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Handout For:
Soft Tissue and Bone Tumors of the Head and Neck with Emphasis on Recently Described Entities and Ancillary Studies

Case 1 – Mesenchymal Chondrosarcoma

Mesenchymal chondrosarcoma accounts for approximately 3% of all chondrosarcomas. It can arise at any age but has a peak in the second and third decades with an equal sex predilection. Tumors arise over a wide distribution of anatomic sites. The craniofacial bones, especially the jaw bones, the ribs, the ilium and the vertebrae are the most common sites. A minority of lesions arise in the deep soft tissues, especially around the skull base. Radiologically, skeletal lesions are lytic and destructive with occasional calcifications.

Grossly, the tumors are grey-white to gray-pink, form soft, and usually well-defined, circumscribed masses ranging up to 30 cm in size. Most lesions contain hard, mineralized areas with some tumors showing a clearly cartilaginous appearance. Necrosis and hemorrhage may be present.

Histologically, mesenchymal chondrosarcoma is composed of nodules of tumors cells with an infiltrative growth pattern. It has a biphasic appearance which is the histological hallmark. The tumors are composed of sheets of small round to oval cells admixed with a cartilaginous component that ranges from primitive chondroid islands to more obviously cartilaginous areas. The cellular areas range from having an appearance similar to Ewing sarcoma to those lesions resembling poorly differentiated synovial sarcoma. A myopericytoma-like vascular pattern is common. The amount of the cartilaginous component is variable and can be almost completely absent/very focal. Cytologically, the lesional cells are uniform, tend to have round to oval nuclei, scant cytoplasm, and mitotic figures can be numerous. Hyalinization, necrosis, and hemorrhage can be seen.

The immunophenotype is non-specific. In particular, CD99 can be positive in a membranous pattern but is usually less extensive than what is seen in Ewing sarcoma. Lymphoma markers (CD3, CD20, CD43) are useful in excluding lymphoma or other hematological neoplasms.

A recurrent *HEY1-NCOA2* fusion is present in virtually all mesenchymal chondrosarcomas, consisting of an in-frame fusion of exon 4 of *HEY1* to exon 12 of *NCOA2.* Since *HEY1* and *NCOA2* are about 10 Mb apart on chromosome 8q, the fusion is thought to arise from a small interstitial deletion.

Mesenchymal chondrosarcoma is an aggressive lesion with the potential for local recurrence and distant metastasis.

The differential diagnosis includes mainly Ewing sarcoma, lymphoma, and poorly differentiated synovial sarcoma. The biphasic appearance is distinctive. It is helpful to submit additional tissue in cases with only focal cartilaginous differentiation. The presence of the *HEY1-NCOA2* gene fusion is diagnostic, since this genetic abnormality is not seen in any other type of tumor.

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Case 2 – Solitary Fibrous Tumor – Giant Cell Variant

If extrapleural solitary fibrous tumor isn't the most common soft tissue tumor, it is one of them. However, there are a variety of histological variants including cellular, myxoid, giant cell-rich and fat-forming (also known as lipomatous hemangiopericytoma) that can be confusing. Giant cell-rich/giant cell angiofibroma variant was originally described by Dei Tos and Fletcher in 1995 as giant cell angiofibroma, a tumor with a predilection for the soft tissue around the eye. Indeed, most of the examples in my files are from around the eye. However, these lesions do occur at other sites less commonly and over time, the existence of hybrid cases with convincing areas of conventional solitary fibrous tumor suggested to soft tissue pathologists that giant cell angiofibroma was a variant of solitary fibrous tumor. In the latest edition of the WHO Classification of Tumours of Soft Tissue and Bone, giant cell angiofibroma has been included in the section on extrapleural solitary fibrous tumor as a histological variant.

Recently, it was discovered that solitary fibrous tumors possess a *NAB2-STAT6* fusion. Chimielecki et al. found the fusion in 100% of SFTs, while Robinson et al. identified it in about 55% of cases. However, it is clear that Robinson's study was suboptimal and they missed a lot of cases. It really looks like *NAB2-STAT6* is pathognomic for SFT and seen in a high percentage (at least 90%) of cases. STAT6 is usually a cytoplasmic protein but NAB2-STAT6 fusion results in nuclear localization and strong expression. This has been exploited immunohistochemically. Several studies have been published showing high sensitivity and specificity for STAT6 IHC as a diagnostic marker for SFT. These studies have also shown that all of the histological variants of SFT, including meningeal HPC are positive for STAT6. STAT is also diffusely and strongly positive in malignant SFTs and CD34 negative SFTs. Finally, the only example of a non-SFT neoplasm that has been identified to be positive for STAT6 is dedifferentiated liposarcoma, which occasionally falls into the differential diagnosis of SFT. STAT6 is sometimes included in the 12q12-15 amplicon which is always amplified in dedifferentiated liposarcoma, explaining while some

cases of dedifferentiated liposarcoma are positive for STAT6 IHC. We haven't really studied it in detail but based on Leona Doyle's paper and our own experience, dedifferentiated liposarcomas show immunoreactivity for STAT6 less than 5% of the time. However, SFTs are not amplified for *MDM2* so they are negative by MDM2 IHC and non-amplified for *MDM2* FISH.

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Case 3 – Epithelioid Hemangioendothelioma

Epithelioid hemangioendothelioma (EHE) is a malignant tumor showing vascular differentiation. It can arise at any age but is most common in young adults. Women are affected more than men, approximately 4:1 for liver lesions. EHE can arise at any anatomic site including visceral organ involvement, skin, soft tissue and bone. The majority of patients present with widespread metastatic disease involving some combination of liver, lungs and bone.

Histologically, EHE is typically composed of a poorly circumscribed/infiltrative proliferation of cords and strands of small epithelioid cells set in a chondromyxoid matrix. Importantly, EHE is a primitive lesion and does not form proper blood vessels. The lesions are often centered on small to medium-sized blood vessels. The lesional cells are monomorphic and have round nuclei with fine chromatin, a moderate amount of pale, eosinophilic cytoplasm and are frequently mono-vacuolated (so-called blister cells), occasionally containing a red blood cell. Mitotic

activity is usually sparse. Larger lesions, especially in the liver can be necrotic, possibly due to ischemia.

Immunohistochemistry reveals the lesional cells to be positive for endothelial markers including CD31, CD34, ERG, and FLI1. Occasional cases are also positive for keratin in a variable proportion of cells from focal to extensive. EHE is also positive for CAMTA1 which is sensitive and specific for the diagnosis of EHE.

At the molecular level, EHE is characterized by a t(1;3)(p36;q23-25) translocation that results in fusion of *WWTR1* (also known as *TAZ*) to *CAMTA1*. The presence of this gene fusion is pathognomonic for EHE and is quite sensitive, being seen in over 90% of cases. TAZ is a transcription factor and fusion of TAZ to CAMTA1 results in a constitutively nuclear form of TAZ that drives oncogenesis. *TAZ-CAMTA1* is a sensitive and specific marker for the diagnosis of EHE. As mentioned above, CAMTA1 IHC is also a sensitive and specific marker for the diagnosis of EHE.

EHE has a fascinating clinical course. Solitary skin lesions have an excellent prognosis while lesions involving deep soft tissue and visceral organs tend to behave more aggressively. While EHE can be quite indolent, with some patients surviving many years with widespread metastasis, many patients eventually progress and succumb to the disease. Pleural and peritoneal involvement has a particularly grim prognosis. Some have suggested that solid growth and increased mitotic activity merits the designation of high-grade EHE. However, I do not use this grading system as this concept was put forward before the discovery of the gene fusion and some of the cases graded as high-grade may actually represent epithelioid angiosarcomas. I do not grade EHE since it has such an unpredictable clinical course.

EHE has a very characteristic histological appearance. The differential diagnosis includes epithelioid hemangioma, pseudomyogenic hemangioendothelioma, epithelioid angiosarcoma, and carcinoma (e.g. lobular breast carcinoma). In contrast to EHE, epithelioid hemangioma is more vasoformative, can be positive for FOSB by IHC and contains *FOSB* gene fusions. Pseudomyogenic hemangioendothelioma (also known as epithelioid sarcoma-like hemangioendothelioma) tends to have a more spindled appearance, lacks prominent chondromyxoid stroma, is always positive for AE1/AE3 keratin, is negative for CD34, *SERPINE1-FOSB* gene fusions and expresses FOSB by IHC. Epithelioid angiosarcoma has a more solid growth pattern with larger cells, prominent nucleoli, increased mitotic activity including atypical mitotic figures, and necrosis. Carcinoma is a notorious diagnostic pitfall since some EHE can have extensive keratin expression. In contrast to EHE, carcinomas lack expression of vascular markers. EHE is the only lesion in the differential diagnosis that is positive for CAMTA1 by IHC and has a *WWTR1-CAMTA1* gene fusion.

Of note, Dr. Antonescu and colleagues described an EHE 'variant' known as *YAP1-TFE3* translocated EHE. This variant is characterized by more solid growth with areas that are vasoformative, reminiscent more of epithelioid hemangioma. The lesions are positive for vascular markers, TFE3 and have *YAP1-TFE3* gene fusions. These are extremely rare – I have

only seen two cases in my consult files. Provisionally, I consider them a different entity than conventional EHE described above. They appear to be more aggressive clinically than epithelioid hemangioma.

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Case 4 – Biphenotypic Sinonasal Sarcoma

Biphenotypic sinonasal sarcoma is a distinctive low-grade sarcoma exclusively involving the sinonasal region. It occurs over a wide age range and has a predilection to occur in middle-aged females. It occurs most frequently in the nasal cavity and ethmoid sinus.

Grossly, tumors are tan and present as polypoid masses with a locally destructive growth pattern with invasion into surrounding bony structures. Histologically, these neoplasms are reminiscent

of monophasic synovial sarcoma. They are cellular neoplasms, composed of a monotonous population of spindle cells arranged in a dense fascicular (herringbone) growth pattern, admixed with hemangiopericytoma-like blood vessels. The nuclei are oval to wavy in shape with fine chromatin and a moderate amount of palely eosinophilic cytoplasm. Mitotic activity is low and necrosis is rare. Rare cases (of a rare neoplasm) show obvious rhabdomyoblastic differentiation.

By immunohistochemistry, the lesions are distinctive and positive for both S-100 and myogenic markers, hence the name "biphenotypic". S-100 ranges from focal to diffuse and smooth muscle actin, muscle-specific actin, and desmin are variably positive. Focal positivity can be seen for keratin and EMA. Recently, Jo and Colleagues demonstrated PAX3 expression to be sensitive and specific for the diagnosis of biphenotypic sinonasal sarcoma.

At the molecular level, *PAX3* gene fusions are seen in most cases. 55% of cases harbor *PAX3-MAML3* fusions, 25% have *PAX3* fusions with an unknown partner, 7% have *PAX3-NCOA1* fusions, 2% have *PAX3-NCOA1* fusions, 2% have fusions with *MAML3* and an unknown partner and 9% are fusion negative.

Biphenotypic sinonasal sarcomas have locally aggressive clinical behavior with frequent invasion of bony structures but no cases have metastasized thus far.

The differential diagnosis includes monophasic synovial sarcoma, malignant peripheral nerve sheath tumor, and cellular schwannoma. All three of these neoplasms can have a similar appearance to biphenotypic sinonasal sarcoma. However, their immunohistochemical and genetic characteristics are very different. Synovial sarcoma is focally positive for EMA and cytokeratin and harbors *SYT-SSX* gene fusions. Malignant peripheral nerve sheath tumor is variably positive for S-100. Cellular schwannoma is diffusely and strongly positive for S-100 and SOX10. Biphenotypic sinonasal sarcoma is positive for S-100 and myogenic markers and typically harbors *PAX3* gene fusions.

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Case 5 – Spindle cell/Sclerosing Rhabdomyosarcoma

Spindle cell/sclerosing rhabdomyosarcoma is an uncommon variant of rhabdomyosarcoma with spindle cell morphology. It affects both children and adults with a pronounced bias in males of about 6:1. In children, most tumors arise in the paratesticular region while in adults, the head and neck region is most common with about 50% of tumors arising in this location.

Grossly, tumors appear well circumscribed but unencapsulated with an average size of 4-6 cm. The cut surface is gray and white and whorled. Histologically, tumors are infiltrative and composed of intersecting fascicles of uniform spindle cells. The lesional cells have ovoid or elongated nuclei, vesicular chromatin, inconspicuous nucleoli and scant, palely eosinophilic cytoplasm. Occasional rhabdomyoblasts may be present and cross-striations can also be seen rarely. Occasionally, there is extensive collagen deposition with tumor cells arranged in nests or trabeculae with a pseudovascular appearance – this is the sclerosing variant which is on a continuum with spindle cell rhabdomyosarcoma. Nuclear hyperchromasia and mitotic activity are common.

Spindle cell/sclerosing rhabdomyosarcoma is positive for desmin, muscle specific actin, and nuclear expression of MYF4 (myogenin) and MYOD1. Smooth muscle actin tends to be less positive. Tumor cells are negative for S-100, GFAP, caldesmon and HMB-45.

At the molecular level, spindle cell rhabdomyosarcoma in adults possess recurrent mutations in *MYOD1* while spindle cell rhabdomyosarcoma in children harbor recurrent *NCOA2-VGLL2* gene fusions.

Spindle cell/sclerosing rhabdomyosarcoma in children has a favorable prognosis while in adults, it is an aggressive tumor with a poor prognosis in adults.

The differential diagnosis in the head and neck region includes mainly leiomyosarcoma, metaplastic carcinoma, desmoplastic melanoma, malignant peripheral nerve sheath tumor with rhabdomyoblastic differentiation and monophasic synovial sarcoma. In contrast to spindle cell rhabdomyosarcoma, leiomyosarcoma is uniformly positive for smooth muscle actin and can be positive for H-caldesmon. It is negative for myogenin and MYOD1. Metaplastic carcinoma tends to be more pleomorphic, is positive for keratins and is negative for myogenic markers. Desmoplastic melanoma is positive for S-100 and SOX10 and negative for myogenic markers.

MPNST and synovial sarcoma tend to have a much higher nuclear to cytoplasmic ratio, imparting a “blue” appearance to the tumor. Rhabdomyoblasts can dominate MPNST but when this happens, they typically have an appearance more similar to embryonal rhabdomyosarcoma.

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Case 6 – Low-grade Myofibroblastic Sarcoma

Low-grade myofibroblastic sarcoma (LGMFS), is classified by the World Health Organization as an intermediate (rarely metastasizing) fibroblastic / myofibrobastic tumor. It falls into the differential diagnosis of fibromatosis because it has a similar histological appearance.

Clinically, it occurs mostly in adults and has a wide anatomic distribution but it has a tendency to arise in the head and neck, especially the tongue and mouth region. Grossly, the lesions are poorly circumscribed and firm and tan on cut section. Histologically, they have a very infiltrative growth pattern, similar to desmoid-type fibromatosis. They are composed of fascicles of spindle cells with pale eosinophilic cytoplasm. In contrast to desmoid-type fibromatosis, LGMFS has at least moderate cytological atypia with enlarged, hyperchromatic nuclei. Mitotic figures can be identified but they are typically not numerous. By immunohistochemistry, the lesional cells show variable immunoreactivity for actin and/or desmin, consistent with a myofibroblastic phenotype. Calponin and CD34 may also be positive. S100, epithelial markers, and β-catenin are negative. There are no consistent genetic aberrations identified so far.

LGMFS has a propensity for local recurrence but metastasis is very rare.

The differential diagnosis includes mainly extra-abdominal desmoid fibromatosis. In contrast to desmoids, LGMFS has prominent cytological atypia and is negative for nuclear β-catenin.

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Case 7 – Spindle Cell/Pleomorphic Lipoma

Spindle cell / pleomorphic lipoma is an important neoplasm because it is very common and has a range of histological appearances that are not often appreciated, leading to diagnostic confusion. Historically, spindle cell and pleomorphic lipomas were thought to represent different tumor entities. However, as is seen with many other soft tissue tumors, the shared clinical features and lesions with combined features led to the realization that they were part of the histological spectrum of a single entity – spindle cell / pleomorphic lipoma.

Typically, spindle cell lipomas occur in the subcutaneous tissues of the upper back / neck or around the face of middle-aged to elderly males. While cases are reported in women, they are rare. Also, in my experience, the diagnosis of spindle cell lipoma in other anatomical sites is almost always wrong and often times, the mistaken neoplasm is aggressive or malignant. Thus, I don't recommend that anyone other than bona fide soft tissue pathology experts make the diagnosis of spindle cell / pleomorphic lipoma at other anatomical sites besides the subcutaneous tissues of the upper back / neck or face of middle-aged to elderly males. Conversely, one of the golden rules of soft tissue pathology is that any lesion in the subcutaneous tissues of the upper back / neck of an elderly to middle aged male is a spindle cell lipoma until proven otherwise.

Grossly, spindle cell / pleomorphic lipomas are composed of an admixture of fatty and fibrous tissue, which can vary greatly depending on the proportions of the individual components. Occasional examples are grossly gelatinous, corresponding to myxoid change histologically.

Histologically, spindle cell / pleomorphic lipomas have three major components, well-differentiated adipose tissue, benign appearing spindle cells, and 'ropey' collagen. The proportions can vary greatly and there are some additional histological features that can be mixed in, making for a great variety of histological appearances. Tumors with a predominance of adipose tissue appear fatty while those tumors with a predominance of spindle cells (so-called "low-fat" or "fat free" spindle cell / pleomorphic lipomas) can mimic spindle cell sarcomas. The adipocytic component is well-differentiated adipose tissue but occasionally, some of the fat cells can be multi-vacuolated lipoblasts. The spindle cells are benign appearing, mitotically inactive, with short nuclei and fine chromatin. The spindle cells are usually distributed randomly but can form short fascicles with palisading reminiscent of Schwannoma, which is one of the lesions in the differential diagnosis of "fat free" spindle cell /pleomorphic lipoma. Some spindle cell lipomas can have extensive myxoid stroma with some of the more myxoid lesions also adopting a distinctive pseudoangiomatous appearance. On the pleomorphic end of the spectrum, rosette-type multinucleated cells can be seen in spindle cell / pleomorphic lipoma. When they are few, it's not usually a diagnostic problem. However, they can be numerous and rarely, there are atypical mitotic figures in the pleomorphic cells. Overall, the spectrum of histological changes can be quite bewildering to the unwary surgical pathologist. Remember the rules about age, sex, and anatomic location of spindle cell / pleomorphic lipoma. It's important.

By immunohistochemistry, the spindle cells are always diffusely and strongly positive for CD34. While CD34 is not specific, it's comforting to see CD34 immunoreactivity in morphologically challenging lesions. Genetically, loss of 13q corresponding to loss of RB1 protein is typical of spindle cell / pleomorphic lipoma, distinguishing it from conventional-type lipoma and atypical lipomatous tumor, which harbors *MDM2* gene amplification.

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Case 8 – Tenosynovial giant cell tumor, diffuse-type (also known as pigmented villonodular synovitis.

Tenosynovial GCT, diffuse-type tends to involve the hip and knee joints. However, it can arise rarely from the temporomandibular joint. Over the last several year, I've encountered a few cases that present as facial masses with involvement of the parotid gland, such as the current case.

These tumors are infiltrative and grow as diffuse sheets of cells. The lesions are composed of a mixture of four cell types: osteoclast-type giant cells, mononuclear ganglion-type cells/siderophages, foamy histiocytes, and lymphocytes. These cells can be present in varying proportions, making the diagnosis difficult and presenting a broad differential diagnosis, depending on which cell type predominates. The siderophages are variably pigmented/hemosiderin-laden, depending on the extent of bleeding in the area. Lesions surrounding large joints tend to invoke blood effusions so they tend to have more hemosiderin. Mitotic figures are common and can be numerous. However, atypical mitotic figures are rare as is nuclear pleomorphism. Necrosis is unusual.

By immunohistochemistry, the mononuclear cells are positive for clusterin and can be positive for desmin. The foamy histiocytes are positive for CD68, CD163, and CD45. The osteoclasts are positive for CD68.

At the molecular level, these lesions are characterized by *CSF1* gene fusions that activate the CSF1R pathway, which is targetable by CSF1R inhibitors. Recent clinical trials with these inhibitors have shown a dramatic response rate.

Tenosynovial GCT are infiltrative tumors with aggressive local behavior.

The differential diagnosis depends on the relative percentages of the different components and can range from rhabdomyosarcoma for those tumors with numerous desmin positive mononuclear cells to giant cell tumor of soft tissue for lesions with a predominance of osteoclasts to xanthoma for those lesions with lots of foamy macrophages.

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Case 9 – Malignant myopericytoma

Myopericytoma and glomangiomyopericytoma lie on a morphologic continuum with myofibroma and myofibromatosis. They are essentially a spectrum of tumors showing perivascular myoid differentiation.

Myopericytomas can arise at any anatomic location but have a predilection for the extremeties. Myopericytoma occurs over a large age range with a peak and middle age, and has a male predominance.

Typically, myopericytomas are circumscribed but unencapsulated nodules composed of ovoid or plump spindle cells with eosinophilic cytoplasm arranged around many blood vessels in a concentric or whorling fashion. The tumors cells often infiltrate the walls of the smaller vessels. The tumor cells range in appearance from cells that look more glomoid to those with the appearance of smooth muscle. It has been suggested that myopericytomas are on a spectrum with angioleiomyomas. Rarely, as in the present case, myopericytomas are malignant with prominent pleomorphism, mitotic activity, necrosis, etc.. These criteria are vague and subjective.

By immunohistochemistry, the tumors cells are positive for smooth muscle actin and H-caldesmon while desmin is usually focally positive. Tumor cells are negative for S-100, EMA, keratins, and CD34.

At the molecular level, a group of malignant myopericytomas has been found to have *NTRK1* gene fusions.

The differential diagnosis of myopericytoma is a bit hard to characterize and includes vascular lesions, smooth muscle tumors, schwannoma, and possibly other things. I find the pattern of concentric whorling of tumor cells around the vessel lumina to be the most characteristic feature of this entity. Glomangiopericytomas tend to have more dilated vessels surrounded by rounded cells with sharp borders that have a “glomoid” appearance.

References

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Case 10 – Adamantinoma-like Ewing Sarcoma

Unlike conventional Ewing sarcoma showing keratin immunoreactivity, adamantinoma-like Ewing sarcoma shows complex epithelial differentiation in the form of squamous pearls and or immunoreactivity with p40. While these were originally described to occur in long bones, more recently, it has been realized that these lesions can also present in the head and neck region.

The largest case series of head and neck lesions by Bishop et al. described 7 cases. They arose in the sinonasal tract, parotid gland, thyroid gland, and orbit. The patients ranged in age from 7-51 yrs with a mean of 31 years. There was a female predominance (5:2).

Histologically, the lesions consisted of sheets and trabeculae of uniform, small cells with minimal to moderate amount of pale eosinophilic to clear cytoplasm. The nuclei were round with fine chromatin. Mitotic rates ranged from 5-12 mitotic figures/10 HPFs. Tumor necrosis was identified in 4 cases. In contrast to typical Ewing sarcoma, the tumor cells showed areas with lobules of tumor cells separated by prominent fibrous bands. There were also areas of palisading that was reminiscent of basaloid squamous cell carcinoma. Two cases demonstrated hyaline basement membrane-like material. Squamous pearls were seen in two cases. One of the sinonasal tumors showed areas of intraepithelial growth in the overlying sinonasal epithelium. One of the thyroid tumors showed microcystic growth with a prominent myxoid stroma. The thyroid cases showed colonization of thyroid follicles.

Immunohistochemically, the tumors cells were uniformly positive for CD99 in a membranous pattern. The tumors cells were also positive for pan-cytokeratin and p40. Synaptophysin was positive in 50% of cases and focal chromogranin was seen in 1 of 6 cases. Three of seven tumors were positive for S100 and actin was positive in 1 case. Desmin and NUT-1 were negative. Interestingly, p16 was positive in 2 of 5 cases but all 5 cases that were tested were negative for HPV. An additional report found that these tumors are positive for NKX2.2, a marker of Ewing sarcoma that is sensitive and specific for this diagnosis.

At the molecular level, all tested cases harbored *EWSR1-FLI1* fusions, the most common gene fusion found in Ewing sarcoma.

Clinically, they are potentially aggressive lesions. Of the four patients with follow-up, two had no evidence of disease, 1 patient was alive with residual tumor, and 1 patient died of disease 52 months after initial diagnosis.

The differential diagnosis is broad including poorly differentiated carcinoma including squamous cell carcinoma, NUT midline carcinoma, olfactory neuroblastoma, myoepithelial carcinoma, desmoplastic small round cell tumor, poorly differentiated synovial sarcoma, and CIC-DUX sarcoma. There are so many pitfalls that it indeed seems very unlikely to recognize this

very rare entity. However, knowledge of its existence and the presence of diffuse and strong membranous positivity for CD99, immunoreactivity for NKX2.2 and the typical *EWSR1-FLI1* gene fusion are helpful in making the diagnosis.

References

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