

**HEAD AND NECK SARCOMAS****Dr. Jaspreet Singh Badwal\***

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Article Received on 11/07/2017

Article Revised on 01/08/2017

Article Accepted on 22/08/2017

**ABSTRACT**

Sarcomas of the head and neck are heterogeneous tumours with different biological behaviour depending on their histological type and degree of differentiation. The purpose of this review is to present the classification, diagnosis and prognosis for head and neck sarcomas.

**KEYWORDS:** Sarcomas head and neck, classification, diagnosis, etiology, prognosis.

Cancer has been recognized from antiquity. Celsus (25 BC to AD 50), a native of Greece practicing in Rome, separated benign tumors, eg. lipoma, from malignant growths, cancer. Galen (AD 131–200), another Greek physician who settled in Rome, described sarcoma as “fleshy excrescence” having the appearance of raw meat “sarkos.” Under the term of sarcoma, he combined swellings, benign tumors, as well as undefined tumours, such as “fungus.”<sup>[1]</sup> With regard to treatment, Celsus, Galen, and most physicians and surgeons for centuries advised refraining from the surgical excision of tumours, including sarcomas, that were irregular in shape, livid in colour, insensible, ulcerated, or could not be moved with fingers. Theodoric of Salerno (1205–1296), a priest physician, noted that lipomatous tumours that were dark in colour and firm to touch were cancerous, and treatment was not appropriate for such lesions. A French surgeon, Guy de Chauliac (1300–1368), who was the physician to 3 Popes in Avignon, held a different view. He recommended wide excision for cancer at an early stage when the cancer was small and superficial.<sup>[2]</sup>

Sarcomas are rare neoplasms, constituting only 1% of all cancer diagnoses in the United States.<sup>[3,4]</sup> Furthermore, these tumours do not commonly manifest as primary malignancies in the head and neck region, except in the paediatric population where as many as 35% of all sarcomas affect head and neck sites.<sup>[5]</sup> Nevertheless, sarcomas account for only 1% of all head and neck primary cancers.<sup>[6]</sup> The rarity of sarcomas, and the multitude of histologic subtypes, can make definitive diagnosis difficult, and an experienced pathologist is key to the initial evaluation. Appropriate pathologic characterization forms the basis for prognosis and subsequent treatment selection. The biology of a neoplasm and its propensity for locally aggressive growth and systemic dissemination are clearly reflected

in its histology and grade. The size and location of the lesion, which have become more precisely delineated with improvements in radiographic modalities, also impart reliable prognostic information. These factors, along with the complexities of head and neck anatomy, especially regarding function and cosmesis, make optimal treatment difficult to determine in many cases.

Traditionally, surgery has formed the cornerstone of therapy for head and neck sarcomas. Multimodality treatment of these tumours, however, which incorporates a multidisciplinary approach, has yielded encouraging results. Data collected by ongoing cooperative studies, such as the Intergroup Rhabdomyosarcoma Study Group (IRSG), have demonstrated improved outcomes for patients treated with surgery and other nonsurgical modalities.

**Incidence**

Approximately 37,800 new cases of head and neck cancers are diagnosed in the United States each year; most of these tumours are of the squamous cell type involving sites of the upper aerodigestive tract, such as the oral cavity, oropharynx, hypopharynx, and larynx.<sup>[3]</sup> Only 11,700 sarcomas of all body sites (2400 bony and 8300 soft tissue) were estimated to occur in the United States in 2002.<sup>[3]</sup> In most studies, head and neck primary sarcomas represent only 5% to 15% of all sarcoma cases in adults.<sup>[7,8]</sup> In the paediatric population, however, 35% of all sarcomas manifest in the head and neck.<sup>[9]</sup>

**Classification**

Sarcomas can be classified according to various criteria that are also useful in determining prognosis and formulating treatment strategies. In general, these neoplasms are designated by their tissue of origin, histologic grade, and anatomic subsite of the head and

neck region in which they are found. Sarcomas can arise from either bony or soft tissue elements, depending on the mesenchymal cells from which they derive. Most tumours, approximately 80%, are of the soft tissue type; only 20% are of bony or cartilaginous origin.<sup>[8]</sup> Muscle, vessel, nerve, fat, and fibrous tissue can each give rise to a heterogeneous group of malignancies whose histologic characteristics reflect their tissue of origin (Table 1). Some types have no clear association with any particular tissue, and it remains unclear which soft tissue elements potentiate these lesions.

**Table 1: Histologic classification of Head and Neck Sarcomas.**

Histologic type
Bony
Osteosarcoma
Cartilaginous
Chondrosarcoma
Fibrous
Malignant fibrous histiocytoma
Fibrosarcoma
Dermatofibrosarcoma protuberans
Muscular
Rhabdomyosarcoma
Leiomyosarcoma
Vascular
Angiosarcoma
Hemangiopericytoma
Neural
Neurogenic sarcoma
Fatty
Liposarcoma
Histogenesis unclear
Synovial sarcoma
Ewing sarcoma
Alveolar soft part sarcoma
Unclassified

Histologic grade is a reliable predictor of prognosis and is a designated component of the American Joint Committee on Cancer staging system for sarcomas. Osteosarcoma, MFH, RMS, angiosarcoma, synovial sarcoma, alveolar soft part sarcoma (ASPS), and Ewing sarcoma are considered, as a general rule, to be high-grade lesions.<sup>[8,10,11]</sup> Dermatofibrosarcoma protuberans, desmoid tumours, and atypical lipomatous tumours are almost universally low-grade neoplasms.<sup>[6,12]</sup> Other types of sarcomas, including chondrosarcoma, fibrosarcoma, leiomyosarcoma, liposarcoma, neurogenic sarcoma, and hemangiopericytoma, require individualized grading according to pathologic analysis.

Finally, the classification of sarcomas according to anatomic location in the head and neck region has proved to be helpful because of the influence of location on disease management decisions. Lesions of the scalp and face, sinonasal tract and anterior skull base, ear and lateral skull base, parotid gland and neck, and the upper aerodigestive tract ultimately mandate different surgical considerations and approaches. Furthermore, postoperative functional outcomes and the potential for negative margins are directly related to tumour location and serve as critical factors on which operative therapy is based.

### Etiology

Genetic and environmental factors can contribute to the development of sarcomas. Several hereditary disorders are clearly associated with an increased risk of these neoplasms. Li-Fraumeni syndrome is an autosomal dominant disorder involving a germline mutation of the p53 tumour suppressor gene.<sup>[13]</sup> Affected individuals suffer from breast cancers, soft tissue sarcomas, central nervous system malignancies, leukemia, and adrenocortical carcinomas.<sup>[14]</sup> Another tumour suppressor gene, Rb1, is known to cause the hereditary form of retinoblastoma. These patients are also afflicted with other types of bony and soft tissue sarcomas.<sup>[15]</sup> Neurofibromatosis type I is associated with elevated rates of childhood RMS, liposarcoma, and fibrosarcoma. Neurogenic sarcomas commonly develop later during adulthood in these patients.<sup>[14,16]</sup> Many other genetic disorders, including Gardner syndrome, nevoid basal cell carcinoma syndrome, Carney triad, hereditary hemochromatosis, and Werner syndrome, have also been linked to sarcomas.<sup>[14]</sup>

In addition to predisposing host factors, there are several environmental exposures that have been proposed as causative agents in the development of sarcomas. The relative risks, however, are difficult to determine because of the rare incidence of these tumours. Nevertheless, ionizing external-beam radiation (EBRT) to the head and neck area is believed to contribute to the risk of sarcomas according to several large-scale studies.<sup>[17-20]</sup> The true calculated risk of developing a sarcoma after radiation remains elusive because of inadequate observation of these patients and the relative rarity of these tumors.<sup>[21]</sup> In a large-scale series of patients treated in Taiwan for nasopharyngeal carcinoma using radiotherapy, MFHs were later diagnosed in 0.38% of the long-term survivors. The 15-year cumulative incidence was 2.2% in these individuals.<sup>[22]</sup> Increased risk has also been reported in people exposed to various radioisotopes<sup>[14,23]</sup> and in electrical workers who work near high electromagnetic fields.<sup>[24]</sup> Certain chemical agents, such as phenoxyacetic acid-based herbicides, agent orange, and dioxin, have been implicated in the formation of soft tissue sarcomas. Polyvinyl chlorides, thorium oxide (Thorotrast), and inorganic arsenic are all well documented risks for hepatic angiosarcomas.<sup>[14,25]</sup>

Parental drug use, particularly cocaine and marijuana, in the year preceding the birth of a child increases risk of pediatric RMS as much as five-fold.<sup>[26]</sup> Finally, tobacco has been associated with development of soft tissue sarcomas, especially in the upper aerodigestive tract in users of smokeless tobacco products.<sup>[27,28]</sup> Despite these known risk factors, only a minority of sarcomas can be attributed to a defined hereditary syndrome or known environmental exposure. Other agents and genetic abnormalities that contribute to the formation of sarcomas remain to be identified. No single cause is apparent, and an interaction between environmental and genetic elements likely occurs in many cases of head and neck sarcoma.

### Diagnosis and evaluation

Most sarcomas of the head and neck region present with nonspecific signs and symptoms. In 80% of patients, these tumours manifest as a painless mass.<sup>[6]</sup> A variety of symptoms can occur, however, depending on the subsite of the head and neck affected. Patients with disease in the sinonasal tract and anterior skull base may complain of nasal obstruction, proptosis, diplopia, or epistaxis. Involvement of the ear and lateral skull base may present as hearing loss, vertigo, tinnitus, or facial paralysis. Masses that affect the oral cavity can induce dental pain and occasionally loose teeth. Tumours of the neck can impinge on vital structures, causing dysphagia, hoarseness, and even dyspnea. Similar symptoms may arise from sarcomas of the upper aerodigestive tract if they involve the oropharynx, larynx, or cervical esophagus. Furthermore, masses in the hypopharynx and oropharynx commonly cause otalgia through referred sensory pathways; therefore, persistent otalgia in the absence of obvious ear disease warrants evaluation of these areas. Examination generally reveals a submucosal mass of the upper aerodigestive or sinonasal tract or a subcutaneous mass of the neck, possibly with distortion or destruction of adjacent structures. The submucosal location of the neoplasm is one clinical aspect of sarcomas that may help distinguish them from squamous cell carcinomas of the head and neck. Skin and soft tissue lesions in the scalp and face may reveal the violaceous macular characteristics of an angiosarcoma or the reddish-blue colour associated with dermatofibrosarcoma protuberans. Findings are usually nonspecific, however, and the full extent of the mass cannot be ascertained with history and examination alone.

Imaging studies augment the physical examination by more accurately assessing the size and location of sarcomas in the head and neck. In addition, information regarding bony involvement, intracranial extension, and regional nodal disease can be better delineated. High-resolution CT scans and MRI are the studies of choice in nearly all cases. CT scanning is rapid and presents fewer problems with motion artifact. Increased sensitivity for bony abnormalities with CT compared with MRI is yet another advantage to this modality. In addition, CT

imaging is less expensive. MRI, however, offers much better soft tissue resolution and is therefore better able to evaluate the primary lesion, perineural extension, dural involvement, bone marrow replacement, and orbital invasion. Multiplanar imaging also assists in more accurate views of the tumour and adjacent structures. Other advantages of MRI are the lack of exposure to radiation and iodinated contrast material. Because of the unique qualities of CT and MRI, they can often be used in a complementary fashion, especially for surgical planning.<sup>[29]</sup>

Certain findings on radiographic images can indicate specific histologic subtypes of sarcomas, thereby assisting in the actual diagnosis. For example, osteosarcomas classically demonstrate a sunburst periosteal reaction seen on both plain radiographs and CT scans. Bony destruction or peripheral calcifications with new bone formation may also be visualized. Extraskelatal Ewing sarcoma typically is hypodense, with irregular enhancement seen with CT. The mass usually shows significant infiltration of muscle planes and subcutaneous tissues. On MRI images, these neoplasms are hypointense on T1-weighted studies and hyperintense on the T2 projections. MFHs, however, are isointense and hyperintense on T1- and T2-weighted MRI images, respectively, whereas CT can reveal aggressive bone destruction and remodelling. MRI evaluation of liposarcomas, however, results in hyperintense T1 images and only an intermediate signal on T2 images. Leiomyosarcomas may appear as non-enhancing masses with areas of cystic necrosis on CT scans. Cystic necrosis along with speckled calcifications can also be seen on CT images in cases of hemangiopericytoma, but intense hypervascular enhancement distinguishes these tumours from the leiomyosarcomas. ASPS tends to be hyperintense on T1 and T2 images. None of the imaging characteristics can be considered diagnostic, however, and heterogeneity in appearance can be expected.<sup>[29]</sup>

Regardless of how strongly the history, physical findings, and radiographic studies suggest sarcoma, a biopsy is necessary to definitively establish the tissue diagnosis. The biopsy should be performed, if possible, after imaging is completed. An initial biopsy can be done with simple fine-needle aspiration (FNA), although occasionally core-needle specimens may be necessary to accurately subtype the tumour. Nevertheless, some institutions and pathologists still prefer an open biopsy. If an open approach is required, careful consideration should be given to the technique. In sarcomas of the head and neck, a transmucosal biopsy is appropriate for lesions in the sinonasal and aerodigestive tracts. Endoscopic methods can also be used to obtain the tissue from these sites. One must be cautious, however, not to cause tumour contamination in uninvolved regions, such as adjacent paranasal sinuses, while performing the procedure.

Complete surgical resection of sarcomas in the parotid, neck, and parapharyngeal space is preferable to incisional biopsy if the FNA is non-diagnostic. In certain cases, especially in a child or if dysfunction and disfigurement will result, complete resection is not possible or desirable. Incisional biopsy then becomes an acceptable alternative. In such cases, the incision must be oriented in a fashion that allows it to be incorporated into any future definitive resection, and the extent of dissection should be as limited as possible. Once an adequate biopsy specimen has been obtained, the tissue must be reviewed by a pathologist experienced with sarcomas. Special immunohistochemical stains and cytogenetic studies can greatly assist in confirming the diagnosis of sarcoma. If any doubt remains regarding the final histologic interpretation, a second opinion at an outside facility should be considered. Few centers have significant pathologic expertise in this area, however.

After the diagnosis is confirmed, distant metastases should be excluded. Sarcomas most commonly spread to the lungs. Consequently, imaging of the chest is necessary; this may entail only a chest radiograph in patients with low-grade lesions, but CT of the chest is required for high-grade tumors.<sup>[30,31]</sup> Findings such as elevated liver function tests, abnormal bone profiles, neurologic deficits, and bone pain warrant further evaluation with appropriate studies.

#### Prognosis in head and neck sarcomas

For adult soft tissue sarcomas of all anatomic sites, tumour diameter larger than 5 cm, high histologic grade, local extension to skin or bone or major neurovascular structures, and positive surgical margins correlate with increased local recurrence, distant failure, and reduced disease-specific survival rates in multivariate logistic regression analyses.<sup>[32,33]</sup> When tumour location is considered, head and neck sarcomas are associated with the highest rates of local recurrence and the worst disease-specific survival rates.<sup>[32,33]</sup> Several studies of head and neck soft tissue sarcomas of various histologic types have attempted to quantify outcomes based on tumour factors.<sup>[6-8,10,34,35]</sup> All but one of these reports found tumour size greater than 5 cm to predict reduced survival.<sup>[6-8,10,34,35]</sup> Four of the studies that examined tumour grade demonstrated significantly worse survival for patients with high-grade lesions.<sup>[7,10,34,35]</sup> Two studies have evaluated the impact of local extension on outcome.<sup>[10,34]</sup> Based on univariate analysis, Farhood et al.<sup>[10]</sup> found that patients with bony involvement had poorer outcomes. LeVay et al.<sup>[34]</sup> demonstrated by multivariate analysis that local extension predicted local recurrence, distant metastases, and disease-free survival.

Surgical margin status has been repeatedly linked to local control and survival rates.<sup>[6-8,10,34]</sup> Two studies have confirmed this association with multivariate analysis.<sup>[7,34]</sup> Other factors, such as subsite within the head and neck region, may influence prognosis, but this relationship is not as clearly defined.<sup>[6,35]</sup> Furthermore, whether the

sarcoma is a primary lesion or a recurrent tumour does not appear to influence either local control or survival rates.<sup>[7,8,34]</sup> Recently, Kattan et al.<sup>[36]</sup> published a nomogram for predicting the probability of death from a soft tissue sarcoma within 12 years of surgery. Points were assigned based on tumour size, depth, site, histologic type, and patient age. Because pathologic grade is such a powerful prognostic factor in itself, the nomogram incorporated two separate parallel linear axes accounting for the difference between low- and high-grade lesions. A tumour located in the head and neck region represented the extreme on the site axis of the nomogram. This nomogram is statistically valid and allows clinicians to calculate sarcoma-specific survival for individual patients. In addition, this tool may allow oncologists to assign patients to various treatment regimens based on risk assessment.<sup>[36,37]</sup>

#### AUTHOR CONTRIBUTIONS

Participated in the conception and design of the manuscript, drafting of manuscript and literature search.

#### CONFLICT OF INTERESTS

The author declares that there is no conflict of interests that could influence this work.

#### FUNDING ACKNOWLEDGEMENTS

The author declares that there was no financial aid obtained from any source for the preparation of this manuscript.

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