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거골에서 발생한 유윙 육종/원시신경 외배엽종양
- 1예 보고 -

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= **Abstract** =

Ewing's Sarcoma/PNET of the Talus
-Report of a Case -

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Ewing's sarcoma (ES)/PNET is common in both axial and appendicular skeletons, but is extremely rare in the talus.

Here, we report a case of ES/PNET of the left talus in a 29-year-old male patient diagnosed by fine needle aspiration cytology, and review the literature on similar cases. The cytological smears were composed of individually dispersed small round cells and occasional clusters of loosely cohesive cells. The tumor cells were fragile, frequently exhibiting naked nuclei. Two distinct types of cells were observed. The light (chief) cells displayed round or slightly oval nuclei with frequent indentations, generally inconspicuous nucleoli, and a thin rim of cytoplasm, which sometimes harbored small vacuoles. The dark cells were smaller, displaying scanty cytoplasm with dense hyperchromatic nuclei, intermixed with chief cells, and often manifesting as small molded groups. However, no significant nuclear pleomorphisms or mitoses were noted. Tumor cells in the cell block revealed positive cytoplasmic glycogen, as determined by a PAS stain with diastase control, and also exhibited positive immunoreactivity for CD99.

Key words : Ewing's sarcoma/PNET, Talus, Cytology, Aspiration

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INTRODUCTION

Ewing's sarcoma/PNET (ES/PNET) is an aggressive, primary malignant bone tumor usually seen in patients between the ages of 5 and 20 years.[1,2] It is common in both the axial and appendicular skeletons,[1,2] but rare in the foot and especially in the talus.[1-10] Since the first description of ES/PNET of the talus in 1953,[3] only 9 cases have been published.[1,3-10] The morphologic features of the ES/PNET cells can be recognized on cytologic examination, which represents an important diagnostic tool, both in bone and in soft tissue lesions.[11-14] The cytologic features of this tumor have not been reported in Korea yet.

We present a case of ES/PNET that originated in the talus and describe the cytologic features of the tumor together with a review of the literatures.

CASE

A 29-year-old male complained of pain and swelling in the left ankle region of three months' duration. He had been treated elsewhere by analgesics and acupuncture etc. with no relief. About seven months ago, he sprained this ankle and had been treated by a below-the-knee plaster cast for 3 weeks. On MRI findings, there was a round mass in the lateral aspect of the talus, about 3 cm in dimension, and the signal intensity of the mass was homogeneously low (isointense to muscle), and bright on T2W1. After the contrast infusion, there was diffuse homogeneous enhancement in the mass and the surrounding marrow and soft tissue (Fig. 1). Imaging studies showed no distant metastases.

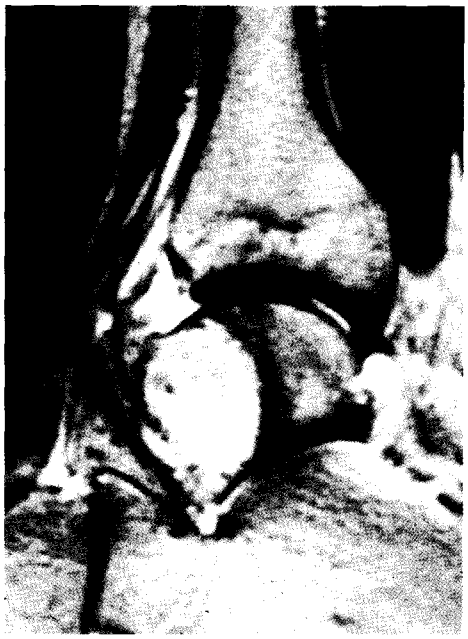

Fig. 1. Ankle MRI finding. There is a round mass in the anterior aspect of the talus with high-signal intensity in T2W2, about 3 cm in dimension.

Cytologic findings

The cytologic smears were composed of individually dispersed, small round tumor cells and occasional clusters of loosely cohesive cells (Fig. 2 and 3). The tumor cells were fragile, frequently showing naked nuclei. There were two distinct types of cells. The light (chief) cells had round or slightly oval, larger, and paler nuclei with frequent indentation, generally inconspicuous or absent nucleoli and a thin rim of cytoplasm, sometimes containing small vacuoles. The dark cells were smaller and had scanty cytoplasm with a dense hyperchromatic nucleus. The dark cells were interspersed, often as small molded groups, between the large paler cells (Fig. 2 and 3). However, no significant nuclear pleomorphism or mitoses were noted. Tumor cells in the cell block revealed both positive cytoplasmic glycogen by a PAS stain (Fig. 4A) with diastase control and positive cytoplasmic membranous immunoreactivity for CD99 (Fig. 4B). Other immunocytochemical stains were positive for vimentin, but negative for chromogranin.

Histologic findings

Needle biopsy was done and the specimen consisted of only scant soft tissue with hemorrhage, 0.4cm in aggregate. Microscopically, sections of the specimen showed almost entirely necrotic, hemorrhagic material, and only a small portion of small round cell tumor (Fig. 5). Tumor cells were small, uniform, and revealed indistinct cell outlines, resulting in a syncytial appear-

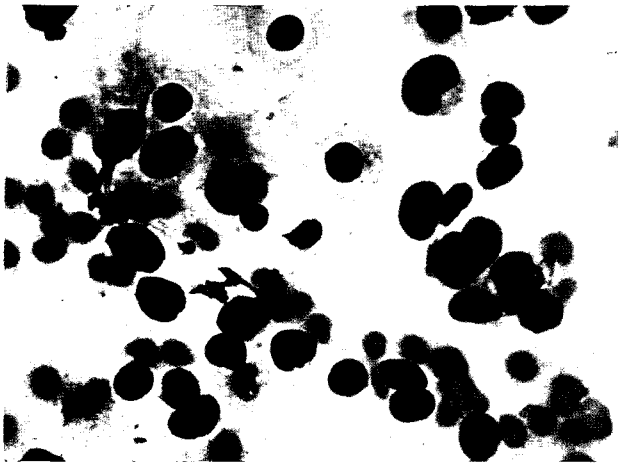

Fig. 2. Fine needle aspiration cytologic findings. The smear shows single cells or small groups of small round tumor cells. There are larger chief cells having round to slightly oval nuclei with frequent indentation and a thin rim of often vacuolated cytoplasm, and smaller dark cells. Nuclear molding is seen(Diff-Quik).

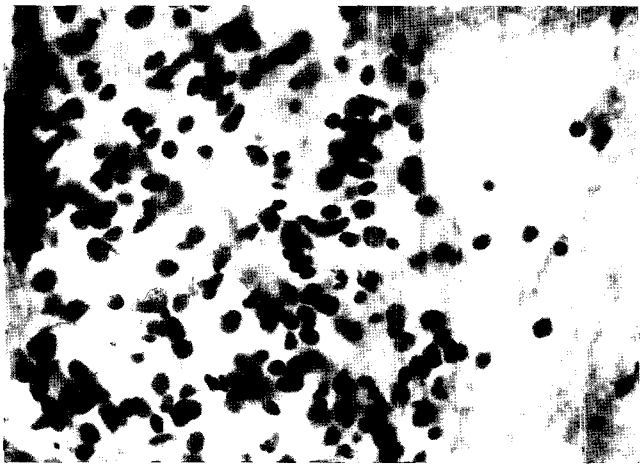

Fig. 3. Fine needle aspiration cytologic findings. The smear shows loosely adhesive clusters or single cells. The smaller dark cells are interspersed, often as small molded groups, between the larger chief cells(Papanicolaou).

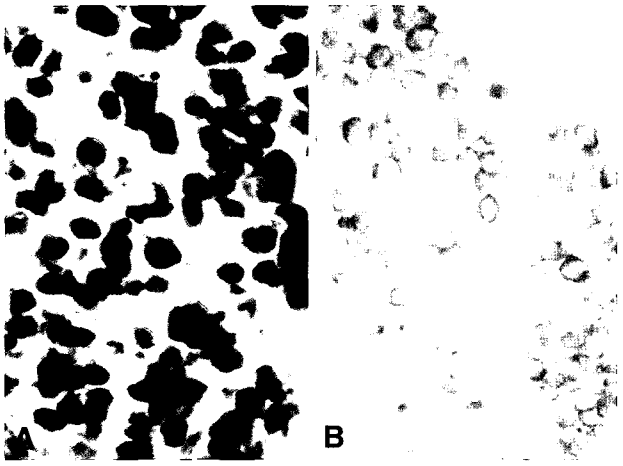

Fig. 4. Special stains of cell block. Tumor cells are strongly positive for PAS stain(A) and show positive immunoreactivity for CD99(B).

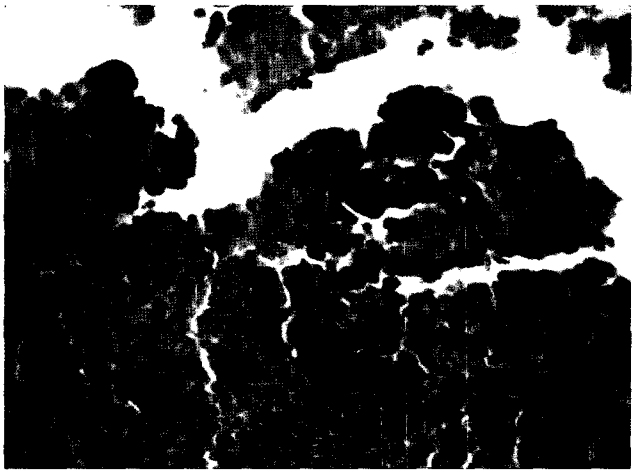

Fig. 5. Histologic findings. There are scant tumor cells with small round hyperchromatic nuclei and indistinct cytoplasm in the hemorrhagic background.

ance. The nuclei were round and hyperchromatic with inconspicuous nucleoli. Immunohistochemical stain for CD99 was positive in tumor cells.

DISCUSSION

Ewing's sarcoma was first described in 1921,[15] and many of Ewing's concepts have been modified.[1,12] Ewing's sarcoma and primitive neuroectodermal tumor (PNET) represent a spectrum of similarly appearing bone and soft tissue sarcomas that usually share the same cytogenetic abnormality, t(11;12)(q24;q12), and the term Ewing sarcoma/PNET(ES/PNET) is currently favored for this tumor family.[12]

ES/PNET in the foot constituted only 0.93 to 4.2% of all ES in bones[6] and most frequently involved the calcaneus and metatarsal.[1] ES/PNET in the talus was first described by Cohen et al.[3] in 1953. Since then, only 9 cases have been reported.[1,3-10] The clinical backgrounds

of the patients were summarized in table 1. The average age was 14 years(range from 3 to 29 years) and our case was the oldest one. The presenting symptoms were mostly pain with swelling and sprain,[1,3-10] and the diagnosis was established at an average of 10 months from the onset of symptoms. Adkins et al.[8] reported that the diagnosis took an average of 22 months in hindfoot ES/PNET from the onset of symptoms. These cases demonstrated the confusing presentation of ES/PNET, often mimicking infection, trauma or fracture. Although this tumor is very rare, these cases illustrate that ES/PNET must be considered in the differential diagnosis of young patients with persistent pain of the foot.[16]

The cytologic appearance of ES/PNET is distinctive, and the cytologic diagnosis is easily established, especially if sufficient material is obtained for ancillary techniques.[11-14] Smears are moderately to markedly cellular, and composed of predominantly single cells with scattered small cohesive clusters. The cells are fragile and naked nuclei as well as a faint grey-blue(MGG) background of detached cytoplasm are common. There is a characteristic mixture of two types of cells.[13,14] One is the light(chief) cell which has round or slightly oval pale nucleus with finely granular chromatin and slight contour irregularities, and one or two small nucleoli or chromocenters. A thin rim of cyoplasm contains small intracytoplasmic vacuoles. The other, the dark cell, is smaller and has scanty cytoplasm with irregular nuclei, dense chromatin and unappreciable nucleoli. The two types of cells are most clearly distinguished within groups and clusters of cells. The small dark cells are interspersed, often as small molded groups, between the large pale cells.[13,14] Rare forms of atypical(large cell) variants may exhibit large irregular nuclei, prominent nucleoli and abundant eosinophilic cytoplasm.[11,12] An intermediate between typical and atypical ES/PNET is also described and shows abundant cytoplasm, intranuclear grooves, and pale vesicular nuclei.[11] Binucleated and multinucleated tumor cells or ganglion-type cells are not observed. Background matrix material(e.g.cartilage or osteoid) or fibrillary background are distinctly absent. Rarely, tumor rosettes may be evident.[12-14] The presence of intracytoplasmic glycogen, in many cells, may be demonstrated with the PAS reaction and with electron microscopy. Expression of the Mic-2 glycoprotein product may be demonstrated by staining with CD99(013) or HBA-71.[11-14] The tumor cells also have consistent positivity for vimentin, and variable positive immunoreactivity for neuron-specific enolase, β_2-microglobulin, neurofilament, Leu-7, and chromogranin.[12,13]

The main differential diagnosis include malignant lymphoma, rhabdomyosarcoma, neuroblastoma and small cell carcinoma.[12-14] Lymphoma shows a dispersed pattern and numerous lymphoglandular bodies in the background as consistent findings, and the cell population found in lymphoma is more monotonous than the bimorphic population characteristic of ES/PNET.[12-14] Embryonal and alveolar rhabdomyosarcomas show a greater degree of morphologic variability from small round primitive-appearing cells to larger, more differentiated forms with obvious myogenous differentiation including cystoplasmic filamentous structures and, rarely, true cross-striations. In addition, the presence of binucleation and multinucleation is helpful in establishing the diagnosis of rhabdomyosarcoma.[13,14] Distinction of ES/ PNET from neuroblastoma can be extremely difficult. A fibrillary matrix in the background and a large number of neurogenic rosettes strongly favor the diagnosis of neuroblastoma.[12-14] Small cell carcinoma shows a tendency to compress or mold adjacent cells and to cluster in cytologic preparations. The cytoplasm is very scanty and often the cells appear as bare nuclei, especially adjacent to areas of necrosis. The nuclear chromatin is coarse and the nucleoli are absent or inconspicuous. The nuclei show a considerable amount of crush artifact, and the salt-and-pepper chromatin appearance on Papanicolaou staining is characteristic.[13,14] Ultrastructural studies combined with cytogenetic analysis are the most valuable diagnostic adjuncts in differential diagnosis. Immunocytochemistry, including reactivity for CD99, is also of value, although CD99 is reported to be positive in other malignant small cell tumors.[11-14] Our case showed a typical cytologic appearance of ES/PNET supported by both positive cytoplasmic glycogen in PAS stain with diastase control and positive immunoreactivity

Table 1. Summary of ES/PNET in the talus

Case	Authors	Age (years)	Sex	Affected side	Symtoms	Duration (months)	Metastasis	Therapy	Survival (Months)
1	Cohen, et al, 1953	3	M	Left	Painful limp of the left leg	30	Widespread dissemination	-	32
2	Falk and Alpert, 1965	8	M	ND	Painful ankle	3	-	RT	45
3	Weissman, et al, 1966	18	F	Left	Sprained ankle	6	-	Deep RT	6
4	Pandy, 1970	16	F	Right	Low-grade fever swelling & pain	3	-	Deep RT	4 1/2
5	Shirley, et al, 1985	12	F	ND	Pain & swelling	2	-	RT & CT	42 (alive)
6	Maletz, et al, 1986	13	M	Right	Pain & swelling	24	Lung	CT & B-K amputation	30 (alive)
7	Adkins, et al, 1997	20	F	ND	ND	ND	Lung	RT & CT	8
8	Serrano, et al, 1998	14	M	Left	ND	ND	ND	CT	ND
9	Rasit, et al, 2001	4	F	ND	Osteomyelitis	8	Pleura & spine	–	8
10	Present case	29	M	Left	Sprain	7	-	ND	48(alive)

ND: no data, RT: radiotherapy, CT: chemotherapy

for CD99. The biopsied tissue specimen revealed extensive necrosis with scant cellularity, so fine needle aspiration cytology was very useful for the diagnosis.

The recommended treatment of ES/PNET in the foot is local control with radiation or operation and systemic control with chemotherapy.[8] Surgical treatment appears to have an important role in local control and survival.[8,16] Adkins et al.[8] describes that survival of ES/PNET in foot bones is worse in patients who present with metastatic disease. The clinical summary of ES/PNET in the talus (Table 1) revealed metastases in four out of the ten patients, and six (including three patients who had metastases) out of the ten patients died after an average survival of 17 months, ranging from 4 months to 45 months. But three patients including our case survived 30, 42 and 48 months, respectively, but it is not known whether they are still alive.

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