Ewing sarcoma and primitive neuroectodermal tumor

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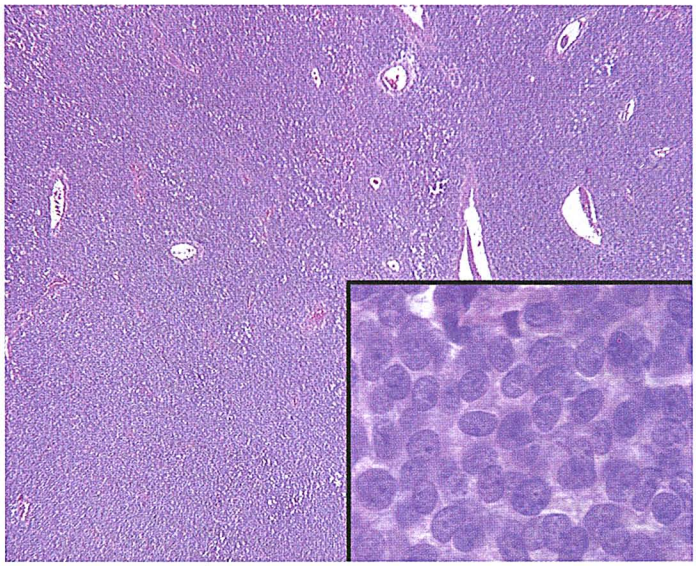

Figure 1. Diffuse sheets of small, round, blue cells make up this Ewing sarcoma. The cells have a high nucleus-to-cytoplasm ratio and small nucleoli (inset).

Ewing sarcoma (ES) and primitive neuroectodermal tumor (PNET) are closely related, high-grade, round-cell tumors with a neuroectodermal phenotype. These tumors are histologically considered on a morphologic spectrum, and they express similar genetic alterations. ES usually develops in bone and is more undifferentiated, while PNET tends to involve soft tissue and demonstrates more pronounced neuroendocrine features.

ES/PNETs are more common in children and young adults, with about 20% of ES/PNET patients developing head and neck disease. There is a minor male preponderance. These tumors are often polypoid, and they can become quite sizeable (up to 6 cm). They are often associated with bone erosion with ulceration and bleeding. In view of the anatomic confines of head and neck sites, tumors in this region are usually much smaller at presentation than those at other anatomic sites.

Histologically, ES/PNETs are made up of diffuse, densely cellular sheets of uniform, small to medium-sized round cells with scant vacuolated cytoplasm (figure 1). The nuclei are round with a fine, delicate to coarse chromatin distribution and small nucleoli (figure 2). Mitotic figures are common. Coagulative necrosis is frequently identified. Occasionally there is a greater degree of nuclear pleomorphism with a rosette formation. Conceptually, the tumor is classified as a *small, round, blue-cell neoplasm*, which requires the application of special studies to confirm the diagnosis. The tumor cells contain glycogen, which is highlighted with a periodic acid-Schiff (PAS) stain (figure 2). CD99 and vimentin are almost always expressed in ES/PNET, while neuron-specific enolase and synaptophysin are expressed less often. FLI-1 (a portion of the gene fusion product of EWS/FLI-1) can be detected by immunohistochemistry, although the characteristic chro-

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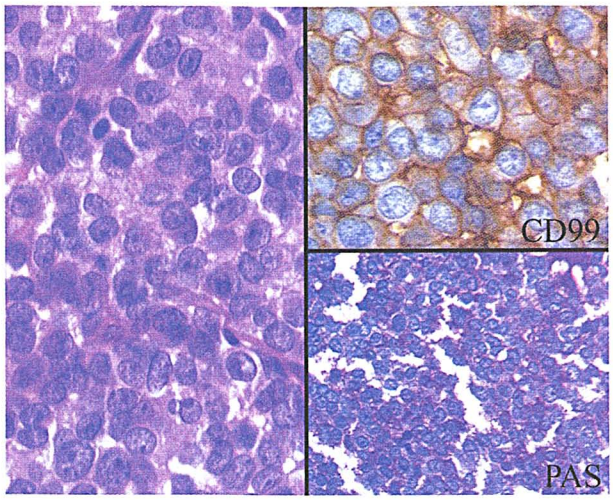

Figure 2. This diffuse arrangement of small cells exhibits a delicate nuclear chromatin distribution with margination to the periphery (left). The neoplastic cells are strongly and diffusely immunoreactive with CD99, although this finding is nonspecific (top right). The slightly pink reaction in the cytoplasm with a PAS stain demonstrates glycogen (bottom right).

mosomal translocations at t(11;22) (q24;q12) or t(21;22) (q22;q12) can be identified by polymerase chain reaction or fluorescent in situ hybridization.

The differential diagnosis includes other small, round-cell tumors, such as lymphoma, rhabdomyosarcoma, olfactory neuroblastoma, melanoma, sinonasal undifferentiated carcinoma, and pituitary adenoma. Different clinical presentations, patterns of growth, immunohistochemistry findings, and molecular studies allow for separation.

Tumor stage is one of the most important considerations in patients with this highly aggressive neoplasm. ES/PNET is managed with multimodal therapy. Patients with sinonasal tract lesions and those with the EWS/FLI-1 fusion tend to have a better prognosis than do patients with thoracoabdominal lesions and those without the fusion.

Suggested reading

Toda T, Atari E, Sadi AM, et al. Primitive neuroectodermal tumor in sinonasal region. Auris Nasus Larynx 1999;26:83-90.

Wenig BM, Dulguerow P, Kapadia SB, et al. Neuroectodermal tumours. In: Barnes EL, Michael L, eds. Pathology and Genetics of Tumours of the Head and Neck. Kliehues P, Sobin LH, series eds. World Health Organization Classification of Tumours. Lyon, France: IARC Press; 2005:66-76.