Case Report

Primitive Neuroectodermal Tumor Presenting with Elevating Carcinoembryonic Antigen

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Abstract.

Primitive neuroectodermal tumor (PNET) is a rare disease and mostly diagnosed in children and young adults. This tumor is presumed to be of neuroectodermal origin, probably developing from migrating embryonic cells of the neural crest. Carcinoembryonic antigen is a glycoprotein and frequently elevated in patients with a variety of epithelial malignancies. We report hereby a 59-year old male patient with pelvic PNET, and the initial presentation was merely elevating serum CEA of unknown origin. This case might help to support the theory that PNET may have a potential for epithelial or neuroendocrine differentiation.

Keywords: PNET, CEA

INTRODUCTION

In 1918, Stout described a tumor of the ulnar nerve with the gross features of a sarcoma, but composed of small round cells focally arranged as rosettes; and it was designated as neuroepithelioma first [1]. The concept of this entity evolved to include a group of small round-cell malignancies, ubiquitous in location and of presumed neuroectodermal origin, probably developing from migrating embryonic cells of the neural crest [2] and was called primitive neuroectodermal tumor (PNET) [3]. This type of tumor is usually diagnosed in children and young adults [4]. Re-
Recently, PNET and Ewing's sarcoma have been classified into the same tumor family on the basis of molecular genetic analysis because of their similar histologic and immunohistochemical characteristics, also sharing nonrandom chromosomal translocations [5,6].

Carcinoembryonic antigen (CEA) is an approximately 180 kDa glycoprotein, originally identified by in 1965 by Gold and Freedman [7,8]. Serum levels of CEA are frequently elevated in patients with a variety of epithelial malignancies [9-11].

There has been only one report of peripheral PNET/ Ewing's sarcoma/with elevated serum levels of CEA in the literature, and the case was a 7-year-old patient [12]. To the best of our knowledge, this is the first case of primary Ewing's sarcoma/peripheral PNET with elevated serum levels of CEA in an adult patient.

**CASE REPORT**

A 59-year-old man was referred to the out-patient department of medical oncology because of incidental finding of elevated CEA in a health examination. His initial CEA level was 44.13 ng/mL (normal value: < 5 ng/ml for non-smokers and < 7 ng/mL for smokers). No headache, chest pain, abdominal pain, bone pain, cough, dyspnea, anorexia, general malaise, bowel habit change, body weight loss, or other symptoms were mentioned. The patient had hypertension and diabetes mellitus with regular medical control. He denied smoking and alcohol use. He was 166 cm in height and 88 kg in weight and was fair looking. There was no abnormal finding in the physical examination. On account of abnormal elevating of CEA without obvious symptoms or signs, we rechecked his

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**Figure 1.** Computed tomography scan of pelvis showing a 3 x 3 cm mass in right rectoischial fossa

**Figure 2.** Formalin-fixed excised round tumor showing lobulated, gray-white, and elastic contents

**Figure 3.** Haematoxylin and eosin section showing malignant tumor composed of moderately uniform round and oval cells, and arranged in sheets and trabecules with cystic space and rosettes. The overall pattern favored a PNET. (Original magnification of 40x10)
serum CEA, which was elevated to 56.9 ng/mL in one month. The hemogram and biochemistry were also in the normal range. The chest X-ray, panendoscopy, colonscopy, and liver echo all showed negative findings. Then, chest, abdomen and pelvic computed tomography scans (CT scan) were arranged. There was no specific finding in the chest or abdomen, but a mass about 3x2 cm in dimension with a suspicious necrotic part was noted in the right rectoischial fossa (Figure 1).

After discussion with the patient, an en bloc excision of the tumor was performed. A lobulated tumor, located at the apex of the ischiorectal space near the right pelvic sidewall was found. The size was 5x6x4 cm, and the tumor had a heterogenous content (cystic and solid component) with no invasion to the surrounding structures (Figure 2).

Hemotoxyline and eosin staining (Figure 3) showed a malignant tumor composed of moderately uniform round and oval cells, arranged in sheets and

**Figure 4.** Immunohistochemical staining showing diffuse positivity of tumor cells for CD99 (A) and CEA (B); focal positivity for vimentin (C) and NSE (D); and negativity for AE1/AE3 (E), EMA (F), and BCL-2 (G). (Original magnification of 40x10)
trabecules with cystic space and rosettes. Tumor nuclei were large with mitotic figures 7-10/10HPF, and necrosis was seen. Immunohistochemical study showed that the tumor was diffusely positive with CD99 (MIC2) (Figure 4A), focally with vimentin and NSE (Neuron Specific Enolase) (Figure 4C,D). It was negative for AE1/AE3, EMA (Epithelial Membranous Antigen), or BCL-2 (B-cell lymphoma 2) (Figure 4E-G). The overall pattern favored a PNET. As elevating serum CEA was noted, the tumor was also stained for CEA, which showed unusually diffuse positivity (Figure 4B).

After the operation, the patient received adjuvant concurrent chemoradiotherapy. His serum CEA, originally 218.49 ng/mL before operation, decreased to 73.4 ng/mL 2 weeks after the operation, and then dropped to 10.7 ng/ml 3 months after the operation when he finished his adjuvant therapy. But his serum CEA never returned to normal, and became gradually elevated during follow up. The repeat CT scan showed negative finding for tumor recurrence. Fourteen months

Figure 5. Computed tomography scan showing lung metastasis

Figure 6. Computed tomography scan showing progressive more extensive lung metastasis (A), local recurrence (B), and left rib metastasis (C)
after the operation, the patient’s serum CEA elevated to 393.48 ng/mL, and a chest CT scan showed multiple pulmonary metastasis (Figure 5). He hesitated for palliative chemotherapy. Five months later, the serum CEA level reached 1250 ng/mL and the CT scan demonstrated more extensive pulmonary metastasis, local recurrence, and left rib metastasis (Figure 6). Therefore, the patient started to receive palliative chemotherapy with epirubicin and ifosfamide. Unfortunately, he died of sepsis. The overall survival was approximately 24 months.

**DISCUSSION**

PNET is a rare and aggressive disease. There were only 17 diagnosed cases of PNET in Taiwan in 2008 [13]. It is defined as embryonal tumors composed of undifferentiated or poorly differentiated neuroepithelial cells which have the capacity for or display of divergent differentiation along neuronal astrocytic, ependymal, muscular or melanotic lines [14]. Morphologically, the appearance of PNET tumors is similar to that of other small round blue cell tumors involving bone and soft tissue, including lymphoma, small cell osteosarcoma, mesenchymal chondrosarcoma, medulloblastoma, dedifferentiated synovial sarcoma, desmoplastic small round cell tumors, and rhabdomyosarcoma. As a group, these tumors often pose difficult diagnostic problems when examined by light microscopy alone. Nowadays, demonstration of MIC2 glycoprotein expression by immunocytochemical staining (CD99) aids in diagnosis of PNET [15,16]. In our case, the H.E staining showed typical findings of PNET, and the immunohistochemistry study also confirmed the diagnosis (positive for CD99). As the initial presentation of the case was elevating serum CEA, we also stained the tumor with CEA to see if the tumor was CEA-producting. The result was positive and the patient’s serum CEA fluctuated as his disease course changed. The fluctuation of the serum CEA levels confirmed the patient’s PNET was CEA-producting.

Carcinoembryonic antigen (CEA) is a 180 kDa GPI-linked cell-surface glycoprotein normally expressed in the fetal gut and on the luminal surface of the adult colon [8,17]. During colorectal carcinoma oncogenesis, CEA loses its polarity and becomes overexpressed throughout the tumor tissue. High levels of CEA expression have also been observed in epithelial tumors in the lung [18,19], breast [20], thyroid [21-23], and ovaries [24].

PNET is in the same family as Ewing’s sarcoma. Ewing’s sarcoma family of tumors (ESFT) have been found to have potential for epithelial differentiation. The immunohistochemical (IHC) study of Machado et al confirmed the epithelial marker expression of EMA and CEA in ESFT. Thus, epithelial marker expression does not necessarily rule out the diagnosis of ESFT. In the study of Machado et al, 57 (20.8%) out of 415 specimens of ESFT had stained positive for CEA. However, no correlation was shown between epithelial marker expression and histological subtypes of ESFT [25]. Further or more advanced molecular genetic techniques are necessary to confirm the diagnosis of sarcoma. Our patient did not have the study of reverse transcription polymerase chain reaction (RT-PCR) to demonstrate the EWS-FLI1 fusion gene because the technique was unavailable in our hospital at that time.

Our case also suggested that PNET might have potential for epithelial or neuroendocrine differentiation. However, more data are necessary to support this statement.

**REFERENCES**

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