Margin Analysis
Sarcoma of the Head and Neck

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KEYWORDS

• Head and neck • Sarcoma • Histologic types • Resection margin • Prognosis

KEY POINTS

- Head and neck sarcomas are rare but are associated with significant morbidity/mortality and management difficulties.
- These tumors are best managed in a multidisciplinary setting.
- Open or core biopsy is essential for histologic diagnosis and grading. Based on histology, the tumors are divided into 3 categories; low grade, intermediate grade, and high grade, which helps in guiding therapy.
- Complete surgical tumor resection with negative margins at the first attempt is the best chance for potential cure.
- In most patients, except those with small resectable low-grade lesions, adjuvant radiotherapy and chemotherapy is added to maximize local control with variable results.

INTRODUCTION

Sarcomas are malignancies arising from mesenchymal (nonepithelial) tissue and are broadly classified into sarcomas of soft tissue and bone. Soft tissue sarcomas can arise from muscle, blood vessels, nerves, fat, and fibroconnective tissues. Sarcomas of bone are mainly osteosarcoma, chondrosarcomas (CS), and Ewing sarcoma (EWS).

Sarcomas are rare compared with carcinoma, accounting for 1% to 2% of all head and neck (HN) malignancies, of which approximately 80% originate from soft tissues and 20% from bone.[1] Although rare in the HN, they represent an important but heterogeneous group of tumors that may be associated with management challenges and risk for morbidity/mortality.

HISTOLOGIC TYPES AND CLASSIFICATION OF HEAD AND NECK SARCOMAS

More than 60 histologic subtypes of bone and soft tissue sarcomas have been described in different parts of the body.[2]

Approximately 70% to 80% of HN sarcomas occur in adults; angiosarcoma, undifferentiated

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pleomorphic sarcoma (malignant fibrous histiocytoma), Kaposi sarcoma, and fibrosarcoma are the most common. Between 20% and 30% occur in children, with most being osteosarcoma, rhabdomyosarcoma and, EWS.[3]

PATHOGENESIS AND PREDISPOSING FACTORS IN HEAD AND NECK SARCOMAS

Several associated/predisposing factors have been implicated in the pathogenesis of bone and soft tissue sarcomas. These include genetic predisposition, acquired gene mutations, radiation/chemotherapy, chemical carcinogens, chronic irritation, lymphedema, viral infections, such as human immunodeficiency virus and human herpesvirus 8 in Kaposi sarcoma, and Epstein-Barr virus in smooth muscle tumors of immunocompromised patients.[4]

GENETIC PREDISPOSITION

Li-Fraumeni Syndrome

Li-Fraumeni syndrome (LFS) is an autosomal dominant inherited germline mutation in the p53 tumor suppressor gene. The syndrome is characterized by soft tissue and bone sarcomas, breast cancer, brain tumors, leukemia, and adrenocortical cancer before the age of 45 years. Sarcomas account for nearly 25% of tumors in affected individuals and they arise at a younger age than those unassociated with LFS.[5]

Retinoblastoma Gene

Different types of sarcomas develop later in life of patients irradiated for retinoblastoma from inherited mutant copy of retinoblastoma-1 gene. Some of these sarcomas did not arise within the irradiated field, suggesting that the gene mutation itself predisposes to secondary sarcomas with radiation therapy shortening the latent period and increasing the risk.[6]

Neurofibromatosis Type-I (Mutations in NF1 Gene)

Some of the multiple benign neurofibromas may transform to malignant peripheral nerve sheath tumor with complex karyotype. The malignant transformation is thought to reflect the 2-hit hypothesis in which one allele is constitutionally inactivated in the germline, and the other allele undergoes a "second hit" by complex molecular aberrations.[7]

Other than a genetic predisposition, acquired cytogenetic events in sarcomas fall into 2 major categories: those with specific genetic alterations that can be used to confirm the diagnosis, predict prognosis, or both,[8] and those with nonspecific complex genetic alterations, as in osteosarcoma, undifferentiated pleomorphic sarcoma (malignant fibrous histiocytoma), angiosarcoma, or leiomyosarcoma. A positive correlation exists between the genomic complexity and more aggressive tumor behavior.[9]

GENERAL PRINCIPLES IN DIAGNOSIS AND TREATMENT OF HEAD AND NECK SARCOMAS

Diagnosis

Patients present with symptoms driven by involvement of adjacent structures. Involvement of the skull base may produce diplopia, proptosis, facial pain, and headache. Involvement of the sinonasal tract may produce nasal obstruction, epistaxis, and pain. Larynx involvement may produce dysphonia or dyspnea. Computed tomography (CT) and MRI delineate the extent of bone and soft tissue involvement. Fludeoxyglucose-PET studies are performed when distant metastasis is suspected. Staging is performed according to American Joint Committee on Cancer guidelines. Open or core biopsy is essential for histologic diagnosis and grading. The tumors are histologically divided into 3 categories; low grade, intermediate grade, and high grade based on the Federation Nationale des Centers de Lutte Contre le Cancer grading system, which considers tumor differentiation, mitosis, and necrosis, and helps guide therapy.

Surgical Treatment

Complete surgical tumor resection with negative margins at the first attempt should be the prime objective to achieve local control, avoids the increased morbidity and costs of second surgery, and is the best chance for potential cure.

Classic teaching based largely on experience in non-HNS dictates the margins of tumor excision/resection may be classified as wide margin when a wide negative margin is present around the resected tumor, as a marginal excision when the excision plane passed through the reactive zone around the tumor (clear but close <1 mm), or an intralesional excision if the tumor is present at any part of the margins.[10]

An ideal "wide" resection margin may be difficult to achieve in HN sarcoma (HNS) without potential considerable functional morbidity from tumor proximity to vital HN structures. Therefore, in HNS, resection should be as wide as permitted by the nearby vital structures, which is commonly accepted clinically as a 1.0-cm thickness of uninvolved tissue around the mass, or an anatomic equivalent, such as periosteum, where appropriate.