or metastatic cSCC not amenable to local therapy can be treated with systemic therapy alone. Current preferred regimens include checkpoint inhibitor immunotherapy, specifically cemiplimab or pembroluzimab. A study of cemiplimab, reported response to phase 1 treatment in 13 of 26 patients (50%; 95% confidence interval [CI], 30 to 70).[8] In the metastatic disease cohort of the phase 2 study, a treatment response was seen in 28 of 59 patients (47%; 95% CI, 34 to 61). In the 28 patients who had a response, the duration of response exceeded 6 months in 57%.[8]

Pembrolizumab is another promising drug used in advanced or metastatic cSCC. In the phase II trial KEYNOTE-629, 159 patients with locally advanced and/or metastatic cSCC were treated and analyzed, including 87% of the patients who had received one or more prior systemic therapies. At median follow-up of 14.9 months, those with locally advanced, unresectable disease demonstrated a response rate of 50%, with complete and partial response rates of 16.7 and 33.3%, respectively. One-year progression-free survival and overall survival rates were 54 and 74%, respectively. Of those with recurrent or metastatic disease, at median follow-up of 27.2 months, the response rate was 35.2%, with complete and partial response rates of 10.5 and 24.8%, respectively. One-year progression-free survival and overall survival rates were 36 and 61%, respectively.[9]

Patients who progress on immunotherapy or have contra-indications to immunotherapy (e.g., organ transplant patients), are considered for traditional cytotoxic therapies such as carboplatin or paclitaxel.

Conclusions

Metastatic cSCC while uncommon, can portend a poor prognosis. This clinical scenario will likely increase as cSCC is expected to increase 2-4% each year.[10] However, newer systemic treatments with immunotherapies offer promising results. In combination with surgical management, more treatment options are now available for management of this aggressive form of cSCC.

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