

Head and Neck Cutaneous Squamous Cell Carcinoma with Perineural Invasion

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Introduction

Head and Neck Cutaneous Squamous Cell Carcinoma (HNCSCC) is one of the most common types of skin cancer found in the head and neck region. This cancer arises from the squamous cells in the epidermis, the outermost layer of the skin, and typically presents as a nodular lesion, often associated with sun exposure. While the prognosis for patients with HNCSCC is generally favorable, certain histological features such as Perineural Invasion (PNI) can significantly worsen the clinical outcome. Perineural invasion refers to the tumor's ability to invade the nerve sheaths, a phenomenon that often leads to aggressive tumor behavior, higher recurrence rates, and a poorer prognosis.

In this paper, we will explore the characteristics of head and neck cutaneous squamous cell carcinoma with perineural invasion, the diagnostic challenges, management strategies, and the implications for patient outcomes. Cutaneous squamous cell carcinoma is a malignancy that arises from the squamous cells of the epidermis. It is the second most common skin cancer, following basal cell carcinoma. CSCC most frequently occurs in areas of the skin that are commonly exposed to sunlight, such as the face, ears, neck, scalp, chest, back, and extremities. The pathogenesis of CSCC is primarily associated with Ultraviolet (UV) radiation, which induces DNA mutations that disrupt the normal cellular repair processes, leading to uncontrolled cell proliferation.

The clinical presentation of CSCC varies but typically manifests as a scaly, erythematous patch or plaque, or an ulcerated nodular lesion. While most CSCCs are localized and can be successfully treated with surgical excision, a small subset of these cancers can exhibit more aggressive features, such as high rates of metastasis, recurrence, and local invasion into deeper tissues. Perineural Invasion (PNI) is a histopathological phenomenon where malignant cells invade the nerve sheaths. In cutaneous squamous cell carcinoma, PNI is considered an indicator of more aggressive behavior and is associated with worse prognosis. The presence of PNI in CSCC can lead to increased tumor size, greater likelihood of local recurrence, and a higher risk of distant metastasis.

Description

PNI is most often encountered in tumors located in the head and neck region due to the complex anatomy and rich neurovascular structures in this area. The craniofacial nerves, particularly the facial nerve, trigeminal nerve, and other branches of the cervical plexus, are at risk of being involved in cases of CSCC with PNI. The invasion of these nerves not only complicates the surgical resection but may also result in significant neurological deficits.

The mechanisms underlying perineural invasion in cutaneous squamous cell carcinoma are not fully understood, but several key factors have been identified. Tumor cells can infiltrate the perineurium (the connective tissue sheath surrounding the nerve) through several mechanisms, including direct extension, local tissue breakdown, and the promotion of nerve growth factors. The interaction between malignant cells and the nerve's extracellular matrix, neurotrophic factors, and cellular signaling pathways contribute to the establishment of perineural invasion. In some cases, nerve fibers may serve as a conduit for the tumor cells, enabling them to spread into deeper tissues, making surgical resection more difficult and increasing the risk of recurrence. The invasion of nerves also facilitates the dissemination of tumor cells to regional lymph nodes and distant organs via the nervous system.

Cutaneous squamous cell carcinoma with perineural invasion may present with nonspecific symptoms, but there are a few clinical signs that should raise suspicion. A well-defined, firm, and sometimes ulcerated lesion, particularly on sun-exposed areas, may suggest a CSCC. When PNI is present, these lesions may grow rapidly. One of the hallmark signs of PNI is pain along the affected nerve, which may be described as sharp, burning, or throbbing. This pain can be referred or localized, often following the distribution of the involved nerve.

If the nerve is significantly involved, patients may exhibit motor or sensory loss in the distribution of the affected nerve. For example, involvement of the facial nerve may result in facial paralysis, while involvement of the trigeminal nerve can cause sensory loss in the face.

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In more severe cases, CSCC with PNI can affect deeper nerve structures, leading to symptoms such as diplopia (double vision), loss of vision, or loss of taste in the mouth. The diagnosis of CSCC with perineural invasion involves a combination of clinical evaluation, imaging studies, and histopathological examination. A detailed history and physical examination are crucial. The physician must look for signs of a skin lesion that may indicate CSCC, along with any associated neurological symptoms.

The definitive diagnosis of CSCC with PNI is made through skin biopsy. Histopathological examination can identify the presence of PNI, which is characterized by the infiltration of tumor cells into the perineural space. Immunohistochemistry can also be employed to enhance the identification of nerve involvement. In cases where there is suspicion of deep nerve involvement, advanced imaging techniques such as MRI (Magnetic Resonance Imaging) and CT (Computed Tomography) scans may be used. MRI is particularly useful in detecting perineural spread, as it can visualize soft tissues and the extent of nerve invasion. In some cases, EMG can be used to assess nerve function and detect any abnormalities in the motor or sensory components of the nerve involved.

Larger tumors and those that invade deeper layers of the skin (dermis and subcutaneous tissue) are more likely to exhibit perineural invasion. Tumors in the head and neck, particularly those near major nerve structures, have a higher likelihood of invading nerves. Certain histological subtypes of CSCC, such as those that exhibit aggressive features like poorly differentiated cells, are more likely to show PNI. Patients with weakened immune systems, such as organ transplant recipients or those with HIV/AIDS, are at increased risk for developing more aggressive forms of CSCC, including those with PNI.

The management of cutaneous squamous cell carcinoma with perineural invasion requires a multidisciplinary approach, often involving dermatologists, oncologists, surgeons, and radiation therapists. The treatment strategy depends on the tumor's location, size, depth of invasion, and the extent of nerve involvement.

Surgical excision remains the primary treatment for CSCC with perineural invasion. The goal is to achieve complete excision of the tumor with clear margins. In cases where perineural invasion is present, the surgeon may need to take wider margins of healthy tissue around the tumor to ensure that no malignant cells remain. If the tumor involves critical structures such as major nerves or blood

vessels, more complex surgical approaches may be necessary, which may include nerve resection, nerve grafting, or even reconstruction of the affected area.

In cases where surgical excision is incomplete or when perineural invasion is extensive, adjuvant radiation therapy is often recommended. Radiation therapy can help eliminate residual cancer cells, reduce the risk of local recurrence, and provide symptomatic relief from pain due to nerve involvement. It is particularly useful when the tumor has spread along the nerve sheath or when nerve involvement is too extensive for complete surgical removal.

Chemotherapy is typically not the first-line treatment for localized CSCC with PNI. However, in advanced cases with metastasis or when the tumor is not amenable to surgery or radiation, chemotherapy may be considered. The drugs commonly used in these cases include cisplatin, 5-fluorouracil, and methotrexate. Close monitoring is essential for patients with CSCC with perineural invasion due to the high risk of recurrence and metastasis. Regular follow-up visits, including physical examinations and imaging studies, are crucial to detect early signs of recurrence or neurological complications. Patients should also be educated on self-monitoring for any new lesions or changes in existing lesions.

Conclusion

The prognosis of patients with head and neck cutaneous squamous cell carcinoma with perineural invasion largely depends on the extent of the invasion, the tumor's size, the success of surgical excision, and the involvement of critical nerve structures. PNI is a poor prognostic factor, as it significantly increases the likelihood of recurrence and metastasis. Tumors with deep or extensive nerve involvement may require more aggressive treatments and lead to more significant morbidity. In general, patients with CSCC and PNI in the head and neck have a higher risk of developing distant metastasis, particularly to regional lymph nodes and other organs. The 5-year survival rate in these patients is lower than that of patients with CSCC without perineural invasion.

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