Head and Neck Sarcomas
Epidemiology, Pathology, and Management

James Paul O'Neill, MB, MRCSI, MBA, MD, MMSc, ORL-HNS[a,*],
Mark H. Bilsky, MD[b], Dennis Kraus, MD[c]

KEYWORDS

• Sarcoma • Surgery • Radiation • Chemotherapy • Grade • Margins • Size

KEY POINTS

- Malignant fibrous histiocytoma, osteosarcoma, fibrosarcoma, angiosarcoma, rhabdomyosarcoma, and liposarcoma are the most frequently reported sarcomas in the head and neck.
- Sarcomas that metastasize to lymph nodes are clear cell, rhabdomyosarcomas, epithelioid, angiosarcoma, and synovial sarcomas.
- Sarcoma surgery demands a significant respect for tumor and pseudocapsule margins in an effort to succeed in gross disease removal with free microscopic margins. This removal can be challenging in an anatomically confined region such as the head and neck.
- Distant metastases occur in approximately 25% to 30% at diagnosis or during follow-up. The common sites of metastases are lung, bone, central nervous system, and liver. Patients require yearly chest imaging for life.

INTRODUCTION

Head and neck sarcomas are a diverse group of cancers. According to the American Cancer Society, in 2010 10,520 new sarcomas were predicted to occur, with 3920 deaths. Head and neck sarcomas account for approximately 2% to 15% of all sarcomas, representing approximately 1% of head and neck malignancies.[1] Sarcomas are classified according to their tissue of origin, which can be bone or soft tissue, whether the tumor is high or low grade, and the anatomic subsite of presentation within the head and neck. There lies an 80:20 distribution between these mesenchymal sarcomas of soft-tissue origin and those of bone and cartilage lineage. The increased use of the immunohistochemistry and molecular oncology markers has furthered our ability to definitively subclassify sarcomas; however, 20% will still remain unclassified, highlighting the challenges that remain.

Malignant fibrous histiocytomas (MFH), osteosarcomas, rhabdomyosarcomas, angiosarcomas, synovial sarcomas, and Ewing sarcomas are all considered high-grade tumors. Conversely, dermatofibrosarcoma protuberans, atypical lipomatous tumor, and desmoid tumor are predominately low grade. Chondrosarcoma, fibrosarcoma, liposarcoma, leiomyosarcoma, neurogenic sarcoma, and hemangiopericytoma require individualized grade characterization.[2] Grade is a key prognostic indicator according to the American Joint Committee on Cancer Staging (AJCC). Five-year survival rates for patients with grade 1 sarcomas was 100% in

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[a] Department of Head and Neck Surgery, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, USA; [b] Department of Neurosurgery, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, NY 10065, USA; [c] New York Head and Neck Institute, North Shore-Long Island Jewish Health System, New York, NY, USA
* Corresponding author.
E-mail address: joneill@rcsi.ie

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one series, compared with 64% for those with tumors of grades 2 and 3.[3]

Computed tomography (CT) and magnetic resonance imaging (MRI) offer 3-dimensional information for tumor locoregional extension, provide assessment of tissue composition (vascular vs avascular, solid vs liquid, fat vs cellular), and assist in successful biopsy and pathologic confirmation, surgical extirpation, and adjuvant radiotherapy planning. Superior soft-tissue resolution on MRI with multiplanar advances provides intimate anatomic information relevant in areas of complex anatomy such as the skull base. ^{18}F-labeled fluorodeoxyglucose (FDG) positron emission tomography (PET) scanning has been used clinically for tumor staging and restaging, monitoring treatment, and predicting prognosis. FDG PET has been found to be superior to conventional imaging in evaluating patients with the more common head and neck malignancies such as squamous cell carcinomas, lymphomas, and salivary gland cancers. PET scanning may also be superior to conventional imaging in staging of miscellaneous cancers of the head and neck, including melanomas, basal cell carcinomas, olfactory neuroblastomas, and sarcomas.[4–6]

Surgery is the primary mode of treatment. Adjuvant radiation therapy (RT) should be considered for patients with locally recurrent lesions and intermediate to high-grade tumors, and for those with close or positive margins. Patients with advanced, marginally resectable tumors should be considered for preoperative RT. Although the role of chemotherapy for head and neck soft-tissue sarcomas remains to be fully defined, adjuvant chemotherapy as a means to decrease the risk for disease recurrence in patients with localized soft-tissue sarcoma at diagnosis has been investigated. The majority of trials reported on have been hampered by patient heterogeneity, short follow-up, and low patient accrual.[7] Neoadjuvant chemotherapy is, however, a strategy used for high-grade sarcomas in many tertiary referral cancer centers.

Patients with unresectable disease have the worst prognosis, and are treated with RT alone or in combination with chemotherapy. It has been difficult to assess the efficacy of RT alone because of selection bias, but it is not considered as effective as surgery alone or combined with RT if used for tumors of similar stage.[8]

MALIGNANT FIBROUS HISTIOCYTOMA

In 1964 O'Brien and Stout[9] published the first article to describe MFH, which is now the most commonly diagnosed soft-tissue sarcoma in the head and neck. Most often MFH occurs in the extremities and the retroperitoneum, and is described as an undifferentiated high-grade pleomorphic sarcoma. This tumor largely presents in the fifth and sixth decades, contributes up to 40% of all sarcomas in the head and neck, and has a male to female predominance of 2:1. Women tend to present nearly a decade earlier. Three percent to 10% of all MFHs occur within the head and neck, with the majority of these occurring in the sinonasal tract. These tumors have a strong association with ionizing radiation exposure, most commonly used for a prior diagnosis of squamous cell carcinoma and lymphoma pathology.[2,10–13]

An MFH tumor is composed of an admixture of spindle-shaped fibroblastic tumor cells and bizarre mononuclear histiocytic tumor cells arranged in a storiform pattern with some multinucleated giant cells. Histopathologic differential of MFH includes anaplastic lymphoma, pleomorphic leiomyosarcoma, pleomorphic liposarcoma, malignant melanoma, malignant peripheral nerve sheath tumor, anaplastic carcinoma, malignant gliomas, or gliosarcoma.[14] There are 5 different histologic patterns of MFH: inflammatory, giant cell, myxoid, storiform-pleomorphic, and angiomatous. Immunopositivity for vimentin, α1-antichymotrypsin, and Ki-67 have been demonstrated in MFH and are of diagnostic importance. The tumor tissue should be immunonegative for S-100 protein and cytokeratins. Histiocytic markers CD68, α1-antichymotrypsin, and factor XIII are no longer used in the diagnosis of MFH, as immunoreactivity to these markers is nonspecific.[15]

Radiation-induced sarcoma tends to occur at the periphery of the radiation field, where the dose of radiation can permanently alter the cell's ability to perform routine repair tasks. To link past radiation exposure and sarcoma, the following criteria must apply. There must be a documented history of irradiation to the head and neck and the new malignancy arising within the irradiated field. The tumor must be histologically distinct from the original primary lesion, and the latency period between the radiation exposure and the development of the new malignancy must be 5 years or more. It is estimated that after head and neck radiotherapy, the incidence of radiation-induced sarcoma ranges from 0.03% to 2.2% in those surviving more than 5 years.[16] The threshold dose for radiation-induced sarcoma is unknown, but the increased risk seemingly correlates with increasing radiation dose.[17] Radiation-induced MFH carries a poor prognosis and accounts for almost 50% of radiation-associated soft-tissue sarcomas.[18] Overall survival from radiation-induced sarcoma ranges from 10% to 30% at 5 years.[19]

Surgery is the main treatment modality for MFH, with chemotherapy and radiation used in the adjuvant setting. The classic behavior of MFH is to recur locally, although rarely it metastasizes to regional lymphatics. Surgical resection for MFH requires wide field dissection with generous margins, and when possible the tumor is never grossly visualized at the resection margin. Of course this is sometimes not feasible, especially within anatomic constraints of the head and neck, but dedicated preoperative planning is essential for successful tumor extirpation and reconstruction of the operative deficit. Despite aggressive surgical management, positive margins are associated with an increase in local recurrence and distant disease. The role of chemotherapy as neoadjuvant or adjuvant therapy remains unproven, and our ability to perform a randomized trial is remote. Distant metastasis appears in one-third of all cases, and those cases mainly involve the lung, regional lymph nodes, liver, and bone.

Five-year overall, disease-free, and disease-specific survival rates are 55%, 44%, and 69%, respectively. The main negative prognostic variables for MFH include positive margins, tumors of the head and neck anatomic region, tumor size greater than 5 cm, and high stage.[20,21]

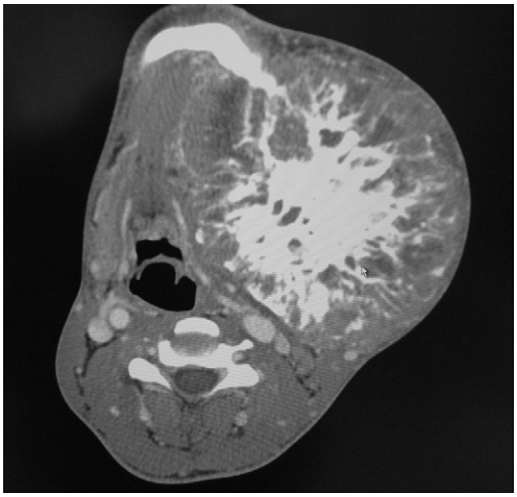

Fig. 1. A destructive mass measuring 11.0 × 11.6 × 12.5 cm in transverse by anteroposterior by craniocaudad dimension involving the left mandibular condyle, coronoid process, ramus, and proximal body with massive sunburst periosteal new bone formation and a large soft-tissue component.

OSTEOSARCOMA

Osteosarcomas (OS) represent approximately 1% of head and neck cancers and fewer than 10% of all osteosarcomas (**Figs. 1–4**).[22,23] Male to female distributions are similar. Patients present with OS of the head and neck in the third and fourth decades, in contrast to OS of the extremities, which generally afflicts teenagers. There are 3 subdivisions of conventional OS: osteoblastic, chondroblastic, and fibroblastic. Most OS will demonstrate components of all 3 subdivisions. There are also many other OS variants including multifocal, telangiectatic, small cell, intraosseous well-differentiated, intracortical, periosteal, parosteal, high-grade surface, and extraosseous OS.

Predisposition to this tumor is related to deletion of chromosome 13q14, which inactivates the retinoblastoma gene, bone dysplasias such as Paget disease, fibrous dysplasia, and enchondromatosis. Li Fraumeni syndrome due to germline TP53 mutations predisposes to osteosarcoma and Rothmund-Thomson syndrome. OS may also present de novo or after RT. These tumors have a classic radiologic appearance. In the extremities, the Codman triangle signifies subperiosteal bone formation. This feature is less frequently seen in the head and neck, where the classic "sunburst" appearance of malignant osteoid formation is observed.

These tumors originate more frequently in the metaphyseal region of extremity long bones, with

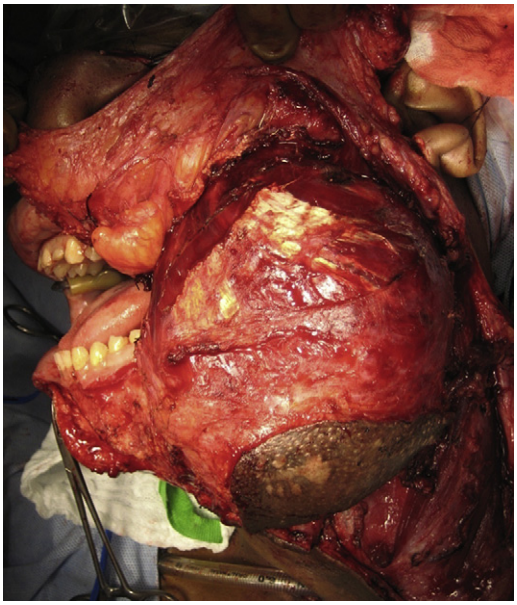

Fig. 2. Intraoperative photo of osteosarcoma. Lower cheek flap is elevated (with the parotid to protect the facial nerve) past the inferior border of the mandible to the level of the zygomatic process.

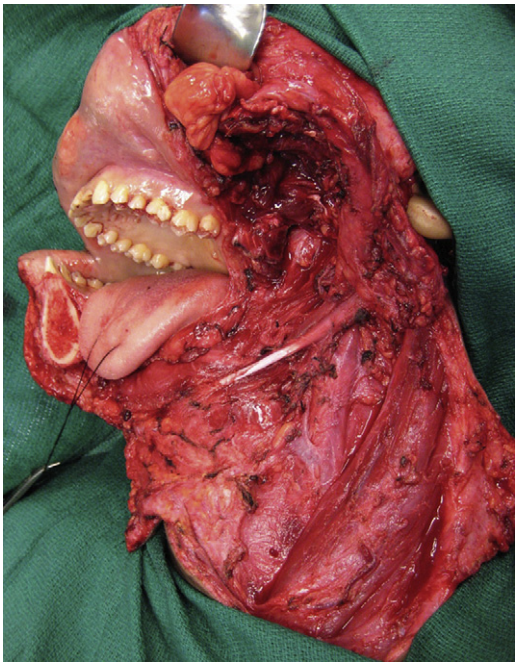

Fig. 3. Osteosarcoma. Tumor en bloc extirpation. Left neck dissection levels I, II, and III (sparing internal jugular, spinal accessory, and sternocleidomastoid muscle), left segmental mandibulectomy, and resection of floor of mouth. The patient then proceeded to have rectus abdominis myocutaneous flap reconstruction.

42% occurring in the femur, 19% in the tibia, and 10% in the humerus (8% pelvis). In 10% of cases, tumors occur within the head and neck. The mandible, maxilla, and skull are the common locations, with the mandible reported as the most common site. The posterior body of the ramus is the classic mandibular location. The alveolar ridge, sinus floor, and palate are classic maxillary tumor locations. As such, the common presenting features of these tumors include dental pain and loose teeth, or a painless mass.

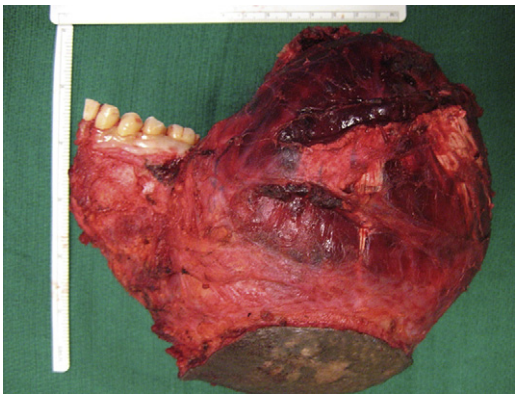

Fig. 4. Osteosarcoma. Operative specimen.

There is no formal consensus on what constitutes "best" treatment for adult OS. Surgery, radiation, and chemotherapy have been used singularly or in combination. Neoadjuvant therapy allows for the evaluation of the response to chemotherapy and can be an effective prognostic tool that helps in the selection of optimal adjuvant therapy. Osteosarcomas metastasize relatively early and there is good evidence that neoadjuvant chemotherapy, surgery, and adjuvant chemotherapy improve disease-free survival and overall survival.[24–26] Several drugs have been used that are active in the treatment of OS, including high-dose methotrexate with leucovorin rescue, adriamycin, cisplatin, ifosfamide, and cyclophosphamide. These drugs are administered in various combinations in an effort to destroy pulmonary micrometastases, which are considered to be present in at least 80% of extremity OS patients at the time of diagnosis.[27] Head and neck OS have a reduced likelihood of distant metastases, with only 7% to 17% of patients developing distant disease, most commonly to the brain or lung.[28,29]

A 3-fold improvement in disease-free survival was realized in the 1980s with the introduction of neoadjuvant chemotherapy in the treatment of extremity osteosarcoma in the pediatric population. The variants, especially dedifferentiated parosteal osteosarcoma and dedifferentiated well-differentiated intraosseous osteosarcoma, are more common in adults than in children, which may account, in part, for inferior prognosis in adults. Can we extrapolate the advantages of neoadjuvant chemotherapy, in particular in the pediatric population, to adults? There are several conflicting studies.[30,31] The Memorial Sloan Kettering Cancer Center (MSKCC) experience for head and neck OS could not demonstrate improved local control, decreased distant metastases, or improved disease-specific survival with the addition of neoadjuvant chemotherapy to conventional management.[32] Furthermore, the response to neoadjuvant chemotherapy is difficult to interpret clinically or radiologically because the bony architecture of the tumor does not allow the mass to "shrink," even if there is significant tumor necrosis. MSKCC reports 3-year overall, disease-specific, and recurrence-free survival rates of approximately 81%, 81%, and 73%, respectively.[32]

What is clear is that complete surgical excision to achieve negative surgical margins, especially of the involved bone, is crucial to local control, as well as recurrence-free and disease-specific survival. A positive margin carries with it a significant drop in survival from 75% to 35%.[28,33] It

would seem reasonable to administer neoadjuvant chemotherapy to patients with high-grade OS or lesions when initial resection is likely to incur the risk of positive surgical margins or a poor functional result. Routine node dissection is not required, given the low rates of cervical nodal metastases. Occasionally removal of neck nodes may facilitate removal of the tumor or be required if there is extension into the soft tissues of the neck. M.D. Anderson indicated that radiation (at doses of 55–60 Gy) improved local control, disease-specific survival, and overall survival for patients with OS of the head and neck with a positive or uncertain resection margin after surgery.[23]

ANGIOSARCOMA

Angiosarcomas represent one of the most challenging sarcomas in head and neck cancer. These lesions are malignant endothelial cell tumors of lymphatic or vascular origin, found primarily in elderly patients (85% of patients >60 years[34]), with men affected twice as frequently as women. There is no agreed treatment consensus, with scattered phase 2 and no phase 3 trials reported in the literature. Angiosarcomas, which are most commonly characterized by immunohistochemical staining for CD31, may arise in any soft tissue or viscera, and cutaneous angiosarcomas typically involve the scalp. Several risk factors exist for the development of angiosarcoma, including radiation-induced (typically 5–10 years postradiation[35]); chronic lymphedema; Milroy syndrome; exogenous toxins including vinyl chloride, arsenic, and anabolic steroids; and familial syndromes including BRCA 1, BRCA 2, Nf-I, Maffucci syndrome, and Klippel-Trenaunay syndrome.[36] Angiosarcomas can be divided into multiple subcategories, including primary cutaneous angiosarcoma, radiation-associated angiosarcoma, primary breast angiosarcoma, and soft-tissue angiosarcoma. A microarray analysis of 222 angiosarcoma specimens describes high levels of expression of VEGF-A, VEGF-C, KIT, phospho-AKT, phospho-4eBP1, and eIF4E, with significant correlative associations between KIT and p-AKT, as well as p-AKT and VEGF-A, VEGF-C, p-4eBP1, and eIF4E.[37]

Angiosarcoma has two clinical presentations in the head and neck. The first is a nodular strawberry-like lesion and the second is an ecchymotic diffuse lesion presenting most commonly on the scalp. Between 20% and 45% of patients have distant metastases on presentation.[38,39] The main prognostic indicators are size (>5 cm), high grade, and anatomic site (scalp) of presentation.[40–43]

Angiosarcoma is such a rare entity that it requires an individual therapeutic approach for each patient. Surgery and adjuvant RT are most commonly quoted treatment strategies; however, diffuse tumor margins often inhibit satisfactory oncologic excision and hence the necessity for an adjunctive and potentially neoadjuvant therapy.[40,43,44] What type of surgery should be performed on these often elderly patients? Given the poor survival statistics that accompany this diagnosis, an efficient one-step surgical procedure to facilitate negative surgical margins when feasible is desirable. Let us consider the scalp and its extensive vascular network. Various arterial branches from the internal and external carotid, for example, occipital, supratrochlear, and superficial temporal arteries, form anastomoses in the subcutaneous and subgaleal layers. There are also draining venous outlets that follow the arteries, and emissary veins drain to the sagittal sinus of the brain.[45] This elaborate communication system allows for rapid malignant dissemination of angiosarcoma. Tumor extirpation, confirmation of surgical margins, and resurfacing with a split-thickness skin graft is a rapid and reliable technique which, though rarely feasible, allows patients to receive adjunctive therapy in a timely fashion. It must be said that in this disease although a negative margin is gratifying, it does not correlate with survival in several studies.[46,47] RT has been shown to improve survival rates in combination with chemotherapy, with reduced local recurrence. Some investigators even suggest definitive radiation without surgical intervention with or without chemotherapy may offer sufficient primary local control.[41,48,49] The fact that 20% to 45% of patients present with distant metastases emphasizes the importance of effective systemic chemotherapy. However, its role in the literature is debated. Some studies report improved outcomes with the administration of chemotherapeutic agents such as doxorubicin, ifosfamide, cyclophosphamide, dacarbazine, paclitaxel, interferon, and interleukin-2.[39,49,50] Other investigators have not shown improved outcomes with chemotherapy.[44,46,51]

In nonmetastatic angiosarcoma, a personalized treatment approach starting with consultation with multidisciplinary colleagues is appropriate. Combined modality therapies are applied with surgical extirpation with wide 2-cm margins and adjunctive RT of 60 to 66 Gy to wide treatment fields. Neoadjuvant or adjuvant taxane (antiangiogenic activity) therapy is used in selected cases. Angiosarcoma tumors of the scalp and neck have a 10-year relative survival rate of 13.8%, highlighting the challenges that remain in offering meaningful cancer care.[34]

RHABDOMYOSARCOMA

Rhabdomyosarcoma (RMS) is a pediatric sarcoma that rarely occurs in adults (**Figs. 5** and **6**). Using the Surveillance, Epidemiology, and End Results Program, between 1973 and 2007 the incidence of RMS of the head and neck has increased significantly, with an annual percentage change of 1.16%.[52]

RMS in the pediatric age groups has changed, with a dramatic improvement in survival from 25% in the early 1970s to 71% by 2001. This improvement can be attributed to the formation of 3 pediatric cooperative cancer study groups, the Intergroup Rhabdomyosarcoma Study Group (IRSG) in 1972, and the more recent Children's Oncology Group (COG) and COG Soft Tissue Sarcoma (COG-STS). These groups stand as an example of the benefits of academic and clinical cooperation, with survival advantages attributed to improved staging, risk stratification, local therapy, and supportive care.[53]

There are two main pathologic entities, embryonal and alveolar, which are pathologically distinct. In contrast to other sarcomas, the head and neck is the common site where it occurs. Success in management has been largely credited to multiagent chemotherapeutic regimens introduced by IRSG. Early response to therapy by radiologic imaging does not predict long-term failure-free survival (FFS). The difficulty is that CT and MRI modalities are poor at distinguishing residual viable tumor from necrotic tumor or scar tissue. The role of PET scanning is actively being investigated in terms of both tumor response to therapy and the role in detecting metastatic disease in bone and lymphatics.[54,55]

Intergroup Rhabdomyosarcoma Study IV (IRS-IV) emphasized that therapy for children with RMS should be risk directed and based primarily on tumor site, histology, and extent of disease.[56] IRS-V used the concept of risk stratification to conduct studies based on clinical and biological prognostic factors. Risk stratification is based on pretreatment staging and a surgical and pathologic clinical grouping established by IRSG.[57,58]

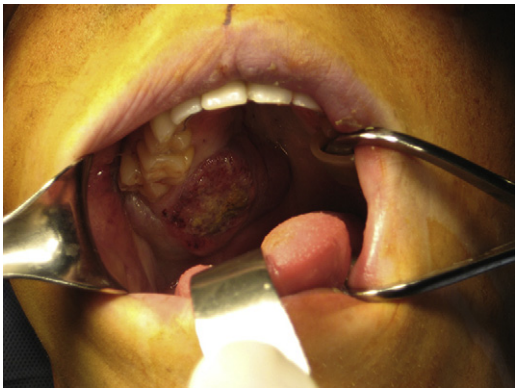

Fig. 5. Alveolar rhabdomyosarcoma of the hard palate in a 22-year-old man after chemoradiation, requiring salvage surgery.

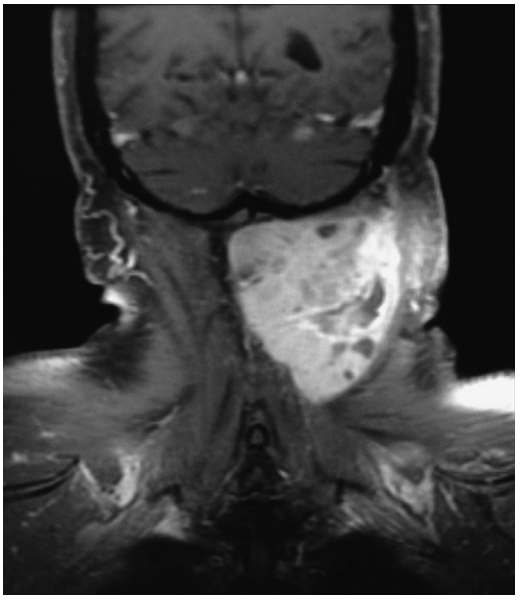

Fig. 6. Adult rhabdomyosarcoma of the posterior neck musculature in a 70-year-old man.

The clinical group is based on the extent of residual tumor after surgery (when possible) with consideration of regional lymph node involvement. The IRS staging system is based on tumor size, invasiveness, nodal status, and site of primary tumor. Two other prognostic factors are tumor histology and age at diagnosis. Clinical grouping and staging are highly predictive of outcome.

Three-year FFS rates for patients on IRS-IV were 83% for group I, 86% for group II, and 73% for group III. Patients with group IV (metastatic) RMS have long-term FFS rates of less than 30%. For IRS-IV, 3-year FFS rates were 86% for stage 1, 80% for stage 2, and 68% for stage 3.[56,59,60]

Pediatric patients younger than 10 years more commonly present with embryonal RMS (ERMS). In patients older than 10 years, alveolar RMS (ARMS) is the most common diagnosis. Age is also an independent prognostic factor in IRS-III and IRS-IV. Infants have a worse outcome because of increased local failure.[61] In infants and adolescents survival is decreased, owing to the higher frequency of undifferentiated or alveolar histiotypes.

The results from IRS-III and IRS-IV facilitate the placement of patients within low, intermediate, and high risk stratifications. Patients with clinical

and biological features that place them in a low risk stratification have a 3-year FFS of 88%, and include 2 subsets of patients. Low-risk subset 1 is stage 1, group I/IIA; stage 2, group I; and stage 1, group III (orbit only) ERMS. Low-risk subset 2 is stage I, group IIB/IIC, or group III (nonorbit).

Nonmetastatic ERMS (stage 2, 3, group 3) are considered to have intermediate-risk RMS and have a 5-year FFS of 73%. In addition, patients with ARMS (stage 1–3, groups I–III), with a 5-year FFS of 65%, are included in the intermediate-risk category. Patients younger than 10 years with metastatic disease were also included within the intermediate category. High-risk stage 4, group IV RMS (ERMS >10 years of age and ARMS of any age) have an estimated FFS of less than 20%.[53]

The more recent COG studies apply varying chemotherapeutic combinations to assess response using the risk-stratified patient populations.[62,63] The many drugs that have been used include vincristine, dactinomycin, doxorubicin, ifosfamide, etoposide, cyclophosphamide, actinomycin-D, topotecan, irinotecan, cixutumumab, and temozolomide.

Outcomes in adult patients with rhabdomyosarcoma are poor, with a 5-year survival rate of approximately 30%. In adolescents and adults there is a greater predilection for alveolar and pleomorphic (malignant fibrous histiocytoma morphologic similarities) histopathologic subtypes and anatomic presentation within truncal or extremity sites. Females may have a treatment and overall survival advantage.[64] One of the questions still unanswered is, can we extrapolate the results and experience of the pediatric populations to adults? This point of conjecture will be a subject of debate at ASCO 2012, and further studies are awaited for clarification.

Another area of RMS that is gaining momentum is the gene status of the tumor. Unlike other pediatric embryonal tumors such as neuroblastoma and medulloblastoma, the current risk stratification does not formally use any molecular or genetic data. The genetic characteristics may eventually be included within the risk stratification, along with clinical features. The *PAX3/FOXO1* fusion gene was discovered in 1993.[65] The *PAX3/FOXO1* fusion gene, resulting from the stable reciprocal translocation of chromosomes 2 and 13, is a signature genetic change found only in ARMS, and is thought to be in part responsible for its malignant phenotype. The presence of PAX3/7-FOXO1 translocation in adult patients is significantly associated with a higher frequency of metastatic disease. There are reports that PAX3-FOXO1 exerts pleiotropic effects, including increasing cell proliferation, promoting cell survival, suppressing terminal differentiation, promoting invasive characteristics, and supporting angiogenesis.[66] Positivity of this gene may have a negative prognostic impact; however, how to incorporate this within the current stratifications is challenging. A recent study reported the *PAX3/FOXO1* fusion gene status can be combined with just 2 other variables (ie, IRS TNM stage and age at diagnosis) to make an effective prognostic risk classifier.[67]

LIPOSARCOMA

Liposarcomas account for 35% to 45% of all soft-tissue sarcomas.[68] Approximately 2% of liposarcomas present within the head and neck region, and as such there is a limited reporting of these tumors in the literature. The remaining liposarcomas are reported within the extremities and retroperitoneum.[69] There is a male predominance, and etiologic factors include Nf-1 gene, trauma, and irradiation. There are several subtypes that include well-differentiated, myxoid, pleomorphic, and round cell tumors. Well-differentiated and myxoid are considered low grade, whereas pleomorphic and round cell are high-grade tumors. Survival is determined by subtype of tumor, grade, size, and anatomic site of presentation.

In a study of 76 patients the principal determinant of outcome was histologic grade. Five-year survival was 100% for well-differentiated, 73% for myxoid, 42% for pleomorphic, and 0% for round cell liposarcomas.[69]

Disease-specific survival in a study of 30 patients reported 100% for well-differentiated and myxoid variants, 60% for round cell, and 45% for pleomorphic liposarcomas.[68] The difficulty with these tumors is local recurrence. In particular, in the head and neck a compartmental resection, which is possible in the extremities, is restricted by vital neurovascular structures. Thus postoperative RT is frequently undergone. Radiation improves local recurrence; however, it may not have any impact on overall survival. Local recurrence can be reduced from 60% to 40% with the addition of radiation.[70] In 1954 a study of 105 patients reported improved 5-year survival of 88% for surgery plus radiotherapy, versus 67% for surgery alone. More recently a study of 76 patients from the Royal Marsden in London reported a 5-year survival rate of 83% for surgery and radiotherapy versus 63% for radiotherapy alone.[69] In 7 trials from Europe (with a total of 2185 patients) with advanced liposarcomas, adjuvant radiation had a significantly higher control rate of 36% compared with other soft-tissue sarcomas.[71]

It is agreed that surgery with negative margins is the gold-standard treatment for all histologic

subtypes of liposarcomas. Adjuvant radiotherapy is used for high-grade tumors, large tumors and positive margins. Round cell and pleomorphic tumors may metastasize to the lungs, and a yearly chest radiograph is advised.

FIBROSARCOMA

Fibrosarcomas and MFHs share common histopathologic similarities. Fibrosarcomas present in the fourth and fifth decades and most commonly present with a painless mass. Radiation exposure is again a well-documented etiologic factor, with 10% of patients having prior radiation exposure.[72]

A study of 29 patients in 1991 reported an absolute 5-year survival of 62%. Tumor grade was the most important prognostic factor, followed by tumor size and surgical margin status identified in the study.[73] A study of 132 cases reported the cumulative probability of distant metastases was 34% at 1 year, 52% at 2 years, and 63% at 5 years. Distant metastases occurred as late as 22 years after surgery, and metastasis was not significantly associated with surgical margin.[74]

Patients with low-grade lesions and adequate surgical margins are sufficiently treated with surgery alone. Patients with high-grade lesions or positive surgical margins should receive adjuvant RT. Fibrosarcomas have an improved prognosis compared with other sarcomas, with 5-year survival of up to 82%.[2]

CHONDROSARCOMA

Chondrosarcomas are rare tumors (**Fig. 7**). The gross appearance of these tumors is similar to that of other benign chondroid tumors; a smooth, grayish-white hue with a pedunculated and/or friable granular appearance. Myxoid and mesenchymal chondrosarcoma subtypes constitute a substantial portion of head and neck cases. The myxoid variant is an extraskeletal tumor arising in soft tissues and most commonly in the extremities.[75] Mesenchymal chondrosarcomas are recognized as aggressive tumors, as they have a tendency to be high grade. Immunohistochemical and cytogenic studies have identified features similar to those of Ewing sarcoma. Low-grade chondrosarcomas may be difficult to discriminate, from a histopathologic perspective, from osteochondroma, enchondroma, or synovial chondromatosis. Conversely, high-grade tumors may also have histopathologic similarities to tumors such as chondroblastic osteosarcoma, fibrosarcoma, or malignant fibrous histiocytoma.

The National Cancer Database Report of chondrosarcomas in 2000 noted that owing to the rarity

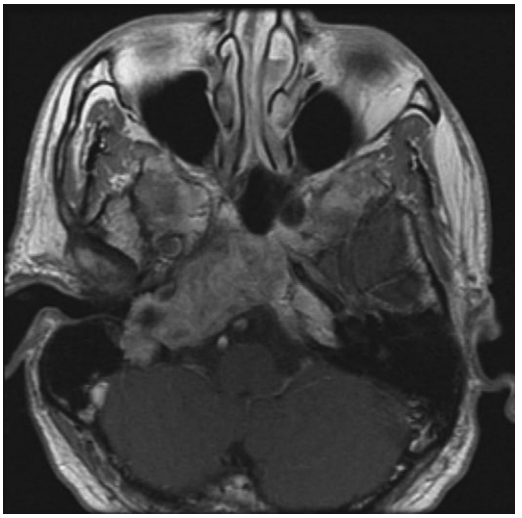

Fig. 7. T1-weighted magnetic resonance postcontrast images of a chondrosarcoma demonstrating enhancement, ruling out other pathology such as a cholesteatoma. The classic paramedian position is noted.

of this disease, it was not possible to accrue a sufficiently large patient population to statistically analyze the impact of proton ocular RT on survival.[76] The anecdotal benefit of RT has long been recognized; however, there are no randomized or nonrandomized prospective studies to suggest where and when RT should be used. Traditionally RT was reserved for inoperable recurrence or inadequate surgical margins. In 1984 Harwood and colleagues[77] reported that chondrosarcomas may indeed be radioresponsive after a long-standing belief that these tumors were radioresistant. This proposal was explained by observations that these tumors had an extracellular matrix, low percentage of dividing cells, and limited vascularity.[78] Further anecdotal reports emerged of an adjunctive response in advanced disease, cases of positive margins, or surgically unresectable tumors.[79,80] Chondrosarcomas are still considered relatively radioresistant tumors and require greater than 65 Gy. Conventional external beam RT with photons has considerable morbidity, especially for lesions at the skull base. Proton beam therapy, on the other hand, has been used to deliver high-energy doses to the tumor while minimizing scatter to adjacent critical anatomic structures; this relates to a minimal exit dose after energy deposition in the target volume.[81] Furthermore, proton therapy has a small but appreciably greater biological effective dose. The first article of the benefits of proton therapy reported 3 cases of skull-base chondrosarcomas treated with surgery and postoperative proton

beam therapy mixed with photons. Local control rates at 5 years of up to 85% to 100% have been reported with mixed photon-proton and proton-only protocols.[82–84]

Intensity-modulated RT (IMRT) allows for the delivery of high-dose conformal photons using either standard fractionation, as with protons, or hypofractionated regimens. No data regarding outcomes for skull-base chondrosarcomas exist, but IMRT allows for the delivery of doses within the range that can control skull-base chondrosarcomas. With regard to other adjuvant treatments for chondrosarcoma, there are no definitive reports in the literature supporting the role of adjunctive chemotherapy in the management of these tumors despite the theoretical advantage of chemotherapy in patients with high-grade tumors, with a high risk of distant dissemination.[85] Similarly, there is no palliative benefit reported in the literature. In the absence of proven tumoricidal effect for chondrosarcomas, chemotherapy has no current role in management. In terms of management of the neck, the authors do not recommend elective neck dissections in clinically and radiographically negative necks. The literature also rarely reports regional or distant metastatic disease at presentation.[86,87]

SUMMARY

Soft-tissue sarcomas are a diverse group of mesenchymal tumors with distinct prognostic implications. These tumors present relatively rarely in the head and neck region, with the exception of pediatric rhabdomyosarcoma. Surgery remains the main therapeutic option with the exception of rhabdomyosarcoma, Ewing sarcoma, and angiosarcoma, for which chemoradiation or neoadjuvant chemotherapy is the preferred first-line treatment. Positive margins, large tumors, and high-grade histology continue to have an impact on local control and overall survival.

The sarcoma story is far from complete, and improved histopathologic classification and combined modality therapy are necessary for translation to improved overall survival in both adult and pediatric patients.

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