Peripheral Primitive Neuroectodermal Tumor Involving the Paravertebral and Retroperitoneal Regions

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A rare case of peripheral primitive neuroectodermal tumor (PNET) is reported. A 68-year-old woman complaining of lumbago was admitted to our hospital. Diagnosis was made based on pathological findings characterized by Homer Wright-type rosettes. Ultrastructural examination showed the presence of neurosecretory granules and short cytoplasmic processes, which were highly suggestive of neural differentiation. Chromosomal analysis of the neoplastic cells revealed translocation (11;22)(q24;q12), which is often found in Ewing’s sarcoma and Askin tumor. These results strengthen the hypothesis of a common histogenesis for these small round cell tumors, and suggest common oncogenesis for these neoplasms.

Key words: translocation (11;22)(q24;q12), neurosecretory granules

Introduction

Peripheral primitive neuroectodermal tumor (PNET) is a rare neoplasm of primitive neuroectodermal cells that usually originates within the peripheral nervous system (1). Clinically, this tumor has a marked predilection for the extremities in any age group. The prognosis is usually poor and the mean survival time is reported to be less than two years (1, 2). This tumor is classified as one of the small round cell tumors that also includes Ewing’s sarcoma, the Askin tumor and neuroblastoma (2). We report a rare case of peripheral PNET involving the paravertebral and retroperitoneal regions (3).

Case Report

A 68-year-old woman was admitted to our hospital in August 1995 for evaluation of lumbar and shoulder pain which had lasted for one month prior to admission. She had been suffering from Parkinson’s disease for four years. A solid mass was pointed out in her lower back area under the intact skin on physical examination on admission. She had no palpable lymphadenopathy. No other remarkable abnormalities were found. Her white blood cell count was 11,100 cells per mm³ and the erythrocyte sedimentation rate was 85 mm in the first hour. Tumor markers were normal except for neuron-specific enolase (NSE) (54.4 ng/ml).

A chest radiograph demonstrated bilateral pleural effusions and alveolar shadows in the right lower lung field. A computed tomographic (CT) scan of the chest showed an infiltrative shadow in the right lower lobe, bilateral pleural effusions and a 2 cm mass in the apical segment of the right upper lobe. No mediastinal or hilar lymphadenopathy was observed. An abdominal CT scan (Fig. 1) showed two huge heterogeneous masses; one was an 18x9x6 cm mass in the subcutaneous tissue of the right back and the other was an 11x6x4 cm mass on the right side of the corpus vertebrae. Abdominal magnetic resonance images (Fig. 2) also showed that the latter large mass was present in the retroperitoneum. A technetium (99mTc) bone scintigram showed abnormal uptake in the lumbar spine at L4 • L5, the right acromial process and right humerus. No other metastasis was detected.

For a more distinct diagnosis, a biopsy specimen was obtained from the subcutaneous tumor of the right back. Light microscopic examination (Fig. 3) showed that the tumor was composed of small round or oval densely aggregated cells arranged in solid sheets or lobules circumscribed by a dense fibrovascular stroma. The tumor cells, the cell-to-cell borders of which were indistinct, contained round-to-oval nuclei with scant eosinophilic cytoplasm. In addition, Homer Wright-type rosettes (Fig. 3a, 3b) whose central area was filled with elongated hair-like cytoplasmic extensions from surrounding cells were observed. Perivascular pseudorosettes were also present. The neoplastic cells were not stained by periodic acid-Schiff (PAS). Immunocytochemical studies showed that the tumor...
cells were immunoreactive for NSE and negative for S-100 protein, cytokeratins, desmin, glial fibrillary acidic protein (GFAP), neurofilaments and vimentin. An antigen determined by the MIC-2 gene was not expressed. Electron microscopic examination (Fig. 4) demonstrated neuronal differentiation of neoplastic cells. Polygonal or short spindle cells, which had scarce cytoplasm and round or oval nuclei with few indenta-

Figure 1. Representative image from a computed tomographic scan of the abdomen taken at the level of the third lumbar vertebra. Large heterogeneous masses can be seen in the retroperitoneum and in the subcutaneous tissue.

Figure 2. T1-weighted images of abdominal magnetic resonance images show large masses as well as T2-weighted images. a) axial image, b) sagittal image.

Figure 3. Microscopic features of the tumor (HE stain). Sheets of poorly differentiated, small round cells with scant eosinophilic cytoplasm and hyperchromic nuclei are shown. Scattered Homer Wright-type rosettes are evident. (a: x20, b: x40) Perivascular pseudorosettes are also shown.
Figure 4. Electron micrographs of the neoplastic cells. Primitive intercellular junctions (white arrowhead) (a) and a cytoplasmic process containing neurosecretory granules (white arrowhead) (b) are shown (x6,000).
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Figure 5. Karyotype of neoplastic cells showing chromosomal translocation (11;22)(q24;q12). Arrows indicate the position of translocation.

Figure 6. The cut surface of the tumor shows the presence of hemorrhagic and necrotic foci.
tions, contained finely granular chromatin and small nucleoli and were connected by sparse, primitive intercellular junctions (Fig. 4a). Short cytoplasmic processes containing membrane-bound neurosecretory granules (Fig. 4b) were observed between cells. These neurosecretory granules were spherical or ellipsoid shaped and ranged from 50 to 200 nm in diameter.

Chromosomal analysis of the neoplastic cells (Fig. 5) revealed chromosomal translocation (11;22)(q24;q12). All of the 20 metaphases analyzed by Giemsa banding showed karyotype 57,XX,+k(1)(q10)x2,+2,+5,+6,+8,t(11;22)(q24;q12),+12,+14,+16,+20,+21. Diagnosis of peripheral PNET was made based on these examinations.

Her lumbar pain worsened day by day as the tumor grew. She suffered from severe dyspnea even during resting ventilation because of respiratory restriction caused by morbid pain. The patient died of respiratory insufficiency and multiple organ failure on the 51st day. Exirpation of the tumor was performed and revealed the continuity of the tumor from the retroperitoneum to the subcutaneous tissue. Macroscopically, the cut surface of the tumor (Fig. 6) was grayish and solid with hemorrhagic and necrotic foci.

Discussion

Tumors consisting of small round cells of neuroectodermal origin are classified as central and peripheral PNET. The term peripheral PNET is used to describe a group of tumors that originate from peripheral nerve tracts (1, 4-6) and have been reported under various terms such as malignant neuroepithelioma, peripheral neuroepithelioma, peripheral neuroblastoma and peripheral medulloepithelioma. In 1918 Stout (4) first described a peripheral neoplasm with rosettes involving the ulnar nerve. Since then a number of cases have been reported. Peripheral PNET probably includes the tumors described as malignant tumors of the thoracopulmonary region in childhood and adolescence as a unique clinicopathologic entity (Askin tumor) (7-9).

Peripheral PNET is uncommon and may occur at any age, though most cases occur in the second and third decades of life (1). The extremities, especially the lower extremities, are most commonly involved (4). This tumor carries a poor prognosis (5); most patients do not survive more than five years following diagnosis (1, 2). Metastases rapidly spread to the lungs, lymph nodes, liver and bones. Recently, however, some cases in which adjuvant chemotherapy with Adriamycin, cyclophosphamide and vincristine proved effective have been reported (6, 10). Histologically, the most characteristic and significant feature is the rosette, especially the Homer Wright-type rosette, formed by the round tumor cells (11). Immunohistochemically, the cells generally stain positively for NSE (5, 6). In addition, peripheral PNET and Ewing’s sarcoma recently have been shown to strongly express the protein products of the MIC-2 gene, suggesting common oncogenesis. In the present case, the histological findings showed the presence of Homer Wright-type rosettes, positive staining for NSE and a typical ultrastructural appearance. These findings confirmed the diagnosis of the tumor as peripheral PNET, though expression of the MIC-2 gene was not recognized.

The MIC-2 gene is a pseudautosomal gene located on the short arms of the sex chromosomes. The gene product, a cell membrane protein, is recognized by monoclonal antibody (MoAb) HBA-71, MoAb 12E7 and MoAb RFB-1. Recently the overwhelming majority of cases of Ewing’s sarcoma and peripheral PNET have been shown to express the MIC-2 gene product in very high amounts and in a highly selective fashion. MIC-2 expression is thought to be a very reliable marker for the two tumors (12, 14).

In the present case, chromosomal analysis revealed the translocation (11;22)(q24;q12). This translocation is a frequent finding in Ewing’s sarcoma and the Askin tumor (8, 15). Recent cytogenetic studies have demonstrated t(11;22)(q24;q12) translocations in peripheral PNET (9, 16). The finding that Ewing’s sarcoma and peripheral PNET share the same chromosomal translocation, with the expression of an identical antigen determined by the MIC-2 gene, suggests a common oncogenesis of the two tumors (17).

The histological and cytogenetic similarities between peripheral PNET and Ewing’s sarcoma, especially extraskeletal Ewing’s sarcoma, have been pointed out (8, 16, 18). The two tumors are generally differentiated histologically by the presence or absence of rosettes, and ultrastructurally by the presence or absence of cytoplasmic processes. Recently, however, certain characteristics of neuroectodermal tumors have been found in cases diagnosed as Ewing’s sarcoma by detailed pathological and immunocytochemical examinations (19). For example, though rosettes have been thought to be present only in peripheral PNET, various rosette forms, fewer and more indistinct than those in peripheral PNET, have been found in Ewing’s sarcoma (19). In addition, in vitro induction of neural differentiation of Ewing’s sarcoma cell lines under certain conditions and the formation of rosettes in recurrent and metastatic lesions of Ewing’s sarcoma have been reported (20-22). Moreover, a common chromosomal abnormality, t(11;22)(q24;q12), of Ewing’s sarcoma and peripheral PNET has been reported recently and the two have been shown to have similar patterns of oncogene expression (23). Therefore, our findings, together with previous reports, support the very close histogenetic relationship between peripheral PNET and Ewing’s sarcoma and suggest the hypothesis that these tumors derive from a common stem cell (16, 20) although the exact histogenesis remains to be confirmed.

Currently, “a broad definition of peripheral PNET” is advocated by some researchers (18, 20). Assuming a tumor family showing different degrees of differentiation made up of neural crest cells or equivalent multipotent cells creating various phenotypes such as neurogenic tumors and mesenchymal tumors, Ewing’s sarcoma is considered to be located at the bottom of the
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differentiation scale. Ewing’s sarcoma consists of quite undifferentiated tumor cells though it has the potential to take various forms. Narrowly defined peripheral PNET is considered to be located just above Ewing’s sarcoma. It consists of undifferentiated tumor cells as does Ewing’s sarcoma; however, it is comparatively more likely to display neural features.

The present case is important as the common chromosomal abnormalities associated with Ewing’s sarcoma were identified and it supports the broad definition of peripheral PNET. Further research on this chromosomal translocation should lead to greater insight into this tumor family.

References

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