A Case of Metastatic Epithelioid Sarcoma

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Epithelioid sarcoma (ES) is a very rare, unique soft tissue sarcoma, which was first fully described by Enzinger in 1970. The tumor chiefly occurs in young adults and affects the soft tissue of the distal extremity.

A 46-year-old male patient had slowly growing masses on his left plantar surface, which were diagnosed as ES and mass excision and radiation therapy were done. Eight months later, about 1 x 1 cm sized, well defined multiple erythematous nodules on his scalp were discovered. Although he was treated with chemotherapy, no improvement was gained.

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Key Words : Epithelioid sarcoma, Metastasis

Epithelioid sarcoma (ES) was characterized as a rare but distinctive type of soft tissue malignancy with cutaneous manifestations by Enzinger in 1970. Chase and Enzinger’s a retrospective review of 241 cases of ES showed its propensity to occur in the distal extremities of young adults. The tumor is generally firm and nontender, and involved the dermis, subcutis or deeper soft tissues, particularly fascial planes, aponeuroses, and tendon sheaths. Follow-up data of 202 cases showed a recurrence in 75% and metastasis in 45%. The most common initial sites of metastasis were the lymph nodes (48%), lungs (25%), scalp (10%), and other skin (6%).

We describe a patient with ES presenting scalp metastasis from a primary lesion in the left plantar region. For the evaluation of the histogenetic origin, immunohistochemical and electron microscopic examination were performed. Although he was treated with chemotherapy, the lesion progressed and worsened.

REPORT OF A CASE

A 46-year-old man visited our department with presenting multiple tender nodules on his scalp in May, 1993. He hit his left sole on the ground by falling down from a height of 2m in spring, 1990. Following this a slowly growing, painless mass on his left plantar surface was identified. One year later, another mass was identified on the distal side of the initial site. Excision of the masses (3 x 4cm, 2 x 2cm in diameter) including parts of the muscle tissue and fascia down to the periosteum was performed at the department of orthopedic surgery in August,

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Fig. 1. On physical examination, the skin lesion showed erythematous, 1 x 1cm sized nodule with some central erosion on scalp.
Fig. 2. Histopathological examination from the skin lesion of scalp. (A) Multiple nodules in the dermis and subcutaneous tissue were composed of peripheral palisading cell infiltration and central necrobiosis (H & E, ×40). (B) They consisted of large ovoid or polygonal cells with deeply eosinophilic cytoplasm and plump spindle cells. Hyperchromatism, cellular pleomorphism was seen, but a distinct biphasic pattern was not observed (H & E, ×200).

Fig. 3. Special staining from the skin lesion of the scalp.

A. The cytoplasm was stained deep-red brown and the intercellular collagen bundle blue (Masson's trichrome, ×40).

B. The surrounding matrix was stained blue (Alcian blue, ×40).

C. The intracellular glycogen was stained red (PAS, ×40).

Table 1. Summary of Immunohistochemical study of this case

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<th>Positive</th>
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<td>Human factor VIII-related antigen</td>
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Fig. 4. Immunohistochemical studies on the skin lesion of the scalp. It showed positive reactivity for staining with primary antibodies to (A) cytokeratin, (×200) (B) epithelial membrane antigen, (×200) (C) vimentin, (×100) (D) α-1-Antichymotrypsin (×200).

Fig. 5. Ultrastructural study on the skin lesion of the scalp.
A: It showed ovoid nucleus in epithelioid cell and paranuclear masses of intermediate filament (×2,500).
B: Indented nucleus in epithelioid cell and paranuclear masses of whorl-like intermediate filament (×12,000).

1992. The tumor was situated in the dermis and the subcutaneous fat with close association to the underlying fascia. Under the diagnosis of ES, it was proposed to amputate but he refused. Radiation therapy was done from December, 1992 to January, 1993 (cobalt treatment of total dosage;
6600 cGy). He discovered multinodular lesions on his scalp in April, 1993. His family history was non-contributory. On past medical history, five years ago, he had pulmonary tuberculosis. On physical examination, the skin lesion revealed about twenty erythematous, variable sized papules and nodules with some centrally erosive and slightly depressed lesions on the scalp (Fig. 1). No other physical abnormalities were detected. Routine laboratory tests including a complete blood cell count with differential cell count, urinalysis, liver function test, ASO titer, CRP, VDRL, stool examination, bone scan, abdominal sonogram, skull X-ray, and chest roentgenogram showed to be negative or within normal limits.

Histopathological examination from the skin lesion of the scalp revealed multiple nodules in the dermis and subcutaneous tissue with central necrosis and normal finding of the overlying epidermis and skin appendages. They consisted of large ovoid or polygonal cells with deeply eosinophilic cytoplasm and plump spindle cells. Peripheral palisading cell infiltration with central necrobiosis, hyperchromatism, and cellular pleomorphism were seen, but a distinct biphasic pattern was not observed (Fig. 2). On the special stains, the cytoplasm was stained deep-red brown and the intercellular collagen bundle blue on Masson's trichrome stain, and the surrounding matrix blue on alcian blue stain, and the intracellular glycogen red on PAS stain (Fig. 3). The result of the immunohistochemical study is summarized at Table 1. (Fig. 4). An Ultrastructural study showed an ovoid or indented nucleus in epithelioid cell and paranuclear masses of whorl-like intermediate filament (Fig. 5).

We concluded that the scalp lesions were metastasized from ES of the left plantar region and chemotherapy was done. Two cycles of the regimen of VP-16, ifosfamide and cisplatin were not effective. Therefore, the regimen was changed to ifosfamide and Adriamycin, but with no response. One month later, inguinal, axillary, cervical lymph node involvement was detected and the skin lesions of scalp were worsened with pain and multiple ulcerative nodules extending to the face, and neck.

**DISCUSSION**

ES is a distinctive type of soft tissue malignancy which was first detailedly characterized by Enzinger in 1970, typically as an indolent, relentless clinical course with numerous recurrences, frequently localizes in regional lymph node or pulmonary metastasis.

The age of onset of the disease is usually in the third or fourth decade of life and male to female ratio is about 2:1. A previous traumatic lesion which develops into a tumor occurs in 20% of the cases. The time interval from the trauma to the tumor is immediate to 20 years and the majority of the tumors occur in the extremities. Clinically it most commonly presents as benign-appearing asymptomatic, slow growing papules, nodules, plaques, erosions, ulcers, or any combination of these involving the distal upper extremities (58%), particularly the hands and forearms, distal lower extremities (15%), proximal lower extremities (12%), proximal upper extremities (10%), trunk (3%), head and neck (1%). It usually occurs in the dermis, subcutaneous tissue, fascia and ten-

| Table 2. A clinical review of reported cases of epithelioid sarcoma in Korean dermatological literatures |
|---|---|---|---|---|---|
| Sex/Age | Duration | Lesion | Symptom | Metastasis | Treatment |
| Kook et al. (1990) | M/26Y | 3yrs | Lt. hand & forearm | Asymptomatic → Pain | Lt. upper arm & axilla | Amputation of Lt. U/E & chemotherapy |
| Chun et al. (1992) | M/24Y | 1yr | Lt. palm & wrist | Pain | Lt. axillary L/N & lung | Lt. shoulder disarticulation & chemotherapy |
| | M/29Y | 1yr | Lt. forearm | Pain | Lt. axillary L/N | No |
| Present case | M/46Y | 4yrs | Lt. foot | Asymptomatic → Pain | Scalp & inguinal, axillary, cervical L/N | Chemotherapy |
don. The majority of the patients are asymptomatic, but, pain or tenderness is a complaint of 22% of patients. The clinical features of the cases that have been reported in Korean dermatological literatures and the present case are reviewed (Table 2).

Histologically, the tumor is composed of nodules, 5-50 mm in diameter surrounded by fibrosis, of large, round to polygonal cells with abundant eosinophilic cytoplasm resembling epithelioid histiocytes, as well as more elongated spindle-shaped cells and the transition between the two cell types are always subtle, never abrupt. Individual tumor cells often extend in a cordlike fashion between the collagen bundles. Large and atypical tumor cell nuclei with mitoses are often present. There are frequent erosions of bone with extension into perineural space or vascular invasion. The central portion of the nodule often shows necrosis and/or fibrosis as the appearance of a centrally necrotic carcinoma or granuloma. The microscopic patterns are thus easily confused with a necrotic granuloma, nodular fasciitis, benign and malignant fibrous histiocytoma, synovial sarcoma, “amelanotic” melanoma, ulcerated squamous cell carcinoma, other benign or malignant processes. The most common and most recognizable pattern in recurrent or metastatic lesion is pseudo-granulomatous proliferation. Skin is microscopically involved in 24% of the cases, skeletal muscle in 28%, and fascia, tendons, or the interlobular septa of the subcutis in the remaining neoplasms. On special staining, reticulin and Masson’s trichrome stain highlight the nodular growth pattern and emphasize the intercellular collagen. PAS stain shows many tumor cells contained glycogen. Extracellular acid mucopolysaccharides (hyaluronidase-sensitive) are present but, intracellular mucin production is conspicuously absent. Our case showed typical histopathological patterns of ES.

The histogenetic origin of this tumor has been an unresolved controversy from its original description to the present time. Based on ultrastructural and enzymatic histocytochemical investigations, a unifying concept is proposed suggesting the histogenetic derivation of ES from pluripotent and ubiquitous mesoderm-related stem cells. This unifying histogenetic concept would be compatible with recent reports on the triple expression of vimentin, cytokeratin, and desmin in ES. Therefore, the coexpression of three different classes of intermediate filaments in the ES might in fact plainly indicate the capability for “multidirectional differentiation” acquired during the process of neoplastic transformation. The results of several immunohistochemical studies are summarized (Table 3). Immunohistochemical studies of our case showed similarities to other cases.

The recurrence rate following the initial surgical procedure is 77% and generally occurs proximal to the initial primary sites. Enzinger found that recurrence usually occurred within six months of the initial surgery. Our patient’s clinical course was that distant metastasis in the form of multiple nodules following a asymptomatic period, occurred after about 8 months. Sustained metastases are 45% and the most frequent initial metastatic sites are lymph nodes (48%), lungs and pleura (25%), scalp and nuchal region (10%), other skin (6%), mediastinum, pancreas, gastrointestinal tract, duval space, liver, kidney, and bone. In our case, the initial metastatic site appeared to be the scalp. Adverse prognostic factors are recurrence after the initial local excision, vascular invasion and lymph

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* ND: not done
AAM: α-1-Antichymotrypsin, CEA: Carcinoembryonic antigen.
node metastasis, proximal or axial tumor location, increased size and depth, hemorrhage, mitotic figures, necrosis, less lymphocytes infiltration, and late diagnosis. More favorable prognostic factors are younger individuals, tumors in distal extremities, females between the ages of 10 and 49, early diagnosis and treatment, tumors smaller than 5.0cm of diameter and low S-phase percentage(<5%). A five-year survival rate is reported in 70% and 10-year survival rate is 50%.15,19

Initial wide or radical resection for the treatment of tumor is recommended. Radiation therapy given either before or after surgery can substantially decrease the local recurrence rate in ES to less than 20% while preserving a cosmetically and functionally acceptable limb in a large majority of patients so treated. The addition of adjuvant therapy to wide or radical resection appears to be beneficial, but long-term follow-up is necessary.15,20,21

REFERENCES