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Case Report

A Case of Long-term Survival in a Patient with Primary Primitive Neuroectodermal Tumor of the Lung

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Primitive neuroectodermal tumor (PNET) arising primarily in the lung is an extremely rare and aggressive malignancy with poor chances of patient survival. We present a case of long-term survival by a 29-year-old woman with PNET diagnosed after a hertological and immunohertochemical examination of a biopsy specimen obtained by performing video-assisted thoracic surgery. The patient underwent a left lower lung lobe lobectomy and 6 cycles of adjuvant chemotherapy. The patient has been free of any symptoms of the recurrence of the disease for 6 years after treatment completion.

Key Words: Neuroectodermal Tumors, Primitive; Sarcoma, Ewing; Lung

Primitive neuroectodermal tumor (PNET) is a malignant tumor composed of small round cells originating from neural crests and is classified as belonging to the Ewing sarcoma family.[1] It occurs largely in the bones or adjacent soft tissues of children or adolescents. It progresses very fast, has a high recurrence rate, and therefore has a poor prognosis. Cases of PNET that occur primarily in the lung parenchyma without intrusion into the pleura or the chest wall are very rare and thus far only about 20 cases have been reported worldwide.[2-5] In addition, reports about cases of long-term survival are even rarer due to the poor prognosis of PNET together with the rarity of the disease.

The authors diagnosed a 29-year-old female patient with PNET of the lung parenchyma, conducted a surgical excision and administered post-operative anti-cancer therapy. Follow up observations were made for six years without any manifestation of the recurrence of the disease. We hereby submit our report on this case.

CASE

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Patient: Female, 29 years old

Main Complaint: Left chest pain for five days

Current History: Ordinarily she was healthy but from five days ago, she felt a continuous dull pain in the area below the left chest and therefore visited our hospital. Her chest pain became all the more severe when she moved her upper body or coughed.

Past History and Family History: There was nothing significant to report.

Social History: She was a housewife and did not smoke.

Findings from physical examination: Her blood pressure, pulse rate, respiration rate, and body temperature were 130/80 mmHg, 76 breaths/min, 20 beats/min, and 36.7℃, respectively; she did not look sick and her mental state was clear. In her physical examination, her conjunctiva was not pale, there was no finding of jaundice of the sclera, and lymph nodes of the head and neck were not palpated. Feeble inspiratory rale was heard from the left lower pulmonary area. There was no tenderness in the abdomen and the liver and spleen were not palpated. There was no bilateral costovertebral angle tenderness and edema of the lower limb was not observed.

Findings by the laboratory: Her level of white blood cells, hemoglobin, hematocrit, and platelets was 8,670 /mm^3, 11.1 g/dL, 33.9 %, and 400,000 /mm^3, respectively, and erythrocyte sedimentation rate was 51 mm/hr. According to her serum biochemical test, her level of blood urea nitrogen, creatinine, serum sodium, potassium, and C-reactive protein was 15.1 mg/dL, 0.9 mg/dL, 141 mmol/L, 3.9 mmol/L, and 0.20 mg/dL, respectively.

In her liver function test, her level of aspartate transaminase, alanine transaminase, total cholesterol was 15 IU/L, 12 IU/L, and 202 mg/dL, respectively. Her urine test result was normal.

Findings from imaging: In a simple X-ray test, a round lump was observed with a relatively obvious boundary in the left pulmo sinister lobus inferior (Fig. 1A). In a chest computed tomography, a lump whose size was 5.5 x 4.5 cm with heterogeneous control enhancement was observed in the superior segment of the left pulmo sinister lobus inferior (Fig. 1B). Under positron emission tomography, the maximal standard uptake value of the mass increased to 12.6 and there was no other region where the value increased.

Findings from bronchial endoscopy: An intrabronchial mass was observed in a bronchoscopy test that had a smooth surface and increased blood vessel distribution completely obstructing the superior segment of the pulmo sinister lobus inferior (Fig. 2). In a histological bronchoscopy test, proliferation of small and round tumor cells was observed but was not sufficient to make a confirmative diagnosis.

Surgical findings: For confirmative diagnosis and treatment, video thoracoscopic surgery was conducted; the left pulmo sinister lobus inferior was excised and mediastinum lymph nodes were detached. The lung mass almost filled the left pulmo sinister lobus inferior, and was completely separated from the pleura; synechia or dissemination

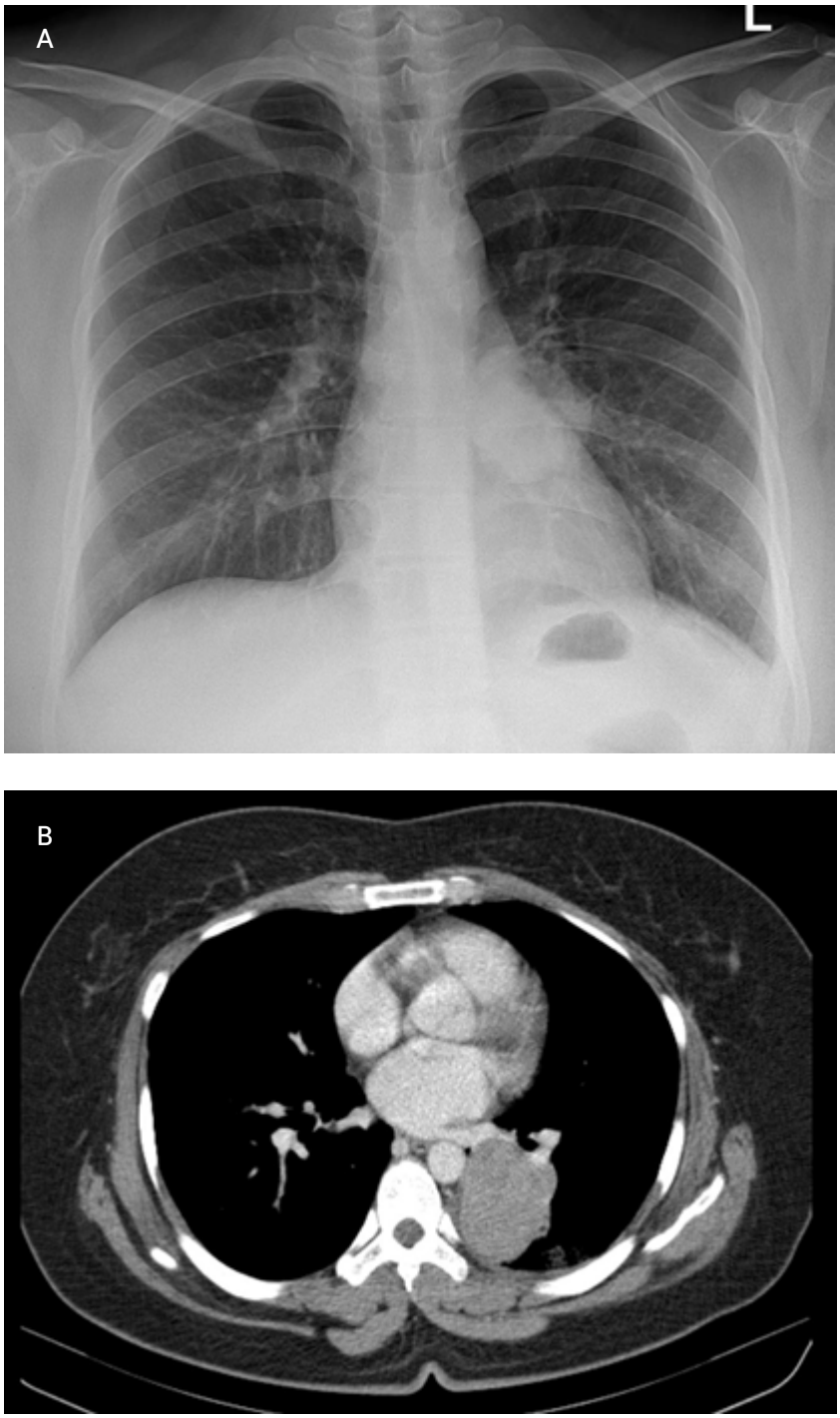

Fig. 1. Radiological findings. (A) Chest radiograph showed a mass in the left lung. (B) Chest computed tomographic image showed a 5.5-x 4.5-cm enhancing mass in the left lower lobe.

was not observed. Lymphadenopathy in the mediastinum macroscopically looking malignant was not observed.

Pathological findings: The excised lung lump was a well-defined yellow lump whose size was 4.5 x 4.4. cm and was accompanied by necrosis in

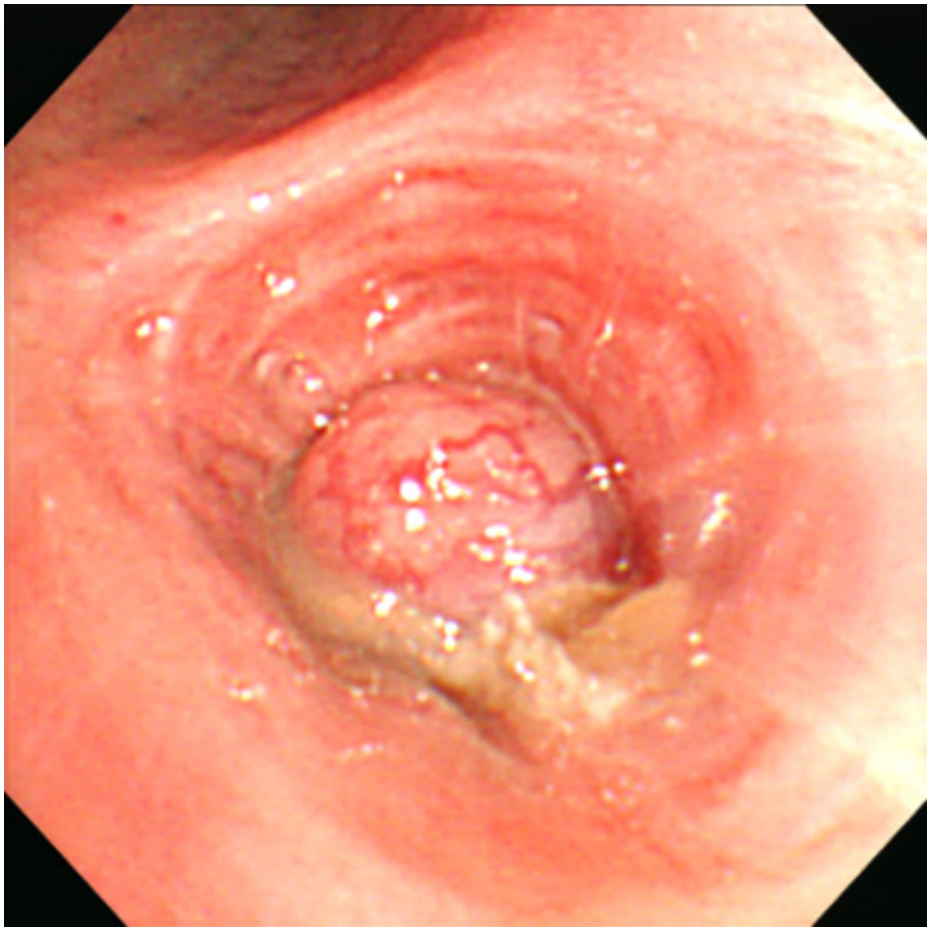

Fig. 2. Fiberoptic bronchoscopic image showed an endobronchial mass obstructing the superior segment of the left lower lobe.

its inside. Hematoxylin-eosin (H&E) staining showed a rosette formation (Fig. 3A, 3B)—round and small tumor cells of homogenous shape forming a lobule. In immunohistochemical staining, she tested positive for CD99 (Fig. 3C), vimentin, CD56, and synaptophysin, and tested negative for LCA, PanCK, S-100 protein, CD34, chromogranin, and EM; Therefore, a final confirmative diagnosis of PNET was achieved. There was no tumor infiltration in the excised bronchus' cross section, lymph nodes, and the pleura.

Treatment and Progression: From the 28th day after the surgery, she received anticancer chemo therapy with the administration of vincristine, cyclophosphamide, doxorubicin ifosphamide, and etoposide for six weeks. Neutropenia of grade 3 and 4 occurred during chemotherapy but she recovered from this soon and completed chemotherapy without major side effects or discomfort. After the last chemotherapy, she was periodically examined. Until the present, the sixth year after completion of the treatment, she has completely recovered and has shown no signs of recurrence of the illness.

DISCUSSION

After Stout et al. reported a disease that occurred

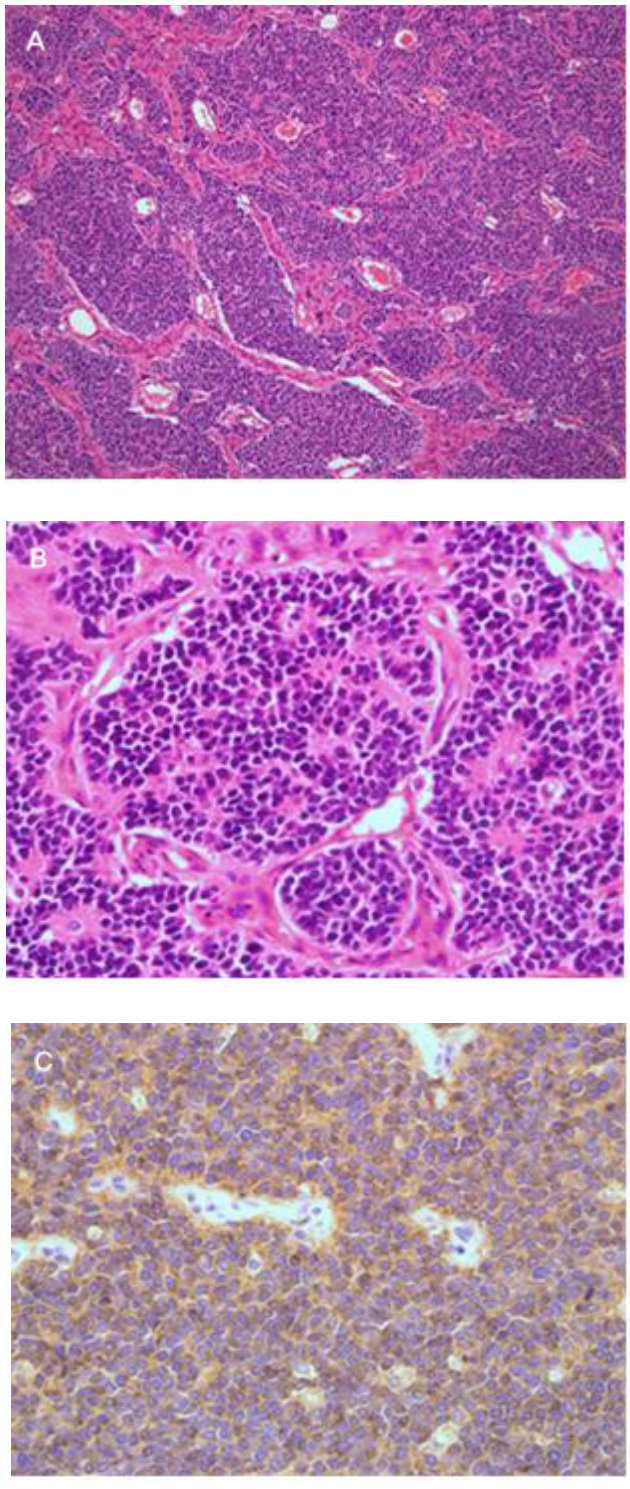

Fig. 3. Pathological findings. (A) Photomicrograph showed diffuse proliferation of small round cells (hematoxylin-eosin [H&E] stain, ×100). (B) Tumor cells showed round-to-oval nuclei with a rosette-like arrangement (H&E stain, ×400). (C) Immunohertochemical staining showed diffuse strong positivity for CD99 (×400).

in the ulnar nerve for the first time in 1918, the term *PNET* was first used by Hart and Earle in 1973.[6] Thereafter, as it was discovered that PNET had a similar and common chromosomal mutation with Ewing's sarcoma in histological findings and findings from immunochemical staining, PNET was regarded as a similar tumor to Ewing's sarcoma with the same origin; PNET is classified as belonging to the Ewing's sarcoma family together with Askin tumor that occurs in the thorax.[1] It is known that as its pathogenic cause is related to the displacement of Ewing sarcoma (EWS) gene located in the 22th chromosome and Friend leukemia integration 1(Fli-1) gene located in the 11th chromosome.[7]

PNET may occur in any part of our body but mostly it occurs in bones or soft tissues adjacent to the bones; on rare occasions, cases that primarily occurred in the duodenum, liver, kidneys, and adrenal have been reported. Cases where PNET primarily occurred in the lung parenchyma without infiltration into the pleura or chest wall are very rare; the number of such cases is just around 20 across the world.[2-5] According to the examination of literature in which the 20 cases reported thus far have been compiled, the number of male cases is 12 and the number of female cases is 8, indicating a slightly higher frequency of occurrence in males. The average age was 30.6 years old (range: eight to 75 years old) and it largely occurred in young people aged 35 or younger.[2] Its common symptoms included coughing, sputum, and chest pain; it was non-specific. Chest computed tomography showed a lump in the lung with heterogeneous contrast enhancement largely accompanying infiltration into the surrounding tissues and there was no characteristic finding that could clearly differentiate it from other tumors.

Diagnosis of PNET is done through histopathological findings, immunohistochemical staining, and chromosome test. The diagnosis rate by percutaneous needle biopsy was about 43% and most cases needed surgical diagnosis. A tumor was suspected in this case after a histological examination by bronchoscopy but confirmative diagnosis was made after surgical excision. H & E staining was able to identify Hormer Wright rosette; round and small tumor cells were differentiated as lobules by the fibrous vessel wall. Thereafter, neural differentiation was identified using immunohistochemical staining and differentiation from other tumors such as small cell lung cancer, lymphoma, and sarcoma could be made. With regard to immunohistochemical staining, two or more of neural differentiation markers—CD99, vimentin, NSE (neuron specific enolase), neurofilaments, S-100, Leu 7, secretogranin— tested positive and the testing positive for CD99 was most useful for identifying the disease.[3] Recently, t(11;22)(q24;q12), an EWS-FLI1 fusion gene, may be identified through a molecular genetic diagnosis method; it is found in about 85 to 89% of patients with PNET.[8] In the present case being discussed no molecular genetic diagnosis method was undertaken.

For successful treatment of PNET, a vigorous therapy program including surgical excision, an-

ti-cancer chemotherapy, and radiological treatment is necessary. It is known that at the time of diagnosis, 25 to 50% of PNET has already metastasized to other organs and the survival rate for five years is just 45 to 55%.[9] The prognosis of PNET that occurs primarily in the lungs is even less sanguine. According to the literature examination by Dong et al.[2], the two year survival rate among the aforementioned 20 cases was 37% in the eight cases where the patients received postoperative anticancer chemotherapy and 33% in the six cases where the patients received chemotherapy followed by surgical excision. Accordingly, the prognosis of PNET that primarily occurs in the lungs is poor but long-term survival is expected when complete surgical excision is performed after being diagnosed with a local occurrence of the disease at an early stage. Sirivella et al.[10] reported that when 23 chest PNET patients (including four primary lung tumors) received active combined therapy in a prospective observation study, they had a high ten year survival rate of 76% when it was possible to completely excise the disease locally. The prognosis of local Ewing's sarcoma that occurs in adults is gradually improving as the combined therapy of different anticancer agents is being developed.[11] In the 1970s, the combined therapy of vincristine, dactinomycin, cyclophosphamide, and doxorubicin (VDCA) was largely used. Thereafter, Grier et al.[12] verified in a randomized study that the prognosis of Ewing's sarcoma in the group to which ifosfamide and etopocide were added to VOCA significantly improved. After the study result was reported, a prescription composed of the five agents—vincristine, cyclophosphamide, doxorubicin, ifosfamide, and etopocide—was gradually used as a preferential therapy method and this prescription was used in the present case as well. The main reason why in this case the patient made a complete recovery and showed no signs of recurrence for six years after surgical and anticancer treatments was mainly because of the diagnosis of a local disease at a relatively early stage and the vigorous utilization of a combined therapy of surgical excision and active anticancer chemotherapy.

In conclusion, PNET that primarily occurs in the lung parenchyma is very rare and has a poor prognosis but when, as in this case, an active combined therapy program, including surgical excision based on an early diagnosis, is implemented, long-term survival can be expected. Hereby, the authors report this case together with an examination of relevant literature to highlight the clinical importance of early diagnosis and active treatment and the influence of these on the prognosis.

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