

Multifocal epitheloid sarcoma A case report with EM study

Piti Palungwachira, MD*
Hitoshi Yaguchi, MD.**
Kunio Iwahara, MD.**
Hideoki Ogawa, MD**

Abstract

A case of multifocal epitheloid sarcoma with cervical lymph node metastasis was studied clinically, light microscopically, ultrastructurally. The tumour was located in multifocal area at the scalp. Light microscopically, the tumour consisted of well-circumscribed nodules situated in the dermis. The cells varied from spindle to epitheloid in appearance. Ultrastructurally, the lesions showed a pattern of epithelial component and spindle cell component having, microvilli, macula adherens, cytoplasmic filaments, pinocytic vesicles and many filopodia like cytoplasmic surface extensions in many cells without well-defined basal lamina. Some ultrastructural features resemble those of classic synovial sarcoma. These similarities support the concept that the epitheloid sarcoma is derived from synovioblastic mesenchyme, which may be the cell of origin of epitheloid sarcoma in this case.

บทคัดย่อ

Multifocal epitheloid sarcoma

ปิติ	พลังงวชิรา	พ.บ.*
ฮิโตะชิ	ยาอูชิ	พ.บ.**
คุนิโอะ	อิwahara	พ.บ.**
ฮิเดโอะกิ	โอกาวา	พ.บ.**

รายงานผู้ป่วย 1 ราย ซึ่งมาด้วยเนื้องอกหลายแห่งบริเวณศีรษะ ได้รับการวิจัยเป็น multifocal epitheloid sarcoma ร่วมกับการแพร่กระจายไปยังบริเวณต่อมน้ำเหลือง จากการศึกษาดังกล่าวพบว่ามีลักษณะของเนื้องอกเป็นเซลล์ลักษณะผสมระหว่าง spindle และ epitheloid โดยพบลักษณะของ microvilli, macula adherens, ใยเล็กในไซโตพลาสซึม, pinocytic vesicles ร่วมกับ filopodia รอบๆ เซลล์โดยไม่พบลักษณะของ basal lamina ซึ่งจากลักษณะดังกล่าวทำให้เชื่อว่า epitheloid sarcoma ในรายนี้จะมีต้นกำเนิดมาจาก mesenchymal tissue ชนิด synovioblastic mesenchyme (MJS 1998 ; 2 : 91-97)

* Skin Center, Srinakharinwirot University.

ศูนย์ผิวหนัง มหาวิทยาลัยศรีนครินทรวิโรฒ

** ภาควิชาตจวิทยา มหาวิทยาลัยจุนเท็นโด, โตเกียว

Department of Dermatology, Juntendo University School of medicine, Tokyo

Introduction

Epitheloid sarcoma has been accepted as a malignant tumors of the somatic soft tissue which characterized by slow growth, multiple recurrences, late metastasis, and frequent culminates in regional lymph node or pulmonary metastasis. On pathologic examination it may be confused either carcinoma or necrotizing granulomatous inflammation. When it occurs at unusual sites, the diagnosis is further complicated.

According to enzinger the commonest epitheloid sarcoma located in the extremities of young adults and appeared to grow in relation to fascial planes and tendon.¹ A primary epitheloid sarcoma of an area besides the extremities is rare, but such lesions have been reported in the abdomen, shoulder, lower back and head.^{2,3} Histogenesis of this tumour is uncertain, but ultrastructural studies suggest a synovial rather than a fibroblastic origin.^{4,5,6,7} Because of its rarity and histologic peculiarities, the neoplasm may be a perplexing one for both dermatologists and the pathologists. In the present report, we record one case of multifocal epitheloid sarcoma, with unusual location and metastasis occurred early to cervical lymph node at both sides of the neck.

REPORT OF A CASE

A 70-year-old man with good general health has had a history of trauma at this right fronto-parietal region 4 months prior to admission to the hospital. Two months prior to an admission to the hospital, he noticed a proliferative tumour had begun growing and the mass increased in size.

The physical examination revealed a fungating, ulcerated 4 x 5 cm lesions on the right fronto-parietal region, two 1.5 x 1.5 cm subcutaneous



Fig. 1 Photograph of patient's scalp showing area occupied by tumour with ulceration.

nodules on the right temporal region (Fig. 1), and a 3 x 3 cm subcutaneous nodule, with slight overlying erythema, on the left fronto-parietal region. Small lymph node diameter about 0.5–1 cm was palpable at both sides of neck.

A biopsy specimen was taken from the tumour and metastasis work up included CT scan of the chest and abdomen, bone scan, liver-spleen scan, routine blood test, chest roentgenogram and upper gastrointestinal studies. There was no evidence of metastatic disease or bone involvement.

The involved area of skin and subcutaneous tissue was treated by α interferon 8,000,000 IU/week. Three months after the treatment he was symptom-free without evidence of recurrent or metastatic tumour.

Materials and methods

Small pieces of excised tumours were fixed in 10% neutral-buffered formalin and embedded into paraffin for EM. Tissue sections were stained with hematoxylin and eosin, periodic acid Schiff (PAS), with or without pretreatment with diastase; and reticulin stains. Some of the specimens were processed for EM. They were fixed in 2.5% phosphate-buffered glutaraldehyde for 24 hr, post fixed in 2% osmium tetroxide for 2 hr, dehydrated in ascending series of ethanol and embedded in Epon. Thin section cut using LKB ultratome were stained with Uranyl acetate and lead citrate. They were examined with a Hitachi H-500 Electron microscope.

Results

(Macroscopic and microscopic)

Macroscopically, the tumour is characteristically multinodular, gray-white to gray-tan in colour with brownish mottling.

Microscopically, the tumour was chiefly composed of nodular aggregates of large, round polygonal, deeply eosinophilic with epithelioid cells

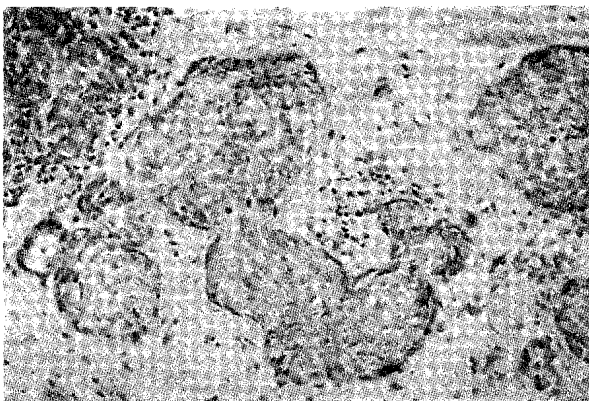


Fig. 2 The tumors infiltrate in a characteristic nodular pattern. Notice, however, the infiltration of epithelioid sarcoma outside of the well-defined borders of the nodules (bottom) (H & E x 40)

merging with spindle cells that simulated fibroblastic elements, abundant collagen and scattered lymphocytes (Fig.2,3). The cytoplasm of spindle cell was basophilic, with poorly circumscribed margins. The nuclei varied from oval to fusiform with coarse chromatin, and occasionally exhibited a prominent acidophilic nucleolus. Irregular clefts or spaces are commonly seen, which probably are the result of poor cellular cohesion and/or artifact of fixation^{1,2,6,8}. This can be so marked that the tumor may simulate a vascular neoplasm (Fig. 4). Between the individual cell, mucinous extracellular material was observed. This material stained with H & E, alcian blue and mucicarmine but failed to take PAS stain. A few polygonal cells showed finely granular or diffuse cytoplasmic staining with PAS which was removed by prior diastase digestion. A dense network of reticulin fiber is present between the tumour cells. Biopsy of the neck mass revealed lymph node tissue that was extensively replaced by tumour cells.

ELECTRON MICROSCOPE

The cells grew in large solid nests and were characterized by irregular cell borders containing microvillus process (Fig. 5). Some

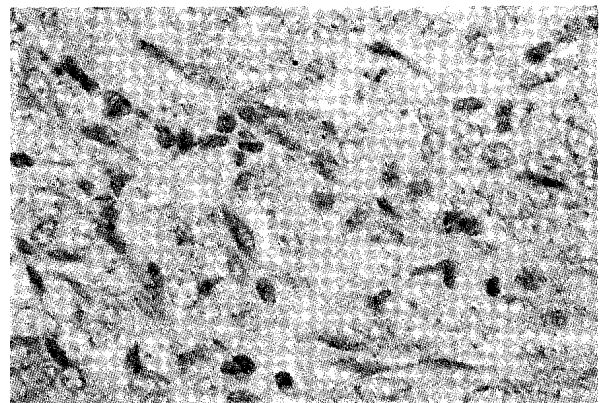


Fig. 3 Area of epithelioid sarcoma exhibiting pattern of spindle and round cells and lying in dense collagenous stroma (H & E x 100)

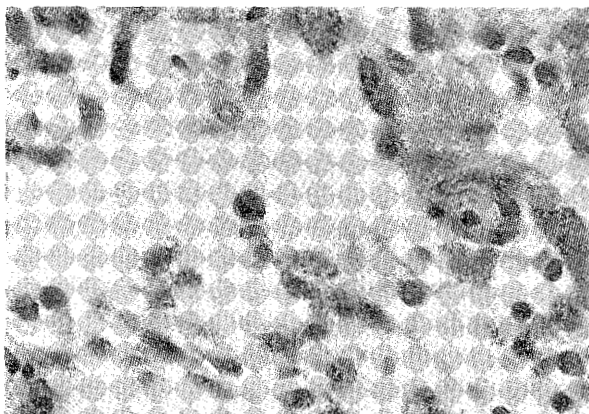


Fig. 4 Loss of cellular cohesion with formation of irregular cleft-like spaces in epitheloid sarcoma. (H & E x 100)

other tumour cells were also connected by poorly developed junctions. The tumour cells had large, often indented nuclei, sometimes multiple nucleoli. The large proportion of the cells had two special features. The predominant cell type was large, spindle and polygonal in shape (Fig. 6). Inclusions of cytoplasmic material were sometimes noted. The cell cytoplasm contained numerous and dilated rough endoplasmic reticulum, mitochondria, and large amounts of ribosomes clusters were seen (Fig. 7). The golgi apparatus was seen in some tumour cells, but was not pronounced. Intermediate filaments randomly dispersed of

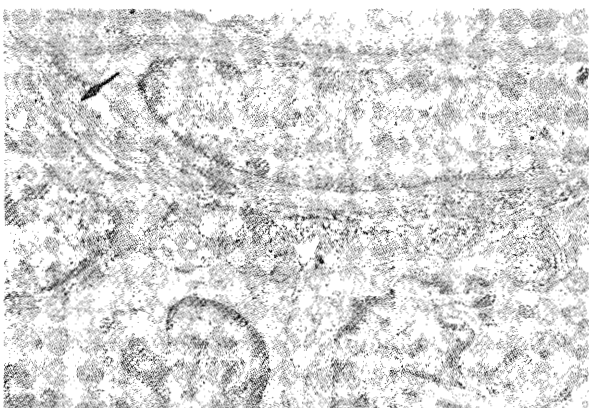


Fig. 5 Portion of cells from epitheloid sarcoma with pronounced interdigitation of cell membranes (arrow) (x 9,600)

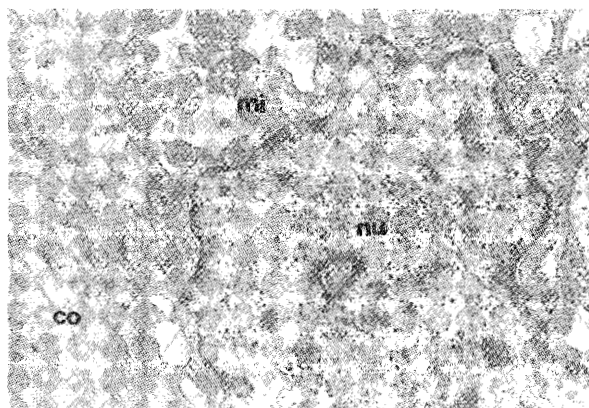


Fig. 7 Numerous mitochondria and dilated rough endoplasmic reticulum. Very indented nucleus of tumour cell. Collagen fibers are next to stromal type tumour cell. (Collagen-Co, mitochondria-Mi, nucleus - nu, x 14,000)

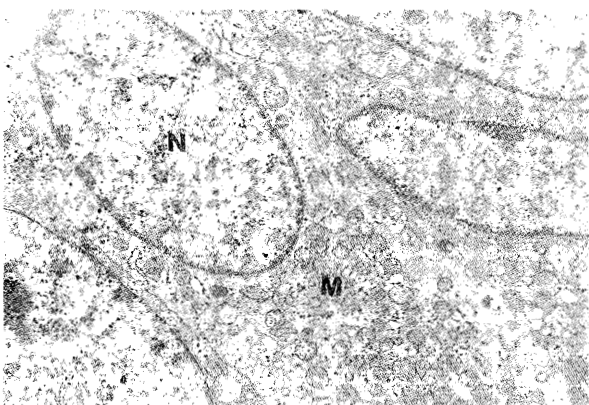


Fig. 6 Stromal tumor cells with spindle-shaped and ovoid nucleus and abundant mitochondria. (N = nucleus, M = mitochondria, x 9,600)

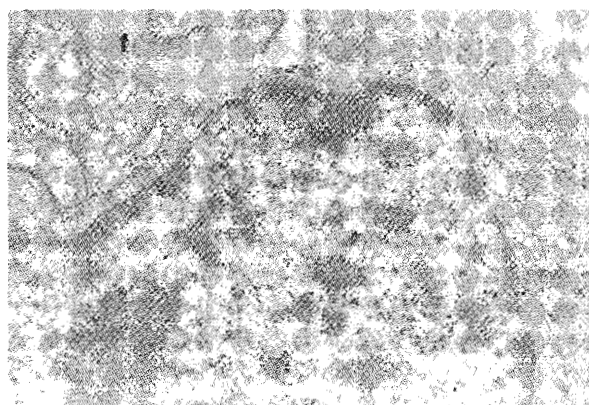


Fig. 8 Epitheloid sarcoma. High power showing extensive accumulation of intermediate filaments (f). (x 30,000)

forming clumps that filled conspicuous array of cytoplasm, or relation to other organelles, as well as lipid droplets, lysosomes, and small glycogen particles (Fig. 8, 9). The significance of this filament is not well established at present. They did not have a definite periodicity and did not appear to be myofibril.

The outer surface of many cells were irregular due to outward projections of filopodia-like cytoplasmic extensions (Fig. 10). Microvilli, are regular, uniform projections of cytoplasm from the cell surface of many cells in contrast to filopodia

which are irregular and infrequent projections of cell cytoplasm, broad at the base and tapering at the end^{9,10}. However, basal lamina can not be observed.

Mature collagen fibers and cellular fragments were observed between cells and focal macula adherens were seen (Fig. 11). Pinocytotic vesicles were observed along the cell membranes as well as linear electron dense condensations consistent with attachment sites (Fig. 12). Dense lysosomal-like bodies of varying density were present mainly in rounded or polygonal cells. In addition, typical



Fig. 9 Epitheloid sarcoma. Several cells in close apposition showing glycogen (G), pinocytotic vesicles (arrow head) and dilated cisternae of Endoplasmic reticulum (ER). (x 18,000)

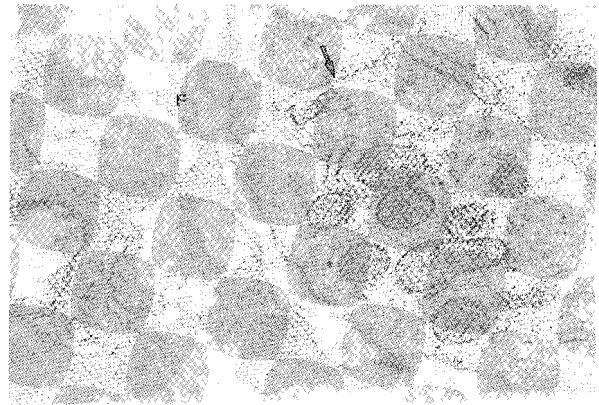


Fig. 11 Epitheloid sarcoma. High power showing interdigitating filopodia (F) with macula adherens (arrows). Fine microfilaments are also seen. (x 42,000)

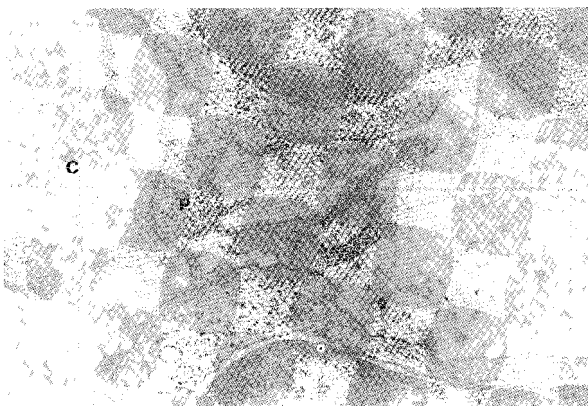


Fig. 10 Portion of cytoplasm of cells comprising epitheloid sarcoma exhibiting pseudopodal extensions. (P). Mature Collagen fiber (C) is evident with in the intercellular space, (x 42,000)

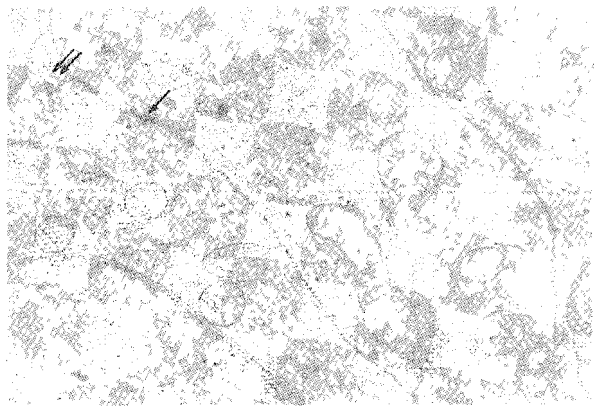


Fig. 12 Focal electron dense condensations consistent with attachment sites (arrow), and pinocytotic vesicles (double arrow), are observed. (x 20,000)

fibroblasts were also present between native collagen fiber.

Discussion

This tumour was presented as multifocal nodule adhering to the tendon sheaths and had extensions into the surrounding tissue ulcerates, and involves the overlying skin. The diagnosis of epitheloid sarcoma must be considered when a primary tumour of mesenchyme is composed of 2 cell types and when it assumes an epithelial appearance. It is then necessary to exclude other possibilities discussed under differential diagnosis which we will discuss later.

Histologically, the occurrence of epitheloid cells is in nodular arrangement. The nodules, enclosed in fibrous bands, are formed by masses of large round or polygonal cells that have a wide eosinophilic and clear cytoplasm (epitheloid cell). The nucleus of these cells are vesicular, and sometimes contain a large nucleolus. Elongated cells similar to immature fibroblasts are present among the epitheloid cells, sometimes they are distributed in small bundles that are separated by dense fibrous connective tissue. Considerable investigation has been addressed toward the question of the cellular origin of epitheloid sarcoma^{2,11,12}. The consensus is that the tumor probably is derived from mesenchymal reserve cells capable of differentiating along either histiocytic or synovial lines^{11,12}.

Ultrastructural features of epitheloid sarcoma^{3,13,14,15} include characteristic intercellular cytoplasmic interdigitations, abundant cytoplasm with rough endoplasmic reticulum, intermediate-sized cytoplasmic filaments that lack condensation plaques, golgi complexes, moderate numbers of small, elongate mitochondria, lipid droplets, lysosomes,

glycogen, cytoplasmic inclusions and focal macula adherens. The nuclei frequently contain finely dispersed chromatin, complex nucleoli, however, basement membrane was absent. These ultrastructural features of our cases are similar to those we have observed in other cases of epitheloid sarcoma, and the clinical features and light microscopic histology are consistent with this diagnosis. And from these ultrastructural features, we can conclude that these tumors have some features of a synovial derived neoplasm^{2,3,12,13,14,15}

Electron microscopy has revealed sufficient dissimilarities of the epitheloid sarcoma from other tumors with which it might be histopathologically confused. Melanin stain was negative and melanosomes were not found with electronmicroscopy. No epithelial clustering was seen in these tumor, and no primary tumour was clinically found. These exclude them from malignant melanoma and metastatic carcinoma. The absence of axon development differentiates it from Schwannoma¹⁶. The lack of cellular tonofibrils and desmosomes readily allow for its distinction from squamous cell carcinoma. The cytoplasmic filaments encountered in cells of the epitheloid sarcoma lack the organization into sarcomere that is encountered in cells of Rhabdomyosarcoma¹⁷. It also lacks the variety of cells and granular aggregates in liposarcoma¹⁸. The absence of cytoplasmic inclusions of paracrystalline material characteristic of alveolar soft part sarcoma excludes them as histogenetic analogs of the epitheloid sarcoma.

The occurrence of epitheloid sarcoma in the scalp area is quite rare. There are only 3 cases reported in the literature¹⁹. The lesions may develop in the dermis or the subcutis, and it often causes changes in the overlying epidermis.

Our patient's clinical course is unique in that multiple scattered lesions occurred over a

period of one and a half year, all with the typical histologic and electron microscopic picture of epitheloid sarcoma. Multiple skin metastasis may be one explanation but this seems unlikely in view of the time interval (one and a half year) because these multiple lesions gradually happened in the period of 3 months from the beginning and the absence of metastasis elsewhere. A tumour of multifocal origin is thought more likely, representing a peculiar susceptibility on the part of the patient to the tumour. This clinical appearance would therefore appear to be one of the characteristic lesion of epitheloid sarcoma. When last seen, he was free of local recurrence and no new lesions were found. Epitheloid sarcoma is not commonly mentioned in Dermatologic literature. Better awareness may help us to diagnose this tumour early and spare the patient avoidable complications.

Acknowledgement

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