19 Primitive Neuroectodermal Tumors and Related Lesions

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19.1 Primitive Neuroectodermal Tumors 317
19.1.1 Introduction 317
19.1.2 Incidence and Clinical Behavior 317
19.1.3 Imaging Characteristics 318
19.1.3.1 Plain Radiography 318
19.1.3.2 Ultrasound 318
19.1.3.3 CT and MRI 318
19.2 Extraskeletal Ewing's Sarcoma 320
19.2.1 Definition 320
19.2.2 Incidence and Clinical Behavior 320
19.2.3 Imaging 320
19.2.3.1 Imaging Studies Other Than MRI 320
19.2.3.2 MRI Findings 321
19.2.3.3 Imaging Strategy 322
References 322

19.1

Primitive Neuroectodermal Tumors

19.1.1

Introduction

Primitive neuroectodermal tumors (PNET) form part of the heterogeneous group of small round (blue) cell tumors of childhood and adolescence. This group also contains conventional neuroblastoma, rhabdomyosarcoma, lymphoma, and Ewing's sarcoma [58, 59, 65].

Purely for practical reasons, Dehner introduced the distinction between central PNET (cPNET) and peripheral PNET (pPNET), as he was well aware that little knowledge was available concerning the actual biology of these neoplasms and of their interrelationships [14]. This classification applies knowledge of neuroectodermal derivatives to the PNET. The neuroectoderm generates the brain and spinal cord, on the one hand, and the entire autonomic nervous system, dorsal root ganglia, adrenal medulla, and part of the neuroendocrine system, on the other, among many other derivatives [33]. It must be stressed that this division of the PNET does not have any clinicopathologic or prognostic implications. In this chapter only pPNET will be discussed.

pPNET and Ewing’s sarcoma form a special group within the small round (blue) cell tumors. Several common characteristics have been discovered that distinguish them from other small round (blue) cell tumors, namely a unique chromosomal translocation, t(11;22)(q24;12) [5, 9, 10, 12, 16, 17, 22, 32, 44, 60, 63, 66], and the expression of a membrane glycoprotein, known as the MIC2 gene product [2, 29, 43, 62]. In addition to pPNET of soft tissue and Ewing’s sarcoma of bone, there are also osseous pPNET and extraskeletal Ewing’s sarcoma [3]. It was also noted that extraskeletal Ewing’s sarcoma and some atypical forms of Ewing’s sarcoma of bone display neuroectodermal features [9, 16, 35, 37, 40]. Because of these shared phenotypical and genotypical characteristics, very typical for Ewing’s sarcoma and pPNET, it is now generally accepted that these two neoplasms are related to each other. They are thought to correspond to distinct neural crest lineages or tumors arrested at different stages of development. pPNET is the most differentiated and can be considered the neural variant of Ewing’s sarcoma [6, 12, 15, 28, 39, 40, 43, 49, 50, 56, 57, 62].

According to the Ewing’s sarcoma/pPNET classification proposed by Schmidt [50], diagnosis of pPNET is reserved to those cases that express at least two different neural markers and/or Homer-Wright rosettes, the others being termed Ewing’s sarcoma. This classification has proven to be useful [6].

19.1.2 Incidence and Clinical Behavior

Most pPNET are diagnosed between the ages of 175 and 250 months, with three-fourths occurring before the age of 30 years [18, 25, 30, 36, 50]. Men are affected more frequently than women [30, 50].
These tumors represent about 1% of all sarcomas [25].

By definition PNET never arise from the sympathetic nervous system. Therefore cases usually occur outside the vertebral axis of the body [18]. They are found most frequently in the thoracopulmonary region, abdomen, pelvis, and lower extremities [27, 50]. Involvement of other areas is rare, but pPNET of the orbit [54], kidney [38], retroperitoneum [13, 26], vulva [48], colon [46], middle ear, diploe, and maxilla [27] have been reported.

The PNET can give rise to symptoms and signs of neurologic failure [18].

According to Schmidt's classification, prognosis is worse for pPNET than for Ewing's sarcoma [50].

A special entity of pPNET is the Askin tumor. This was first described as a “malignant small cell tumor of the thoracopulmonary region of childhood” [4], but it is now classified as a pPNET of the chest wall [24, 53, 61]. It is found principally in young adults and adolescents [7] but can occur at all ages [45].

In contrast to the pPNET in general, Askin tumors seem to have a preference for girls [4, 23, 25]. Usually the mass has already achieved a considerable size by the time of diagnosis [7] and is painful in just over half the cases [47]. Pleural effusion may also occur [4, 7, 20, 22, 24, 31, 52, 55].

pPNET can provoke constitutional symptoms. Fever, anorexia, weight loss, cough, and dyspnea are frequent. In cases of Askin tumor, shoulder pain, Horner’s syndrome, cervical lymphadenopathy can also occur [4, 20, 22, 24, 27, 52, 55].

Askin tumors, as with PNET in general, are highly aggressive. One study of 30 cases showed a 2-year survival rate of 38% and a 6-year survival rate of 14% [11]. Relapse is most common at the thorax, where it presents as local chest wall recurrence or disseminated pulmonary metastasis. Metastasis to mediastinal lymph nodes may also occur. The next most common manifestation of relapse is distant skeletal metastasis. Infrequently the disease recurs in liver, adrenals, brain, retroperitoneum, and sympathetic chain. These sites must be considered in follow-up computed tomography (CT) examinations [4, 20, 22, 24, 52, 55].

Esthesioneuroblastoma, also known as olfactory neuroblastoma, has long been considered a member of the pPNET/Ewing's sarcoma family. Although a primitive neural tumor, recent studies raise doubts about the legitimacy of its membership because of the failure to identify the MIC2 gene product [41].

19.1.3 Imaging Characteristics

19.1.3.1 Plain Radiography

Little is known concerning the radiographic presentation of pPNET. On plain radiographs, Askin tumor commonly presents as a mass of the chest wall with soft tissue density. Rib erosion occurs very often [4, 11, 20, 22, 24, 52, 55]. In about 10% of cases the tumor is seen as a paraspinal or mediastinal mass. In 15% of cases a usually small, pleural effusion is observed. Rarely, calcifications are present [4, 20, 22, 23, 52, 55].

19.1.3.2 Ultrasound

As in the plain radiograph, ultrasound of Askin tumor reveals only nonspecific features. A complex, solid mass may be revealed, with mixed echogeneity and sometimes with cystic components. When present, a pleural effusion can be seen [47].

19.1.3.3 CT and MRI

On CT, pPNET presents as a large, ill-defined mass with a heterogeneous appearance due to extensive cystic degeneration. As a rule, there is no calcification [27], although our series contains a pPNET with extensive calcification (Fig. 19.1). After the injection of iodinated contrast the tumor has a heterogeneous appearance [27, 47, 64].

On T1-weighted images pPNET generally have a signal intensity equal to or greater than that of muscle. Frequently evidence of hemorrhage or necrosis is found. Larger tumors show up as heterogeneous masses, while smaller ones tend to be more homogeneous [19, 27, 64].

On T1-weighted image after intravenous administration of contrast, the tumor shows rapid enhancement [64] (Fig. 19.1). On T2-weighted images these neoplasms tend to show a bright, frequently heterogeneous appearance [27, 64] (Figs. 19.1, 19.2).