Rare Primitive Neuroectodermal Tumor (PNET) of Liver in a Young Woman

Siddhartha Mani, Deep Dutta, Binay K. De
Department of Medicine, Medical College and Hospitals, Calcutta, India

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The peripheral primitive neuroectodermal tumor (PNET), first recognized by Arthur Purdy Stout in 1918, is a member of the family of “small round-cell tumors.” Most of these tumors are diagnosed before the age of 35 years, with a slight male preponderance. Although PNETs can occur in numerous solid-tissue structures, such as the kidney, ovary, vagina, testis, uterus, cervix uteri, urinary bladder, parotid gland, heart, lung, rectum, pancreas, and gall bladder, it is an extremely rare tumor entity. We are aware of a single case report of PNET of the orbit metastasizing to liver; however, primary PNET of the liver has never, to our knowledge, been reported.

Case Report

A 20-year-old woman presented with progressive distension of her upper abdomen, noticed by her mother for the first time 20 days prior to admission, with a dragging sensation and heaviness in the same region for 15 days. She had no other complaints, and her past history was unremarkable. Examination revealed presence of pallor, massive hepatomegaly (liver span 28 cm), and a just-palpable spleen. Liver was firm, smooth surfaced, with sharp borders, and nontender on palpation (Figure 1). Significant laboratory findings included presence of hypochromic microcytic anemia (hemoglobin 9.4 g/dL [normal range 11.5–15 g/dL]) with anisopikilocytosis, elliptocytosis, and occasional polychromatophilic erythrocytes, raised erythrocyte sedimentation rate of 58 mm/h, normal serum albumin (3.9 g/dL [normal range 3.8–5.3 g/dL]), a slightly raised globulin (4.4 mg/dL [normal range 2.3–3.5 g/dL]), and INR of 1.1. Liver enzymes were slightly raised (SGOT 58 IU/L [normal range 10–40 IU/L]; SGPT 52 IU/L [normal range 10–40 IU/L]). Alkaline phosphatase was also slightly elevated (274 IU/L [normal range 110–230 IU/L]). Serum LDH was 200 IU/L (normal range 110–230 IU/L). Serum urea and creatinine were also normal as was urine microscopy. Serum tumor markers, including a-fetoprotein, carcinoembryonic antigen, and CA 19–9, were negative.

Ultrasonography and computed tomography (CT) scan of the abdomen showed an enlarged liver with normal intrahepatic biliary radicles and normal porta hepatis and mildly bulky kidneys with retained corticomedullary differentiation (Figure 2). Using a standard technique, under local anesthesia, she underwent ultrasound guided liver biopsy, using an 8F true cut needle. Microscopic examination (Figures 3–6) revealed a small round blue cell tumor. Nests of medium-sized round or oval tumor cells with enlarged round or oval nuclei with few mitotic figures and scant cytoplasm were seen in the background of hepatocytes. On immunohistochemistry, tumor cells expressed Mic-2 and Fli-1 and were negative for cytokeratin, desmin, hepatocyte-specific antigen (OCHIE5), synaptophysin, and chromogranin A and CD-20. Immunohistochemistry revealed strong expression of CD-99.

Search for other sites of tumor involvement using a CT scan of the chest, MRI of the brain, and a whole-body bone scan yielded negative results. Bone marrow aspiration showed normal cellularity with normal myeloid to erythroid ratio. On Prussian blue staining there was evidence of decreased stainable iron. Kidney biopsy was performed on the left kidney, and seven glomeruli were seen with normal architecture on microscopy.
Twenty-two days after admission, the patient received her first cycle of VAC chemotherapy (vincristine 2 mg/m², doxorubicin 75 mg/m², cyclophosphamide 1200 mg/m²). All drugs were given in a single day. VAC was alternated with IE (ifosfamide 1800 mg/m²/d) given along with mesna over 5 days with etoposide 100 mg/m²/d given over the same 5 days. The cycles were repeated every 3 weeks.

Following the third cycle of VAC, she developed febrile neutropenia. She received two doses of granulocyte-colony–stimulating factor (G-CSF) along with broad spectrum antibiotics. She recovered; however, the subsequent cycle was delayed by 17 days. In subsequent cycles she received doxorubicin 60 mg/m² and cyclophosphamide 960 mg/m². In total, she received six cycles each of VAC and IE over a period of 43 weeks. Blood component transfusions were given as and when required.

Reduction in liver size was observed as early as after the second cycle of VAC and continued throughout therapy. At the end of 43 weeks, she was asymptomatic with liver palpable 2 cm below the costal margin and a nearly normal span. However, a repeat liver biopsy was not done. She is being followed in the Liver Clinic of Medical College and Hospitals Kolkata and has been doing well 1 year after diagnosis.

DISCUSSION

Primitive neuroectodermal tumor is a rare neural crest tumor classified based on site of origin into CNS PNET and peripheral PNET. PNET belongs to the small round blue cell tumor (SRBCT) family. Peripheral primitive neuroectodermal tumor occurs outside the central nervous system and has considerable overlap with Ewing’s sarcoma, both sharing a common and unique translocation \([t(11;22)(q24q12)]\). Fusion gene designated \(EWS/FLI-1\). PNET constitutes approximately 1% of all sarcomas.

Primitive neuroectodermal tumor outside the central nervous system is mostly found within the deep soft tissue of the extremities and the paravertebral areas. Kidney is the most common visceral organ involved by PNET. Liver is often involved in metastasis from other primary sources, which present as liver abscess. However, primary visceral PNETs are extremely rare, and two cases of small intestine and hepatic duct involvement have been reported in children. To the best of our knowledge, this is the first case of PNET to be reported primarily involving the liver.

Once PNET is diagnosed, the standard treatment is with systemic multiagent chemotherapy combined with surgery and/or radiotherapy. Tumor dissemination at the time of diagnosis is associated with a poorer outcome compared to localized disease.
high initial complete response of 94% was observed in patients with PNET treated with vincristine, doxorubicin, and cyclophosphamide chemotherapy plus local radiotherapy. The best responses were reported with combinations based on anthracyclines (doxorubicin) and high doses of alkylating agents (cyclophosphamide or ifosfamide). The most frequently used combination protocols include vincristine, actinomycin D, cyclophosphamide, doxorubicin, and ifosfamide.

Our patient had diffuse involvement of the entire liver without objective evidence of involvement of any other organ. Resection of liver was not an option here, and she responded well to a combination therapy of VAC (vincristine, doxorubicin, and cyclophosphamide) alternating with IE (ifosfamide and etoposide) every 3 weeks over a period of 43 weeks. Radiotherapy was not considered necessary in her case.

Survival in PNET depends on multiple factors, one of the important being the degree of dissemination of disease, and various studies have shown a 5-year survival of 58–61% with a median survival of 120 months. Our patient in this report responded well to chemotherapy alone and is asymptomatic and doing well even 1 year after diagnosis. Isolated liver involvement was probably one of the factors responsible for good response to therapy and survival in her case.

In conclusion, it may be said that PNET of primarily the liver is an extremely rare tumor, and this is perhaps the first reported case. It was observed in a young woman with a subacute clinical presentation of upper abdominal swelling who responded well to combination chemotherapy. Although uncommon, PNET has to be considered in the differential diagnosis of atypical hepatic tumors in young patients.

REFERENCES


