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Extraskeletal Ewing's Sarcoma

-A Case Report-

In Kim, M.D., Seung-Koo Rhee, M.D., Han Chang, M.D. and Jin-Hyoung Sung, M.D.

From the Department of Orthopaedic Surgery, St. Mary's Hospital, Catholic University Medical College, Seoul, Korea

=국문초록=

골격외 유잉씨 육종 -증례보고-

가톨릭 의과대학 정형외과학교실

김 인·이승구·장 한·성진형

Ewing's sarcoma는 흔히 장관골의 골간부 골수강내에서 발생하는 원발성 악성 골 종양이나 극히 드물게 골의 병변없이 연부조직에 발생하기도 한다.

현재까지 Dahlin[2]을 비롯한 여러 저자들이 이와 유사한 골격외 종양을 보고하였고, 국내에서도 오[4]와 곽[5] 등이 각각 1례씩 보고한 바 있다.

그러나 Ewing's sarcoma는 일반적인 조직학적 검사만으로는 근육종, 미분화된 신경 아세포종, 세망세포 육종, 악성 임파종등과 감별이 어려우며, PAS염색등 조직화학적 검사를 한다 하더라도 이들 종양세포들이 glycogen과립을 함유하고 있는 경우도 있기 때문에 정확한 진단을 내릴수가 없다. 따라서 확진을 위하여는 조직학적 검사와 함께 전자현미경 검사를 추가하여야만 한다.

최근 저자들은 가톨릭 의과대학 부속 성모병원 정형외과에서, 43세 여자의 우측 하지에 발생한 골격외 Ewing's sarcoma 1례를 조직학적, 조직화학적 검색 및 전자현미경 관찰로 확진후, 1985년 10월부터 1987년 2월까지 16개월간 항암요법, 방사선조사 및 우하지 절단등으로 치료한 바 있어 문헌고찰과 함께 보고하고자 한다.

Key Words: Extraskeletal, Ewing's sarcoma, Electron microscopic examination.

ABSTRACT

Although Ewing's sarcoma is a primary malignant bone tumor, this tumor can also be occur on soft tissue without involvement of bone, but quite rare. The authors experienced a case of extraskeletal Ewing's sarcoma involving the lower extremity in a 43 year-old female, which was diagnosed by histochemical and electron microscopic examination. We have been follow her for 16 months after diagnosis and treated with chemotherapy, irradiation and finally above-knee amputation.

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INTRODUCTION

Ewing's sarcoma is a primary malignant bone tumor which is usually developed in the medullary cavity of long bone diaphysis. But this tumor is rarely found in soft tissue without any primary bony involvement.

Ever since the tumor of soft tissue which are histologically similar to Ewing's sarcoma was reported first by Dahlin[2] in 1967, several cases of extraskeletal Ewing's sarcoma has been intermittently reported by several authors[1-8]. In Korea, before this report, Oh et al[4]. presented a case of extraskeletal Ewing's sarcoma which was developed on the right up-

per arm. And after then, Kwak et al[3]. also found another case on left leg.

It is well known that the differential diagnosis of Ewing's sarcoma from undifferentiated rhabdomyosarcoma, neuroblastoma, reticulum cell sarcoma, and malignant lymphoma by the histologic studies only are not easy because their histologic findings are nearly similar each other. Moreover because the tumor cells in rhabdomyosarcoma and neuroblastoma often have glycogen granule too, histochemical method such PAS staining only is also not enough for differentiation[7]. Therefore, histochemical method and electron microscopic examination have to be used together to confirm diagnosis.

Hereby we present a case of extraskeletal Ewing's sarcoma confirmed by histological, histochemical and electron microscopic examination.

CASE REPORT

A 43-year-old Korean woman complained of dull pain and hard mass in her right lower extremity. One and half years prior to her admission to our department, a slow growing bean-sized painless mass was found at the anterolateral aspect of her right leg and excision was made by a general surgeon in a local clinic but biopsy was not attempted. Two months later, thumb-tip sized mass was devloped at the previous operation site and at the medial aspect of right thigh. So she was admitted in the department of general surgery of our hospital for biopsy again.

On admission(Oct. 1985), no palpable lymphnode or mass on other part of the body was found and no bony lesion observed through simple roentgenogram. And there was no any increased uptake of radioisotope in bone scan. On operation, a mass was found very well differentiated having hard consistency and no adhesion to surrounding tissue. As the mass was diagnosed as Ewing's sarcoma by histological examination, 90mg of adriamycin and 900mg of cytoxan were admi-

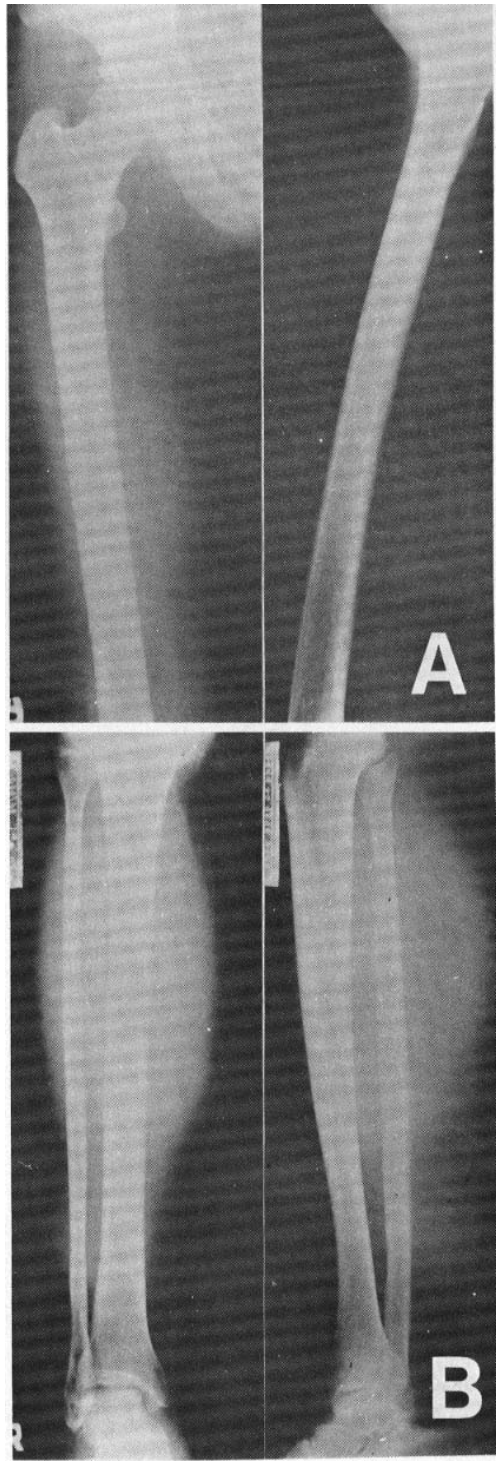

Fig. 1. A) Right femur roentgenogram shows no definite abnormalities. **B)** Right tibia roentgenogram shows only soft tissue swelling(arrows) without bony changes.

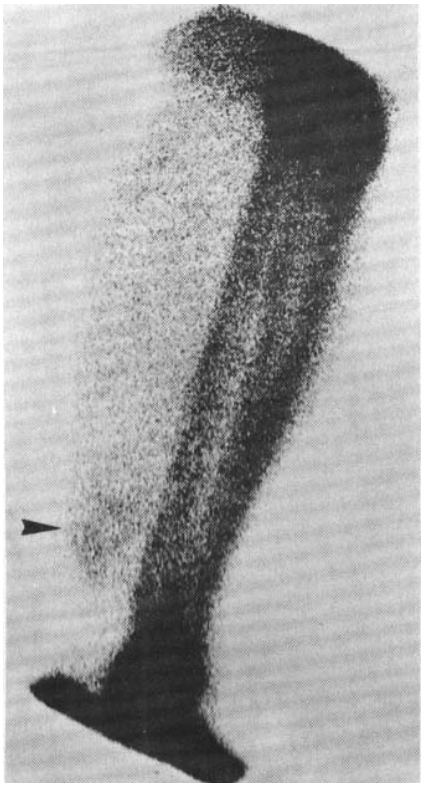

Fig. 2. Bone scintigraphy with pin hole imaging shows a irregular faint hot area in the soft tissue posterior to the distal tibia(arrow) without definite bony involvement. But the uptake are generally increased on the knee, tibia and ankle, suggesting increased turnover rate, rather than active osteolytic change.

nistered after 2 weeks of operation. And one week later, total 5,040 rads of local radiation theraphy were also performed on right thigh and lower leg each for 10 weeks. After then, she was discharged, and we lost her for follow-up.

8 months prior to the second hospitalization, the mass at the previous operation was found again and slowly grew, however she have only got acupunctures and herb medicines without any medical treatment. And two months later, another mass was found at the medial aspect of the right thigh.

On physical examination on the second admission to our department(Jan. 1987), an adult fist sized mass was palpated at the anterolateral and posterolateral aspects of distal one third of right leg, and small amount of pus

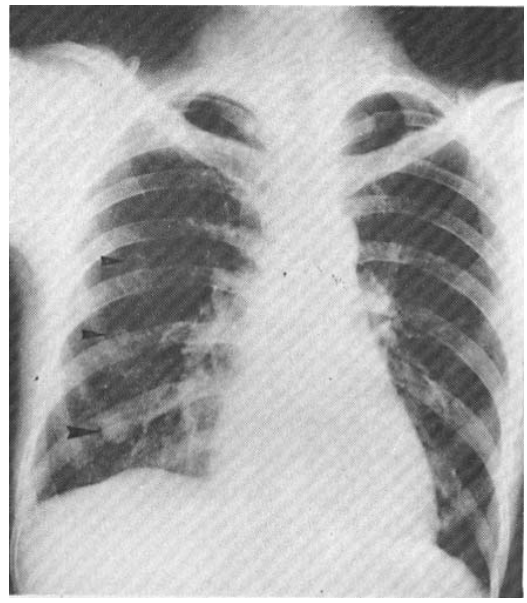

Fig. 3. Chest film shows variable sized multiple round nodular densities scattering both lung fields, suggesting metastasis(arrows).

was drained from the overlying skin due to superficial infection and necrosis. Thumb-tip sized, movable, non-tender mass on the medial aspect of right thigh and a enlarged lymphnode were also noted in the right inguinal region. Otherwise the patient was well.

A roentgenogram of right leg and thigh shows only soft tissue swelling without bony lesions(Fig. 1). Bone scan revealed slight increased uptake of radioisotope on the soft tissue of distal calf(Fig. 2). Chest films on the first admission to our hospital showed free, but a few metastatic lesions of 1~2cm in diameter were found on both lower lung field at the second admission(Fig. 3).

Laboratory studies at this time revealed no abnormal findings except mild anemia. 24 hour urinary V.M.A. excretion was in normal range.

High above-knee amputation were perfomed. A mass from the right thigh, measuring up to 2×2×2cm, was placed on the subcutaneous region outside of fascia and had clear demarcation with hard consistency and no adhesion to surrounding tissue. Its transection was colored gray white and yellow and sho-

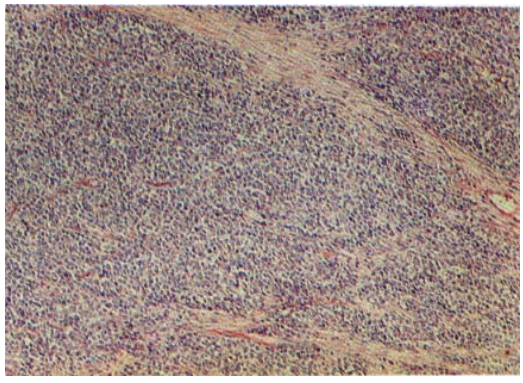

Fig. 4. Closely-packed and uniformal small round tumor cells with interspersed thin-walled vascular structure(H and E, ×100).

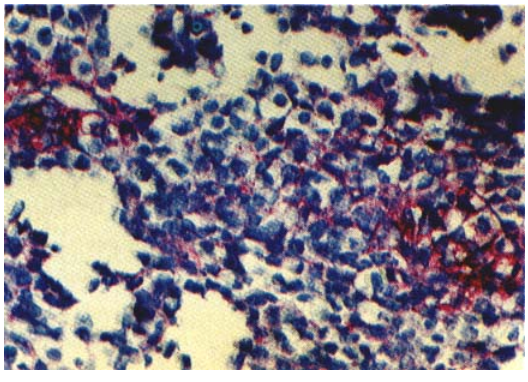

Fig. 5. PAS preparation shows intracelluar glycogen stained with deep purple color(×400).

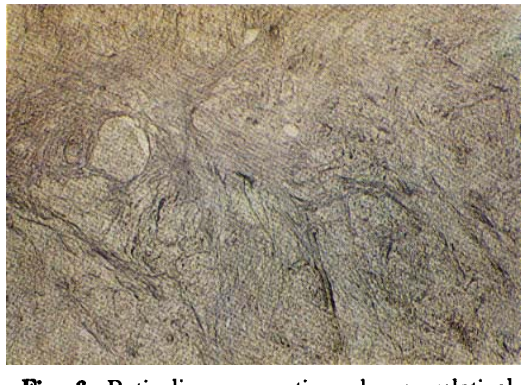

Fig. 6. Reticulin preparation shows relatively lobular arrangement of the tumor, the intervening fibrous septa, and the absence of reticulin fibers between tumor cells(×40).

wed partial hemorrhage in it. When the amputated leg was cut, pus with foul odor was drained. But the ill-defined huge mass on the right calf was extended to the just inferior of knee joint along the gastrocnemius muscle.

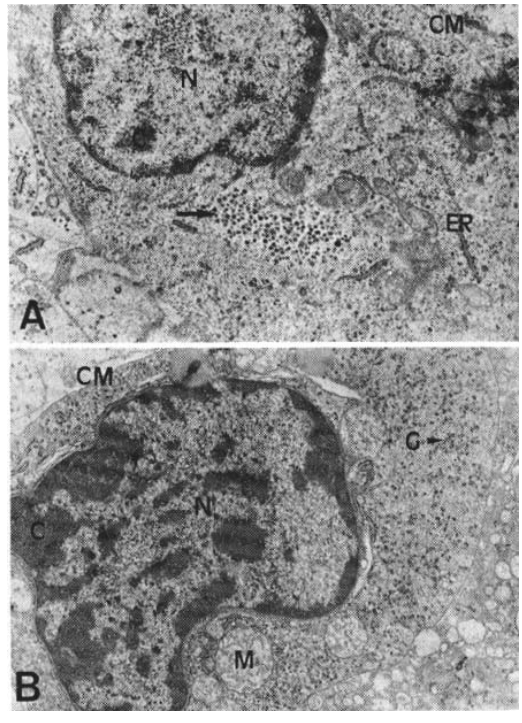

Fig. 7-A, B) Electron microscopic pictures. The individual tumor cell has a prominent nucleus with marginated chromatin, few organelles, and abundant glylcogen. There are no neural tubules or neurosecretary granules(×10,500).
Arrow: focal collection of glycogen granules
CM: cell membrane
N:nucleus
C:nuclear chromatin
M: mitochondria
ER: rough endoplasmic reticulum
G: glylcogen granule

Adhesion and partial invasion into the periosteum of tibia were grossly observed, howerer no actual bony destruction was seen.

The same pathologic findings were found from thigh and calf mass. Relatively small and round cells were closely packed with fibrous connective tissue septa and intervening thin vascular structures(Fig. 4), but bone was clear. In PAS staining, small granules stained in deep purple were observed(Fig. 5), and in reticulin staining, tumor cells were divided into lobule by connective tissue but intercellular reticulin fibers were not found(Fig. 6).

On electron microscopic examination, cytoplasm contained relatively few organelles and

abundant glylcogen granules which were scattered or in the form of focal collection. Nuclear density was increased and irregular clumping of marginated chromatin was observed. There were no neurosecretary granules or neural tubule which can be observed in neuroblastoma(Fig. 7). Extraskeletal Ewing's sarcoma was the final pathological diagnosis.

After the healing of surgical wound, radiation therapy and anticancer chemotheraphy were advised, but she refused and discharged. She was death 4 months later.

DISCUSSION

Extraskeletal Ewing's sarcoma tends to develop in the relatively younger age, predominently adolescents and young adult between 15 and 30 years of age. It chiefly involves the soft tissues of the paravertebral region, adjacent chest wall, retroperitoneum and lower extremity.

Generally tumor grows rapidly to the size of 5~10cm. In principle to make a diagnosis of extraskeletal Ewing's sarcoma there should be shown no bony lesion at roentgenogram, however, according to the report by Angervall and Enzinger[1], bony changes such as slight periosteal reaction and cortical hypertrophy were observed in 10 cases out of 34. The case in this report didn't show any bony changes at the simple roentgenogram and bone scan initially. And even 15 months later, when she was hospitalized in our orthopaedic department, simple roentgenogram revelaed no bony change in spite of extensive soft tissue involvement. In bone scan, increased uptake of radioisotope was found at soft tissue of calf. Although radioisotope uptake was increased a bit on whole tibia when compared with other part of body, it was not clear whether it was the overlap of soft tissue uptake or the increased bony turnover rate.

Operative findings up to the present generally show that tumor is usually devloped at the deep soft tissue, invade muscle and adhere to surrounding tissues or near periosteum and ligament[1]. In the first tumor excision of the present case, the tumor was so well encapsulated that it looked like a benign tumor, and it was located at relatively superficial layer clearly demarcated from surrounding tissues without any invasion. But when she underwent A-K amputation, mass at the right calf had overlying skin necrosis with no demarcation from surrounding tissues and it was extended to the just inferior of knee joint along with the gastrocnemius muscle. The right calf was almost full of tumor tissue and there were adhesion and partial invasion into tibial periosteum but no clear cortical destruction.

The most common metastatic sites are lung and adjacent bone, however the case of lymphnode metastasis is rarely reported. In this case, when the patient was first hospitalized, metastasis was not recognized by physical examination and chest roentgenogram. When hospitalized again 15 months later, an enlarged inguinal lymph node was palpated and chest roentgenogram revealed a few metastatic lesions on both lower lung field.

With the light microscope only, it is known to be very difficult to differentiate extraskeletal Ewing's sarcoma from reticulum cell sarcoma which is a kind of small round cell sarcoma, malignant lymphoma, neuroblastoma and undifferentiated rhabdomyosarcoma[1,5,7]. Rhabdomyosarcoma is characterized by more irregular cell membrane with characteristic alveolar pattern and has typical rhabdomyoblast only in 30%. Reticulum cell sarcoma easily differentiated from Ewing's sarcoma by intercellular reticulin fiber and no intracellular granule at PAS staining. In general, the presence of glycogen within tumor cells has been pivotal in the diagnosis of Ewing's sarcoma. But glycogen alone is unreliable as a pathognomic diagnostic aid due to its presence in several tumors such as rhabdomyosarcoma, malignant lymphoma and even neuroblastoma which is generally known not having glycogen granule.

Therefore, to make an exact differential diagnosis, histological or histochemical study as

well as the age of patient, site of involvement, roentgenogram and urinary catecholamine level are required. And electron microscopic examination must be added to differentiate especially from neuroblastoma. The neuroblastoma is seen, through electron microscopic examination, to have large number of neurosecretary granule and neural tubules or synapses[7]. Ewing's sarcoma of soft tissue is histologically similar to Ewing's sarcoma of bone, however it has relatively abundant cytoplasm with vacuole and its cell membrane is relatively clear demarcated.

For treatment of this tumor, irradiation and chemotheraphy should be used separately or combined after wide local excision. Anticancer drug or radiation theraphy without excision cannot get the local control of tumor.

CONCLUSION

It is known that the Ewing's sarcoma may have originated in the soft tissue but are exceptional. The difficulties usually encountered in making the distinct diagnosis of extraskeletal Ewing's sarcoma was presented here in this report with histological, histochemical studies as well as electron microscopic examination.

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