Adult-Onset Kaposiform Hemangioendothelioma with Early Kasabach-Merritt Phenomenon

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ABSTRACT:
Kaposiform hemangioendothelioma (KHE) is a rare, locally aggressive, vascular tumour with a peak onset within the first year of life. The condition is extremely rare in adulthood, with fewer than 40 cases of adult KHE reported worldwide. A common feature is a single cutaneous erythematous papule, plaque, nodule or tumour with a soft tissue mass on the extremities. Extracutaneous locations such as retroperitoneum muscle, bone, and thoracic cavity can occur and lead to compressive effects or the life-threatening consumptive coagulopathy known as Kasabach-Merritt phenomenon (KMP) which has high morbidity rates. The pathogenesis of KHE involves genetic and environmental factors, the vascular endothelial growth factor-3 axis, and angiopoietin-2 signalling, resulting in dysregulation of angiogenesis and lymphangiogenesis. The diagnosis of KHE requires clinical, histopathological, haematological, and imaging information.
Here, we report a case of a 59-year-old patient presented with solitary painful erythematous to purplish plaque at the left forearm for 4 months. A complete blood count showed profound thrombocytopenia (21,000 cells/mm^3). Coagulogram, fibrinogen and D-dimer were within normal limits. Magnetic resonance imaging revealed mild superficial vein dilatation and subcutaneous fat in the lesion without intramuscular or deep-structure involvement. She was diagnosed with adult onset KHE with early KMP. After a discussion with haematologists, prednisolone (1 mg/kg/day) with topical tacrolimus was initiated as the patient could not afford oral sirolimus. She gradually responded, with a decrease in pain and lesion size and a normal platelet count.
Key words: Vascular tumor, Kaposiform hemangioendothelioma, Kasabach-Merritt phenomenon

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Introduction

Kaposiform hemangioendothelioma (KHE) is a locally aggressive vascular tumor. It is mainly found in childhood, but it is rarely found in adults. It can arise in superficially or deep soft tissue and is mostly located in the extremities. Moreover, it can occur in the retroperitoneum, mediastinum, trunk, head and neck, and visceral organs[1].

The Kasabach-Merritt phenomenon (KMP) is a life-threatening complication which can occur in roughly 70 percent of cases of KHE[2]. Profound thrombocytopenia, together with consumptive coagulopathy, and hypofibrinogenemia that caused from vascular tumors are defined as KMP.

Case report

A 59-year-old woman presented with a 4-month history of a slow progressive, painful erythematous to purplish plaque 5X10 centimeter at the left forearm (Figure1a-b). She denied any history of weight loss, diarrhea and melena. Her underlying diseases were hypertension, aortic regurgitation, and pulmonary hypertension. She was treated with spironolactone, isosorbide mononitrate, furosemide, bisoprolol and amiodarone.

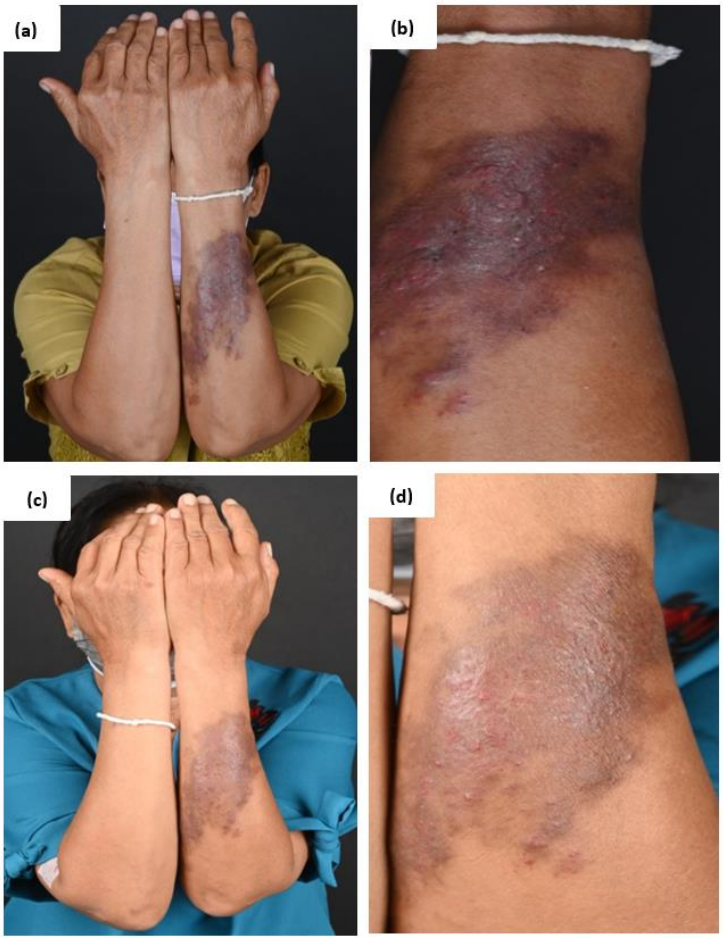

Figure 1 (a-b) Painful erythematous to purplish plaque 5X10 centimeter in size at the left forearm. (c-d) Improvement of the lesion after 4 months of treatment

Histopathology of the lesion revealed multiple dermal-infiltrating nodules of vascular proliferation with fibrous stroma, located from superficial to deep dermis. The neoplasm showed tightly packed spindle endothelial cells with slit-like lumina, intravascular fibrin thrombi, deposits of hemosiderin, and lymphangioma-like areas composed of lymphatic vessels at the periphery of the nodules. The neoplasm was arranged in lobular pattern resembling cannonball appearance. Increased mitotic activity and cytological atypia were not identified (Figure 2a-2c). Immunohistochemistry demonstrated that the neoplastic cells were positive for vascular and lymphatic endothelial markers (CD31, CD34, and D2-40), and negative for HHV8 (Figure 2d1-2d4) and Glut1. A complete blood count showed profound thrombocytopenia (21,000 cell/mm^3). Coagulogram, fibrinogen and D-dimer were within normal limits. Magnetic resonance imaging revealed mild degree of superficial vein dilatation and subcutaneous fat in the lesion without intramuscular or deep-structure involvements. Adult onset KHE with early KMP was diagnosed.

After a discussion with hematologists, prednisolone (1 mg/kg/day) with topical tacrolimus was initiated as the patient could not afford oral sirolimus. She gradually responded to corticosteroids, with a decrease in pain and size of lesion and a normal platelet count. Figure1c-d illustrate her lesion after 4 months of treatment.

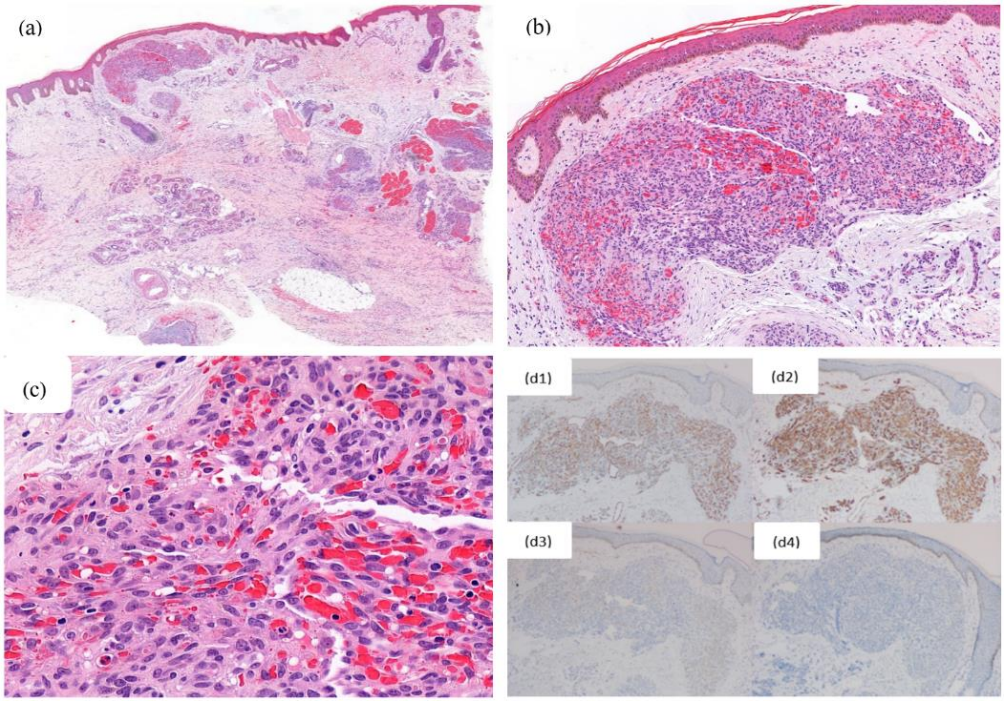

Figure 2 (a) Histological findings showed multiple well defined, round and confluent vascular proliferation involving upper to deep dermis. Slit-like vascular lumina with extravasation of red blood cells and peripheral lymphatic-like spaces were present in the neoplastic nodules. Original magnification (H&E): (a) X40, (b) X100, (c) X400. Immunohistochemistry showed expression of vascular and lymphatic endothelial markers CD31 (d1), CD34 (d2), D2-40 (d3), and was negative for HHV8 (d4). Original magnification: (d1-d4) X100

Discussion

KHE, is a rare locally aggressive vascular tumor, which has a peak onset within the first year of life (90%)[2,3]. The annual prevalence and incidence was reported at 0.91 and 0.07 per 100,000 children, respectively[2,3]. The condition is extremely rare in adulthood, with fewer than 40 cases of adult KHE reported worldwide[4]. A common feature is a single cutaneous erythematous papule, plaque, nodule or tumour with a soft tissue mass on the extremities. Deep masses without cutaneous lesions can occur. Extracutaneous locations such as retroperitoneum muscle, bone, and thoracic cavity can lead to compressive effects, or the life-threatening consumptive coagulopathy known as the KMP[2]. Conceptually, KHE and tufted angioma are the same neoplasm with different severities. The pathogenesis of KHE involves genetic and environmental factors, the vascular endothelial growth factor-3 axis, and angiopoietin-2 signalling, resulting in dysregulation of angiogenesis and lymphangiogenesis[2,5].

KMP, associated with only the vascular tumors (KHE and tufted angioma), is defined as profound thrombocytopenia with consumptive coagulopathy and hypofibrinogenemia. This mechanism can explain by platelet trapping by the tumor and the interplay between abnormally proliferating endothelium of the tumor, the activation of platelets and a secondary activation of coagulation cascades with consumption of many clotting factors[6]. It can occur up to 70% of patients[2]. At the initial presentation, thrombocytopenia is usually severe with a median count of 20,000 platelets per microliter[7]. The risk of KMP is a congenital KHE of a large size, especially more than 8 centimetres, in an intrathoracic or retroperitoneal location[7]. Patients with KHE and KMP have more purpuric, swollen, and painful lesions than KHE patients without KMP[2].

Tufted angioma, mild variant of KHE, is the main differential diagnosis. It usually occurs in children and young adults. However, lesions of tufted angioma are stable in size. Only 10% of tufted angioma develops the KMP[2]. Another differential diagnosis is Kaposi sarcoma which is commonly occurred in patients with human immunodeficiency virus infection. Nevertheless, it can occur in immunocompetent patients (classic Kaposi sarcoma). Kaposi sarcoma can present with red to violaceous macules, patches, papules, and nodules. Skin, mucosal surfaces, respiratory tract, and lymph nodes can be affected[2]. Human herpesvirus-8 latency-associated nuclear antigen which is expressed in endothelial and spindle cells is the most useful to confirm diagnosis of Kaposi sarcoma.

The diagnosis of KHE requires clinical, histopathological, haematological, and imaging information. A biopsy is the gold standard and should be performed if possible. Histopathology and immunohistochemical staining are hallmark pathologies of KHE. Ultrasound is appropriate for small and superficial lesion. However, magnetic resonance imaging is more valuable due to deep infiltrating nature of KHE. Due to its rarity and insufficient randomised clinical trials, there are still no definite guidelines for treating KHE[8]. Systemic corticosteroids and vincristine have been recommended as first-line treatments, especially in KHE with KMP. Since 2010, several studies have demonstrated effective and impressive results with sirolimus[2,8]. Several experts have recommended oral sirolimus plus corticosteroids as the first-line treatment for KHE with or without KMP. Other alternative medical treatments are triclopidine, propranolol, and interferon-α. For superficial KHE, topical sirolimus and tacrolimus were used successfully. Surgical management can be performed for tumors which a complete and safe resection[9]. It is also an option for resection of a fibrofatty residuum or reconstruction of

damaged structures or failure to of pharmacotherapy with cosmetically or functionally problems[10]. Supportive care and monitoring are necessary[2,8].

Conclusion

We report a rare case of adult-onset KHE with early KMP that responded well to an oral corticosteroids and topical tacrolimus. KHE treatment should be individualised for each patient.

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