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Teaching case

A rare case of Ewing sarcoma with elevated plasma pro-gastrin-releasing peptide (proGRP) level

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Abstract We studied a 17-year-old Japanese male with huge mass arising from the left third rib. The mass compressed the left lung and adhered to the pericardium, but the patient had no distant metastasis. He had a high level of plasma pro-gastrin-releasing peptide (proGRP). Histopathological examination of the bone biopsy specimen revealed small round cell tumor which was immunohistochemically positive for CD99 and vimentin. Gene analyses demonstrated EWSR1-FLI1 fusion, confirming the pathological diagnosis of Ewing sarcoma/primitive neuroectodermal tumor (ES/PNET). Several cycles of chemotherapy resulted in clinical good partial response, and plasma proGRP level at that time was normalized. Thereafter residual tumor was resected. Histopathological examination of the resected specimen showed no viable tumor cells, verifying the pathological complete response. High level of plasma proGRP before the chemotherapy and its normalization after the successful chemotherapy strongly suggest that ES/PNET in the present case was a proGRP producing tumor.

1. Introduction

Ewing sarcomas/primitive neuroectodermal tumors (ES/PNETs) are relatively infrequent but the second most common sarcoma of the bone next to osteosarcoma. Nearly 80% of them occur in persons younger than 20 years. Most of them arise from the bone, but 10 to 20% of them from soft tissue. ES/PNETs are pathologically characterized by small round cells which often show CD99 expression by immunohistochemistry (IHC). Approximately 85% of them are known to have a reciprocal translocation of t(11;22) (q24;q12), which makes EWSR1-FLI1 fusion gene [1]. Other fusion genes including EWSR1-ERG and EWSR1-ETV1 have also been reported in ES/PNETs [2]. In Ewing-like sarcomas, fusion genes such as BCOR-CCNB3 [3] and CIC-DUX4 [4] have been demonstrated. Thus, the fusion gene analyses are critical for the definite diagnosis of small round cell tumors including ES/PNETs and Ewing-like sarcomas.

Pro-gastrin-releasing peptide (proGRP) is a precursor peptide of GRP, and elevation of serum or plasma GRP level had been reported to be a useful serological marker for

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patients with small cell lung cancer (SCLC) [5]. Because of instability of GRP in plasma, the improved immunoassay system to measure a precursor form of GRP, i.e. proGRP, which is stable in plasma, has been developed [6]. Now, measurement of serum/plasma proGRP is regarded as a reliable biomarker for SCLC [7]. Although serological tumor markers specific for patients with ES/PNET are not known, some reports demonstrated that serum CEA [8] or serum/plasma proGRP was elevated in several patients with ES/PNET. Elevated serum/plasma proGRP had been reported in two cases of ES/PNET [9,10]. Moreover, Yamaguchi et al. recently reported that elevated level of plasma proGRP was detected in 5 out of 9 ES/PNETs [11]. However, it has been found that expression of GRP in ES/PNETs was not directly regulated by the EWSR1-FLI1 fusion gene [12].

In this report, we described a rare case of ES/PNET with elevated level of plasma proGRP. High plasma proGRP level before the chemotherapy was normalized after the successful chemotherapy which resulted in clinical good partial response and pathological complete response. These results strongly suggested that ES/PNET in the present case was a proGRP producing tumor.

2. Clinical Presentation

A 17-year-old male presented with left chest pain at night. Chest X-ray and chest computed tomography (CT) demonstrated a 90 × 68 mm mass arising from the left third rib. For further examinations, the patient was referred to the Department of Orthopedic Surgery, Hyogo College of Medicine. Chest X-ray and chest CT in our hospital also showed large tumor with destruction of the cortex of the left third rib (Fig. 1A and C). The laboratory data showed slightly elevated serum neuron specific enolase (NSE) (18.7 ng/ml, normal range: 0–16.3 ng/ml) and marked elevation of plasma proGRP (1310 pg/ml, normal range; 0–81 pg/ml). Serum CEA and CA19-9 were within normal range. For the definite diagnosis, bone biopsy was performed.

3. Materials and methods

3.1. IHC

Resected tissues were fixed in 10% buffered formalin and embedded in paraffin. Three-micrometer-thick sections were

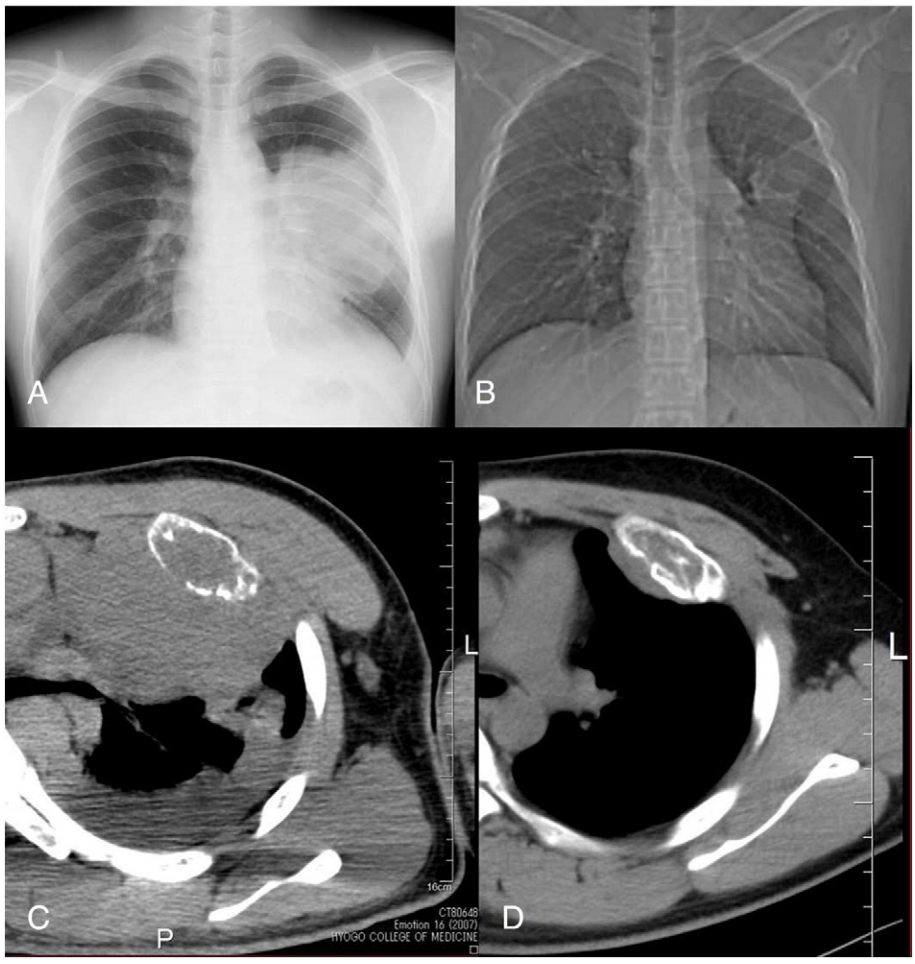

Fig. 1 Radiological findings before and after chemotherapy. A (chest X-ray) and C (chest CT) show that a huge tumor with destruction of the left third rib is expanding to the left thorax at the first visit to our hospital. B (chest X-ray) and D (chest CT) demonstrate a markedly diminished tumor after chemotherapy.