卡波西樣血管內膜瘤

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Kaposiform Hemangioendothelioma

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Kaposiform hemangioendothelioma is a recently described, rare, aggressive vascular tumor that has not been reported previously in Taiwan. We report a female baby who was noted to have a progressive, bluish mass over the medial side of the left foot at 6 weeks of age. Various therapies, including oral prednisolone, interferon-α and laser treatment were tried, but the vascular tumor still showed active proliferating behavior resulting in huge swelling of the left foot and left calf, and was complicated by Kasabach-Merritt phenomenon subsequently. Pathology of the amputation specimen revealed Kaposi's sarcoma-like vascular proliferation and lymphatic-like vascular channels. A diagnosis of kaposiform hemangioendothelioma was made. After amputation, her platelet count returned to normal level. At present, she is still alive with no evidence of recurrence. (Dermatol Sinica 19：243-248, 2001)

Key words: Kaposiform hemangioendothelioma, Kasabach-Merritt phenomenon

卡波西樣血管內皮瘤是一種罕見、新近被描述的侵襲性血管腫瘤。在台灣尚未被報告過。我們在此報告一女童，於出生六週後，被發現在她的左足內側有一進行性之瘀青樣腫塊。各種治療，如類固醇、干擾素注射及雷射治療，均被嘗試過。然而，此血管性腫瘤仍舊展現持續生長之特性，造成左足及左小腿之巨大腫脹。之後，女童並出現Kasabach-Merritt徵候之併發症。截肢標本之病理檢查顯示卡波西氏肉瘤樣之血管增生及淋巴管樣血管腔之特徵。因此，我們診斷此女童爲卡波西樣血管內膜瘤。截肢後，她的血小板數回復正常。術後追蹤至今，女童仍存活且無復發跡象。(中華皮誌19：243-248, 2001)

INTRODUCTION

Kaposiform hemangioendothelioma is a rare, locally aggressive vascular tumor that occurs exclusively in infants and children. It is clinically and histologically distinct from infantile hemangioma. Lesions are characterized by rapid growth with local extension, involving the skin, soft tissue and even bone. It is often

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associated with Kasabach-Merritt phenomenon and lymphangiomatosis. Distant metastasis has not been reported.[1-3] We herein describe a case of extensive, cutaneous kaposiform hemangioendothelioma with typical clinical and histological findings.

CASE REPORT

This female baby was noted to have a bluish, elastic mass over the medial side of the left foot at 6 weeks of age. The tumor grew rapidly and resulted in diffuse swelling of the left foot (Fig. 1). Under the impression of infantile hemangioma, oral prednisolone was given at the dosage of 2-3 mg/kg/day, which resulted in partial reduction in tumor size. Steroid therapy was discontinued due to oral candidal infection after one-month treatment, but was restarted in the next week for the significant re-enlargement of the tumor mass. However, the tumor kept enlarging and was complicated with thrombocytopenia. Thus, interferon-α was administered under the suspicion of Kasabach-Merritt phenomenon. From July 1997 to August 1998, she took daily interferon-α injection, one million units subcutaneously. During this period, she also received three times of dye laser treatment at another hospital. Unfortunately, the vascular tumor still enlarged progressively, and the patient developed severe anemia and profound thrombocytopenia. At the age of 19 months old, she was admitted due to a large facial hematoma after a mild contussion. At that time, physical examination showed diffuse ecchymotic swelling on the left lower calf, huge elephantoid enlargement of the left foot, and several purpuric plaques on the left thigh (Fig. 2). There were two pus-draining wounds on her left big toe and left heel. Her platelet count was down to 3000/μL. PT and PTT were mildly prolonged to 13.8 seconds (12.1) and 46.7 seconds (34.2), respectively. X-ray examination revealed a marked swelling of soft tissue of the left lower leg and foot with bony destruction of the left foot. MRI revealed an extensive tumor diffusely infiltrating in the soft tissue of the left foot and calf. During admission, she received several times of transfusion of platelet and fresh frozen plasma for thrombocytopenic coagulopathy, but the response was only partial and temporary. Finally, below-knee amputation was performed due to persistent thrombocytopenia and complicated osteomyelitis. After amputation, her platelet count returned to the normal level and the infection was under control. Five months later, the patient received the second operation for removing the residual lesions on the left

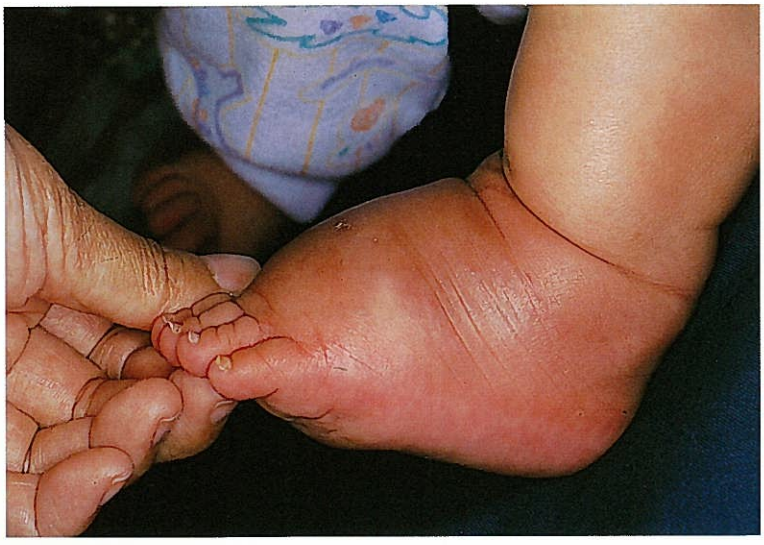

Fig. 1
Diffuse swelling on the dorsum of the left foot when she was 4 months old.

thigh. Histologically, the vascular tumor of the amputation specimen showed an infiltrative lobular growth pattern. From the deep dermis to peri-tarsal bone area, the vascular tumor grew as irregular, interconnecting nodules or sheets (Fig. 3). The tumor nodules were composed of spindle-shaped cells with slit-like vascular spaces between them (Fig. 4). Occasionally, microthrombi in these vascular spaces could be seen. Adjacent to the solid part of the tumor, there were lymphatic-like dilated vascular channels, reminiscent of acquired progressive lymphangioma (Fig. 5). The tumor cells were strongly positive for CD34, and weakly positive for factor VIII-related antigen. Interestingly, the specimen of the second operation showed different pathological findings. The aggregated tumor cells showed a "cannon-ball" distribution, looking like the picture of a tufted angioma (Fig. 6). Base on the clinical and pathological findings, we diagnosed this patient as a case of kaposiform hemangioendothelioma. At this writing, two years after the second operation, she was in a relatively healthy condition and there was no evidence of recurrence.

DISCUSSION

Kaposiform hemangioendothelioma (KHE), designated by Zukerburg *et al.* in 1993,[1] is a distinct, locally aggressive vascular tumor which was named so for its histologic similarities to Kaposi's sarcoma and its intermediate biological behavior between benign hemangioma and angiosarcoma. It affects exclusively the infants and children.[1-3] The clinical presentation falls into two groups. The first group is characterized by visceral involvement, particularly in the retroperitoneum.[3] The other group is characterized by skin involvement, mainly in chest wall, proximal part of extremities, and cervicofacial area.[4] Both types demonstrate locally aggressive behavior by its rapid extension with invasion of the surrounding tissues.[1-3] Although one case was reported to have local metastasis[5], no distant metastasis has been reported.

Alhough KHE is rarely reported in the literature, it may be underestimated as a consequence of misdiagnosis as "unusual" or "alarming" infantile hemangioma. In our case, she was also diagnosed as infantile hemangioma initially. However, reviewing our patient's clinical presentation retrospectively, it is more compatible with the manifestation of cutaneous KHE. There are several hints to differentiate it from infantile hemangioma. First, infantile hemangioma is benign in clinical course and it is very unusual for infantile hemangioma to keep aggressive proliferation beyond 1 year of age.[6-7] Second, the association with Kasabach-Merritt phenomenon favor the diagnosis of KHE rather than infantile hemangioma. The relationship of large vascular tumor with thrombocytopenic coagulopathy (Kasabach-Merritt phenomenon) had been reviewed in Enjolras's[8-9] and Sarkar's[4] series in 1997. None of the underlying vascular tumor was infantile hemangioma. Most of them were KHE and tufted angioma (TA) is another underlying tumor.[8-9] Third, MRI image in infantile hemangioma showed a well-defined, homogenous, enhancing soft tissue mass with fast-flow vessels within them. In contrast, KHE usually lacked a well-defined margin and tended to involve multiple contiguous tissue layers.[4, 10] TA was also considered in our differential diagnosis because of the association with Kasabach-Merritt phenomenon. However, it usually grew insidiously and usually presented as a gradual enlarging plaque instead of a deep-seated, edematous bulging mass.[6, 11-13] Kaposi's sarcomas has never been reported in such a young patient and seldom presented as a solitary, deeply situated mass that in our case.[1,14] Though angiosarcoma is very rare in infants and children,[15-16] it had been suspected for the local aggressive behavior, but the diagnosis was ruled out by the pathology.

Histologically, we can see the typical pathological findings of KHE in our case as those reported in the literature. In the amputation specimen, the neoplasm is characterized by spindle-shaped tumor cells intertwined with slit-

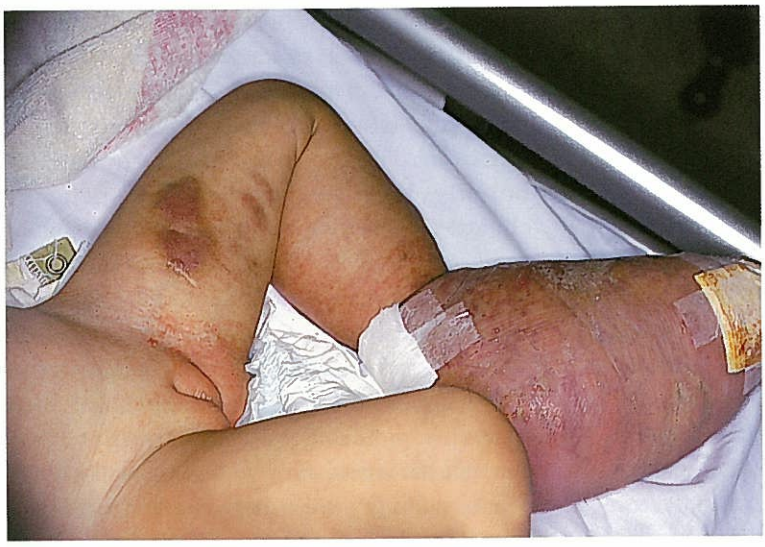

Fig. 2
In addition to the left foot enlargement, several violaceous plaques were also noted on the medial aspect of the left thigh.

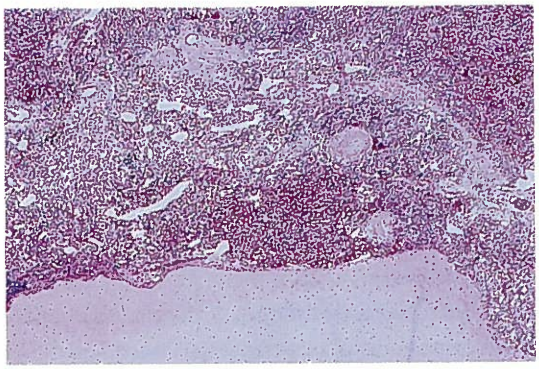

Fig. 3
Interconnecting tumor nodules and sheets invading deeply to the soft tissue and periosteum. (Hematoxylin-eosin stain, x40)

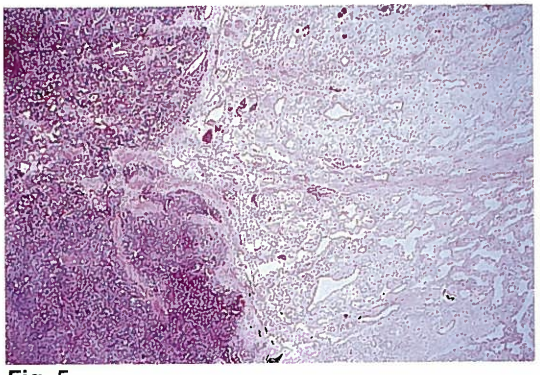

Fig. 5
Adjacent to the solid part of the tumor, thin-walled, lymphatic-like channels can be seen. (Hematoxylin-eosin stain, x20)

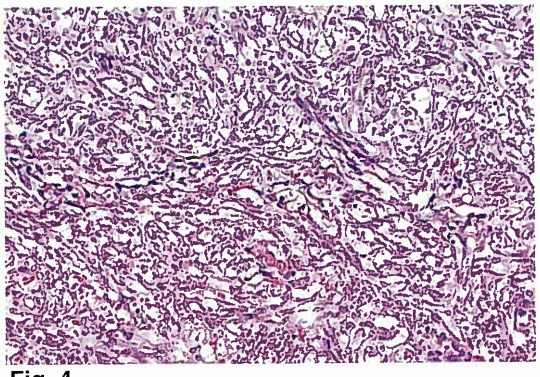

Fig. 4
The tumor nodule was composed of spindle cells with slit-like vascular spaces. (Hematoxylin-eosin stain, x400)

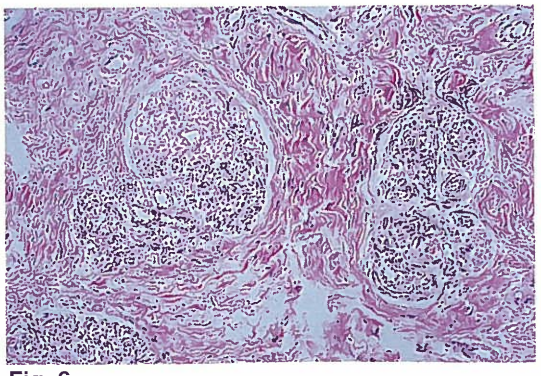

Fig. 6
In deep reticular dermis, multiple, "cannonball-like", vascular tufts can be seen. (Hematoxylin-eosin stain, x200)

like vascular spaces which formed ill-circumscribed nodules or sheets. This picture bears striking resemblance to that of nodular Kaposi's sarcoma. However, the presence of dilated lymphatic-like channels in adjacent to the spindle-cell component and scanty chronic inflammatory cells were contrary to Kaposi's sarcoma.[1-3] Currently, detection of gene of human herpesvirus 8 (HHV-8) by polymerase chain reaction could aid in further differentiation. In contrast with Kaposi's sarcoma, which regularly shows the presence of HHV-8 genes in tumor cells, HHV-8 is not present in KHE lesion.[3] The tumor growth pattern and cell morphology can easily differentiate our case from TA and infantile hemangioma. Sometimes, spindle cell hemangioendothelioma(SCH) and angiosarcoma may need to be differentiated from KHE. In our case, we didn't see large cavernous spaces between spindle tumor cells which are characteristic findings in spindle cell hemangioendothelioma[2,4,16] The lack of cellular atypia, mitotic figures and anastomosing vascular channels rule out the diagnosis of angiosarcoma.[3,17]

Unlike common infantile hemangioma, which usually responds well to prednisolone, the response of KHE to prednisolone was inconsistent.[2, 3, 8, 16] Even in cases responsive to steroid, long-term therapy or combination with other therapy was often necessary. Interferon-α has been demonstrated to have the ability to interfere with angiogenesis[19-22] and was applied in the treatment of KHE. Although one case was reported to be successfully treated with interferon α-2A,[23] the overall effect of which in KHE is still questionable. If feasible, a wide local excision as that in our case is the most successful therapy[1]. Recently, a few case reports demonstrated successful treatments with chemotherapy[24] and multimodal therapy[25] in problematic patients.

In our patient, there is an interesting finding that the local metastatic lesions on the left thigh showed TA-like histologic features without kaposiform spindle component. TA and KHE were recently grouped as in the same disease spectrum. We agree with some authors' view[8] that TA can be regarded as a minor form of KHE. The coexistence of KHE and TA-like lesions in our patient may serve as the supporting evidence for this view.

In conclusion, KHE is a distinct tumor, either clinically or histologically. It is easily misdiagnosed as infantile hemangioma with unusual presentation. Thus, the presence of a rapidly growing vascular tumor in an infant beyond the age for a growing infantile hemangioma should prompt us to take a biopsy to rule out KHE, especially when the tumor is associated with Kasabach-Merritt phenomenon.

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