Two Cases of Epithelioid Sarcoma with Immunohistochemical Study

Duk Kyu Chun, M.D., Kwang Hyun Cho, M.D., Seong Hoe Park, M.D.*

Departments of Dermatology and Pathology, Seoul National University College of Medicine*
Seoul, Korea

Two typical cases of epithelioid sarcoma were examined by immunohistochemical stain using antibodies to epithelial membrane antigen, carcinoembryonic antigen, vimentin and cytokeratin. Both cases showed positive reactivity for the four kinds of antibodies. These results point to the fact that epithelioid sarcoma simultaneously expresses epithelial markers and characteristic mesenchymal phenotypes. Epithelioid sarcoma appears to be a tumor derived from a multipotential mesenchymal cell with multidirectional differentiation.
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Key Words : Epithelioid sarcoma. Immunohistochemical stain

In 1970, Enzinger[1] gave the name epithelioid sarcoma(ES) to a group of polygonal-celled soft tissue sarcomas in 62 cases, which were often confused with necrotizing granuloma or squamous cell carcinoma. Chase and Enzinger[2] reviewed 241 cases of ES, all of which gave a similar picture to our cases of recurrent tumor involving the hand or forearm in young adult males. The histogenesis of this tumor has been debated. Ultrastructural observation using electron microscope has led to various hypotheses of differentiation toward histiocytes,[3,4] or synovium[3,5,6] from primitive cells. Recently, immunohistochemical studies[7,8,9] revealed the coexistence of epithelial markers and vimentin in ES and led to the concept of a multipotential mesenchymal cell origin. We performad immunohistochemical studies in 2 typical cases of ES using epithelial membrane antigen, cytokeratin, vimentin and carcinoembryonic antigen.

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Reprint requests : Duk Kyu Chun, M.D., Department of Dermatology, College of Medicine, Seoul National University, Seoul, Korea

REPORT OF CASES

Clinical findings

Case 1. A 24 year-old male was seen because of crusted plaques with ulceration on his left palm and wrist which had been present for one year. On physical examination, there was an ulcerated, dark brownish to bluish crusted plaque on his left forearm(Fig. 1). Both a flexion deformity of the left hand and left axillary lymph node enlargement were also observed. Although prompt left shoulder disarticulation and post-operative chemotherapy including adriamycin, and dacarbazine, were performed, the patient has developed as demonstrated on chest CT films.

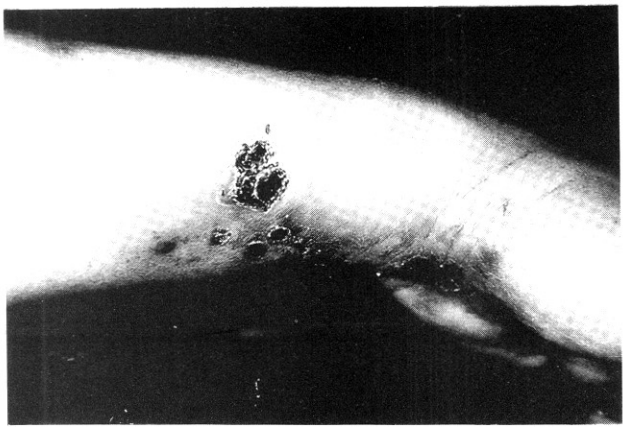

Fig. 1. Dark brownish to bluish crusted plaques, with ulcer on left forearm(Case 1).

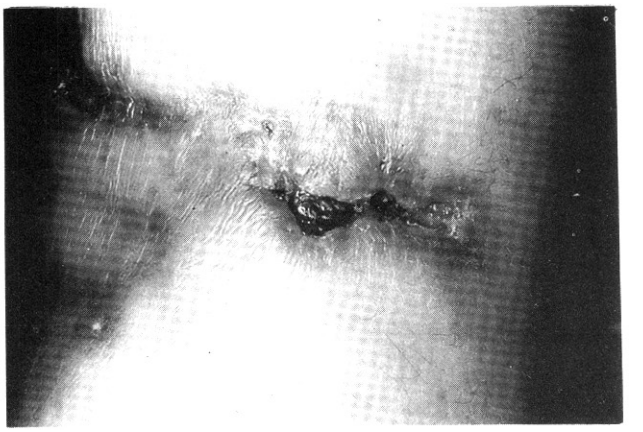

Fig. 2. Indurated, slightly erythematous plaques, with ulceration and scarring(Case 2).

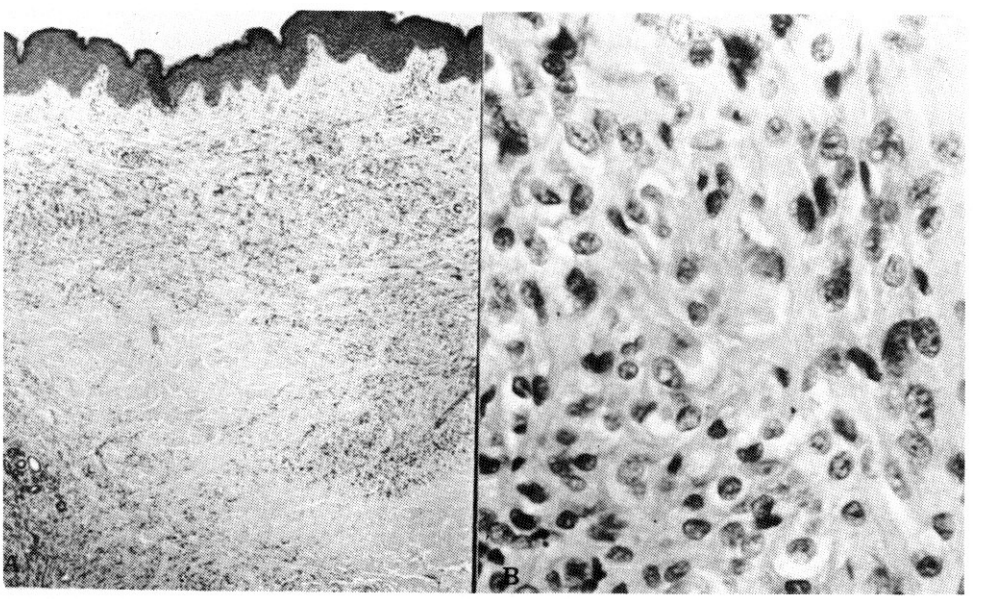

Fig. 3. A : On H & E stain, there are multiple nodules in the dermis with central necrosis(× 40).
B : The constituent cells are oval, polygonal and spindle cells(× 400).

Case 2. A 29 year-old male patient was seen because of a painful ulcerated plaque on his left forearm. Swelling of the left forearm was noted one year ago, which later devoloped ulcerations. Biopsy specimens from the forearm lesion revealed consistent findings for epithelioid sarcoma, while an axillary lymph node biopsy revealed reactive hyperplasia. On physical examination, a 4 × 3㎝ sized, indurated, slightly erythematous plaque was observed. Ulceration and scarring were also present(Fig. 2). Amputation of the left arm was recommended, but refused.

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Histopathology and histochemistry

Case 1. Histopathological examination from the skin lesion revealed multiple nodules in the dermis and subcutaneous tissues with central necrosis(Fig. 3A). They consisted of large ovoid or polygonal cells with deeply eosinophilic cytoplasm and plump spindle cells, but neither a distinct biphasic pattern or cellular pleomorphism was observed(Fig. 3B). On histochemical stain, the cytoplasm stained deep-red brown on Masson's trichrome stain, and the surrounding matrix blue on alcian blue stain(Fig. 4A, 4B). There was a dense meshwork of reticulum fibers between the tumor cells on reticulum stain (Fig. 4C).

Case 2. Histopathological examination including histochemical stain revealed similar findings to those of case 1.

Immunohistochemical study

Immunohistochemical studies were performed by using avidin-biotin-peroxidase complex (ABC) techniques,[10] using 10% buffered formalin-fixed and paraffin embedded tissues. After deparaffinization, the sections were incubated with primary antiserum diluted in PBS, and with diluted biotinylated antibody solution, and ABC reagent, and peroxidase substrate solution, sequentially. Then, the sections were counterstained with Mayer's hematoxyline and mounted with glycerol gel. Both cases showed positive reactivity for staining with primary antibodies to cytokeratin, epithelial membrane antigen, carcinoembryonic antigen, and vimentin (Biogenex, USA)(Table 1). These antigens were expressed preferentially by the epithelioid cells, but spindle-shaped cells were also frequently stained(Fig. 5A, B, C, D). Cytokeratin staining was mostly in the cytoplasm and the epithelial membrane antigen in cell membranes (Fig. 5A, B).

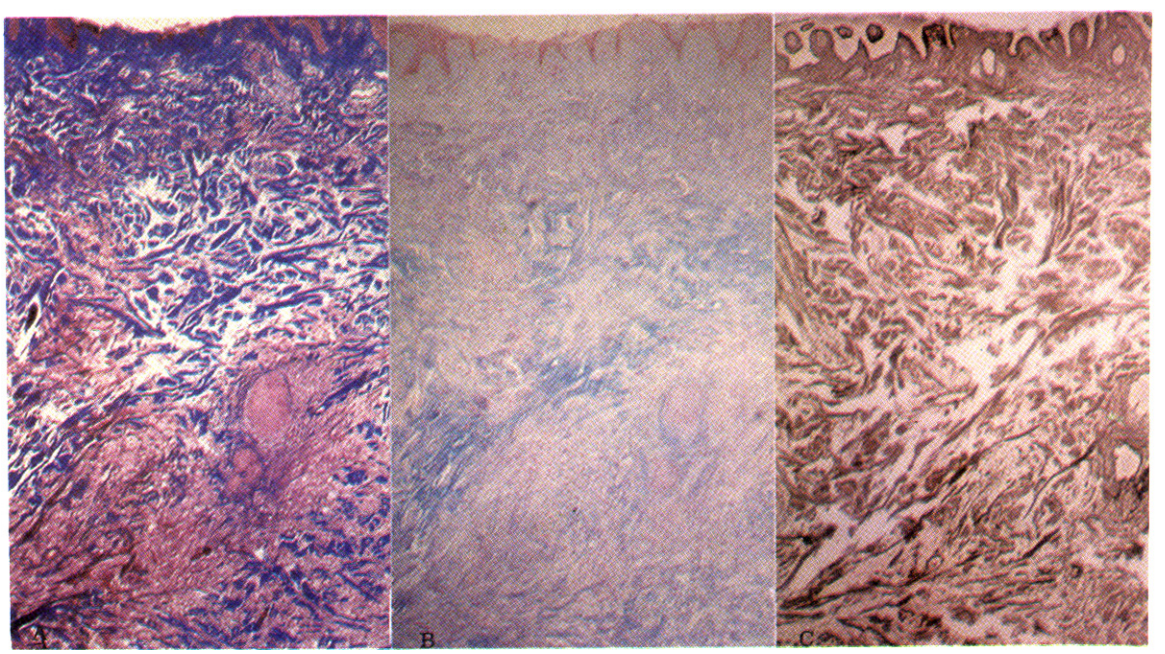

Fig. 4. A : Masson's trichrome stain:The cytoplasm stains deep red brown(×40).
B : Alcian blue stain:Surrounding matrix stains blue(×40).
C : Reticulum stain:Dense meshworks of reticulum fibers are seen(×40).

Table 1. Results of immunohistochemical stains in two cases

	CEA*	EMA**	Vimentin	Cytokeratin
Case 1	++	+	+	±
Case 2	+	+	+	+

*CAE:Carcinoembryonic Antigen, **EMA:Epithelial membrane Antigen
+ :mild to moderate reactivity
++ :strong reactivity
± :doubtful reactivity

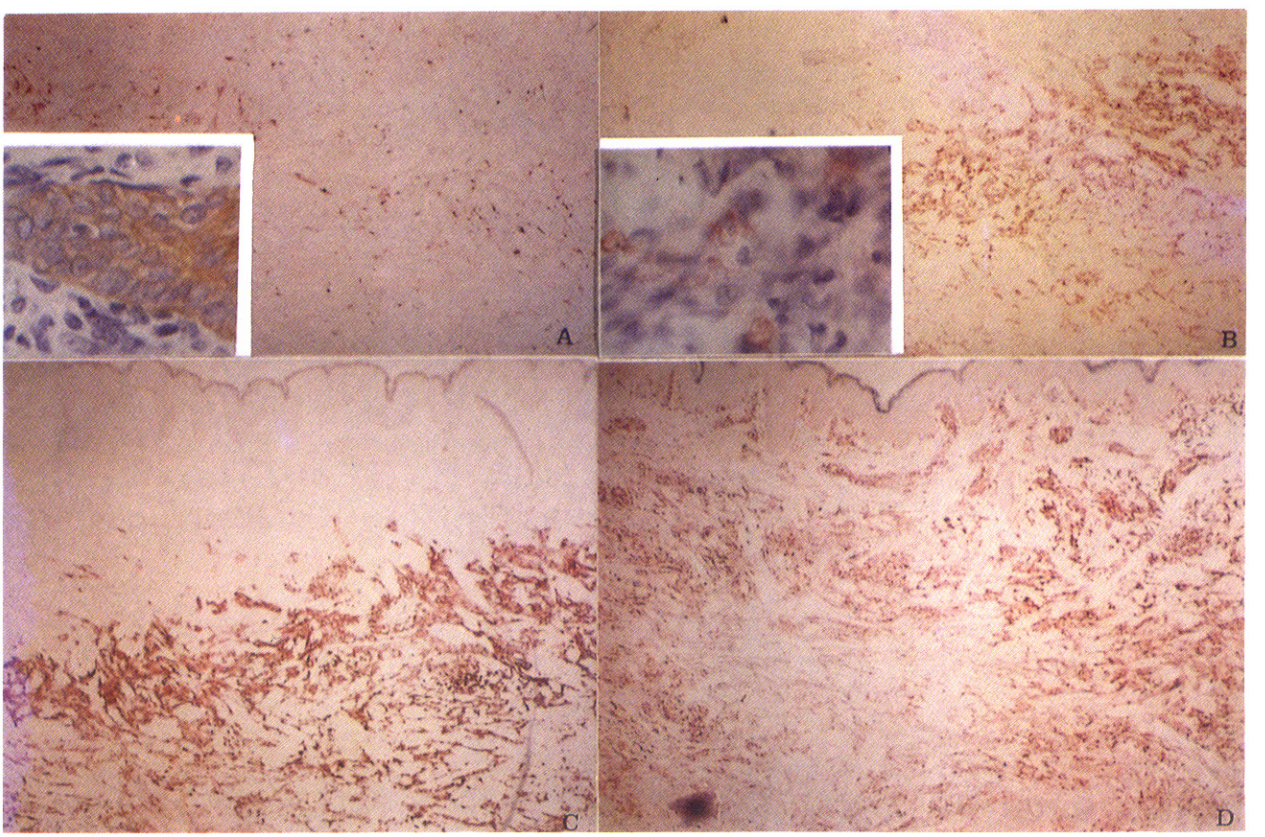

Fig. 5. Immunohistochemical stain by ABC(avidin-biotin-peroxidase) technique in case 1(×40).
A : cytokeratin. Inset, staining mostly of cytoplasm(×400).
B : EMA(Epithelial Membrane Antigen). Inset, staining mostly of cell membranes(×400).
C : CEA(Carcino-Embryonic Antigen)
D : Vimentin

DISCUSSION

ES is malignant soft tissue tumor first described by Enzinger[1] in 1970 which chiefly occurs in young adults. The tumor most commonly affects the soft tissue of the fingers, hands and forearms. It tends to grow in a nodular or multinodular manner along fascial structures

and tendons. Histologically there are irregular nodular aggregates of tumor cells embedded in fibrous tissue with central necrosis. The constituent cellular elements range from plump spindle cells to large polygonal cells with deeply eosinophilic cytoplasm resembling epithelioid cells. As a rule, cellular pleomorphism is minimal.[11] There is no stainable intracellular mucin, but alcian blue-positive and hyaluronidase-sensitive mesenchymal mucin is often found in the surrounding matrix. A dense meshwork of reticulin fibers is present between the tumor cells. The histogenesis of ES is still a subject of discussion. Because of the deep origin of the tumors in soft tissues and its association with tendons and fascial structure, a mesenchymal derivation was favored originally. A primitive mesenchmal nature, with differentiation along either fibroblastic or histiocytic lines has been suggested.[12] A synovioblastic origin was also proposed by some authors.[13,14] Electron-microscopic studies revealed cellular features common to fibrocytes,[6] histiocytes[3,4,6] and synovial cells,[3,5,6] and several authors suggested a primitive pleuripotential mesenchymal cell that can differentiate along several cell lines.[3,15]

Enzymatic histochemical studies[4,16] showed strong reactivity for hydrolytic enzymes, such as acid phospatase, non-specific esterases which are known to be functional markers for cells of the histiocyte series. Synovial sarcoma is also known to show positive staining for these hydrolytic enzymes which is explained by the presence of macrophage like functioning type-A synoviocyte.[17] Therefore those studies suggest two possible hypotheses for the histogenesis of ES deriving either from mesenchymal macrophages versus from monocytic macrophages.

Recently, immunohistochemical studies[7,8,9,18] revealed the coexistence of epithelial markers and vimentin on ES and led to the concept of a multipotential mesenchymal cell origin. Immunohistochemical studies by Chase and Enzinger[2] revealed positivity for cytokeratin in 34(77%) of 44 cases and other stains including actin(73%), carcinoembryonic antigen(38%), lysozyme(17%), S-100 protein(8%). Fisher[7] reported positivity for vimentin and epithelial membrane antigen, and cytokeratin in all 7 cases. Our study also confirms these previous findings of reactivity. The presence of epithelial membrane antigen and cytokeratin has come to be regarded as evidence of epithelial differentiation. On the other hand, the presence of vimentin is known to represent mesenchymal origin.

Therefore our immunohistochemical findings support the hypothesis that ES is derived from pleuripotential mesoderm with multidirectional differentiation. Although most epithelial tumors are derived from components of embryonic ectoderm and endoderm, the mesoderm also contributes to the formation of specific types of epithelial tissues such as mesothelia of celomic cavities, metanephrons, the adrenal cortex, and synovial membranes of the joints and tendons.[19] Therefore the simultaneous expression of both epithelial markers and vimentin in ES is understandable.

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