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Case Report

Digital subtraction angiography and trans arterial embolization in preventing massive hemorrhage of Kaposiform hemangioendothelioma: A case report ☆

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ABSTRACT

The management of hypervascularity tumor in infants and children is challenging due to its hemorrhage risk which can be life threatening. A proper and precise approach should be performed in preventing massive bleeding. A one-month-old male infant came with hypovolemic shock due to intratumor hemorrhage on the right chest that presented at birth and grew progressively with a size of 20 × 15 × 7 cm. After stabilization, Magnetic resonance imaging and Doppler ultrasonography of the tumor showed a solid lesion with an increase in vascular flow. He underwent two rounds of digital subtraction angiography (DSA) and trans arterial embolization (TAE) on the internal mammary, superior thoracic, and right thoracoacromial arteries. On the sixth day after second embolization and ensure significantly reduced vascularity using the ultrasound Doppler modality, he performed tumor removal surgery and skin grafted closure. There were no post-embolization or post-operative complications. Histopathological examination with immunohistochemistry staining on the tumor tissue indicated as Kaposiform hemangioendothelioma. Fluoroscopic technique of DSA and TAE should be considered prior to the tumor removal surgery has been proven to be safe and effective options in progressive large mass with high vascular flow management.

Introduction

Kaposiform hemanigoendothelioma (KHE) is a vascular tumor that is associated with a high rate of morbidity and mortality. The prevalence of KHE is not well-documented due to the asymptomatic nature of the disease which often leads to unsuccessful diagnosis. When KSE lesions present with symptoms, it is often diagnosed as a variant of infantile hemangioma (IH) or other vascular anomalies. Thus, the true

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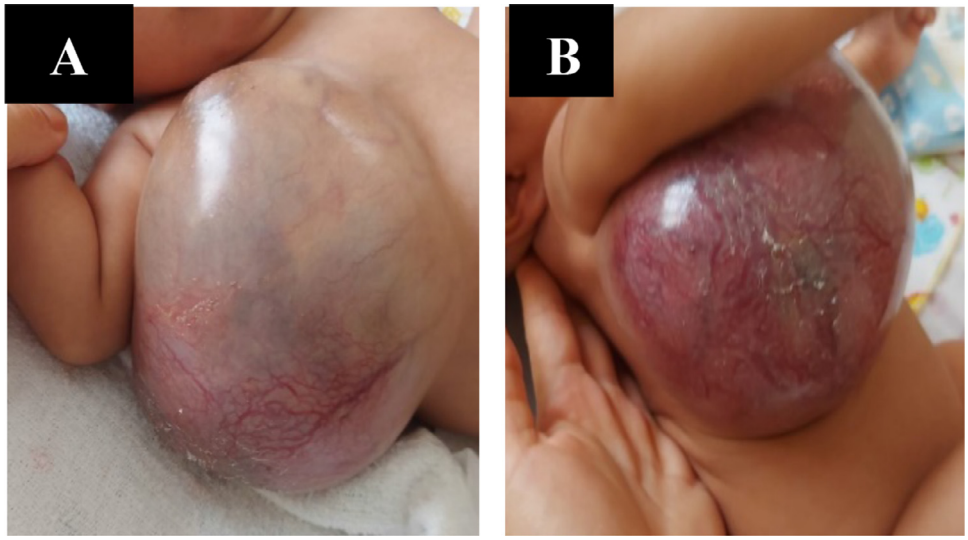

Fig. 1 – Mass on the right chest before embolization (A and B).

prevalence and incidence of KHE are thought to be higher than previously reported numbers. Most reported cases of KHE occur in male patients in the first year of life. Almost half of cutaneous KHE lesions can be spotted and/or diagnosed at birth. The etiology of KHE has not been described. Current theories hypothesize that KHE is multifactorial. The most considered factor is genetic role in the form of a somatic translocation mutation of chromosomes 13 and 16. Other contributing factors are trauma, infection, and manipulation of the tumor which are also thought to contribute to *Kasabach-Merritt* phenomenon (KMP). A common pathological finding is abnormalities in vascular and lymph angiogenesis. The clinical presentation of KHE varies widely and can cause thrombocytopenia and consumptive coagulopathy known as *Kasabach-Merritt* phenomenon (KMP). Trapping of intralesional thrombocytes followed by activation and aggregation of thrombocytes leads to activation of the coagulation cascade and consumption of coagulation factors. This theory can be found in histological findings of KHE cases with or without KMP. Another hypothesis states that endothelial damage and changes which occurs in KHE cause the exposure of extracellular matrix components, which can become a ligand for thrombocyte adhesion. Podoplanin is commonly found in dysmorphic blood vessels in lymphatic malformation. Microvascular thrombus will lead to venous occlusion causing disturbance of normal blood flow, which increases the risk of a stress tear. Lesions in KHE can present as a soft tissue mass in the form of papules, plaques, or purplish erythematous nodules found in the extremities, mediastinum, retroperitoneum, or head and neck. KHE is diagnosed through clinical approach with supporting examinations such as imaging, complete blood count, and biopsies. At the time of writing, there is yet to be a consensus on the management of KHE and it remains a challenge to manage. This study presents a case report of KHE on a 1-month-old male presenting with a cystic lump on the right chest [1–3].

Case

A 1-month-old male baby came to the emergency department with complaints of poor feeding of breastmilk, and lethargy, and the patient's parents also spotted bleeding from a mass on the right chest several hours before admission to the hospital. The mass had been detected at a pre-natal checkup in the third trimester and visible since birth with the size of a tennis ball and had doubled in size at the time of admission. On physical examination, signs of hypovolemic shock were found such as exceeding pulse rate to 160x/minute, cool extremities, and lethargic appearance. A cystic non-compressible lump was found on right chest, sized 20 × 15 × 7 cm with indistinct borders and without bruit (Fig. 1). Fluid resuscitation was immediately administered along with urine output monitoring to stabilize the patient.

Laboratory examinations revealed a low hemoglobin count of 6.2 g/dL and the patient was diagnosed with severe anemia due to intratumor hemorrhage. As soon as the patient was stable, thorax magnetic resonance imaging (MRI) with contrast and Doppler ultrasonography of the tumor were performed. The results showed a solid lesion with an increase vascular flow. MRI features indicated a large tumor in the soft tissue region of the right superior thoracic wall which exhibited a heterogeneous enhancement along with squamous pattern and hemorrhagic component. The patient's MRI and Doppler ultrasonography appearances results supported to Kaposiform hemanigoendothelioma diagnosis (Figs. 2 and 3).

A clinical meeting was done in discussing the choice of management for the patient. The final decision was to perform tumor removal surgery preceded by tumor embolization to reduce risk of intraoperative hemorrhage.

The patient then underwent two rounds of Digital Subtraction Angiography (DSA) and trans arterial embolization using 500-700 microns of polyvinyl alcohol (PVA), optima coil sys-

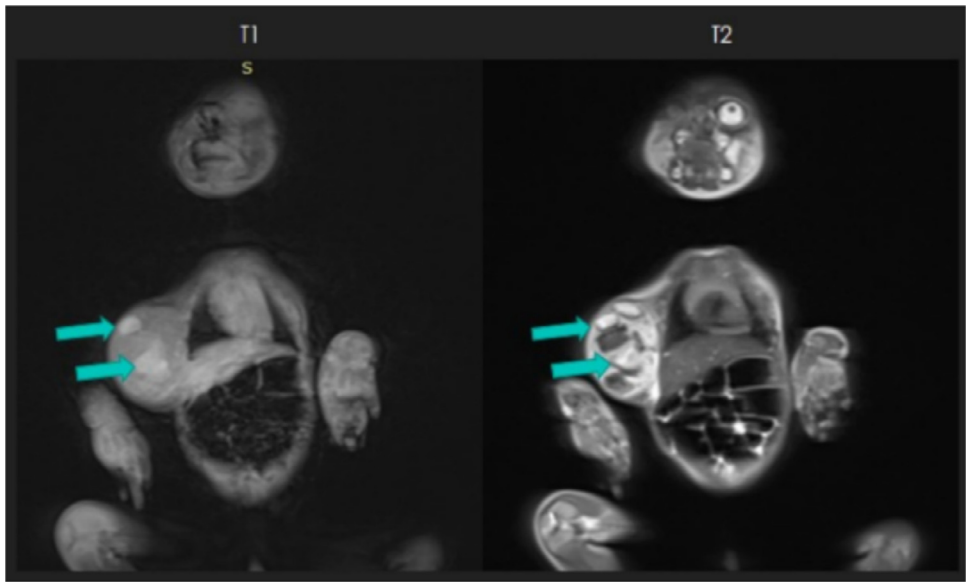

Fig. 2 – MRI showing lesion with solid component accompanied with hemorrhage (blue arrows).

tem, and gel foam. Transarterial embolization was performed on the internal mammary, superior thoracic, and right thoracoacromial arteries (Fig. 3). Post-DSA embolization, the tumor showed no flow of contrast and hypervascularity lesion. (Figs. 4 and 5)

The patient received a blood transfusion post-embolization, elevating hemoglobin levels to 13.2 g/dL. The patient then underwent tumor removal surgery six days after the second embolization. Excisional surgery was performed after no active bleeding and no significant decrease in hemoglobin levels (Fig. 6).

There were no post-embolization or post-operative complications. Patient was discharged two weeks after tumor removal surgery with skin graft technique (Fig. 7). Histopathological examination revealed a Kaposiform hemangioendothelioma (Fig. 8). In addition, it was confirmed by immunohistochemical staining that showed positive for CD34 and negative for D240 in dilated vascular area (Fig. 9). Patient then planned for chemotherapy.

Discussion

The patient presented in this case report fulfilled the epidemiological criteria of KHE patients, a male in the first year of life with a mass on the thorax [1–3]. The mass on the patient's right thorax also fulfilled the common characteristic of KHE lesions which is a purplish erythematous nodule on the skin [4]. The patient's laboratory examination did not show any signs of thrombocyte disorder which indicates the absence of consumptive coagulopathy leading to the patient's diagnosis of KHE without KMP.

Due to rapid tumor growth, structural abnormalities caused can be seen and lead to intralesional hemorrhage, severe anemia, and deeper tissue infiltration. Severe anemia may also be caused by the formation of a hematoma. Presentation of these symptoms worsens the prognosis of the patient because it supports tumor growth and infiltration, hemodynamic instability, and compression of vital structures in the body. As the laboratory examination did not show any signs of coagulation disorder the anemia was most likely caused by the location and rapid growth of the tumor [5,6].

Ultrasonography is the first imaging technique that can be performed although it cannot provide a specific image [7]. Ultrasonography often becomes the first modality used to evaluate superficial vascular tumors. CT scans may be used to evaluate bone involvement. MRI is the imaging modality that can give a specific image, especially in vascular anomalies [8]. The previously mentioned imaging techniques were also performed on the patient in this case. Doppler ultrasonography is performed for identification of tumors that previously described as hemangioma, to determine the size, appearance, hemangioma layers, and relation to peripheral blood vessels [9]. MRI of KHE patients can show a mass invading several layers of tissue and exhibiting post-contrast enhancement. Bone involvement is not uncommon and may have an infiltrative growth pattern [10] On histopathologic examinations, KHE is usually dominated by glomeruloid proliferation of blood vessels by endothelial cells positive for CD31 and CD34 markers. These structures are the site of sequestration and destruction of red blood cells and thrombocytes. Perisitic cells on the actin component of smooth muscle cells can be found around endothelial cells. In the neighboring area, a zone with an indistinct border can be found, composed of lymphatic canals positive for D2-40, LYVE-1, dan VEGFR3. These foci can show proliferation of spindle cells giving an image similar to Kaposi Sarcoma with the formation of slit-like chambers. The diagnosis of Kaposi Sarcoma can be excluded by identifying the glomeruloid proliferation and the absence of HHV-8 on Immunohistochemical or other molecular methods [3]. In this patient's histopathological and immunohistochemi-

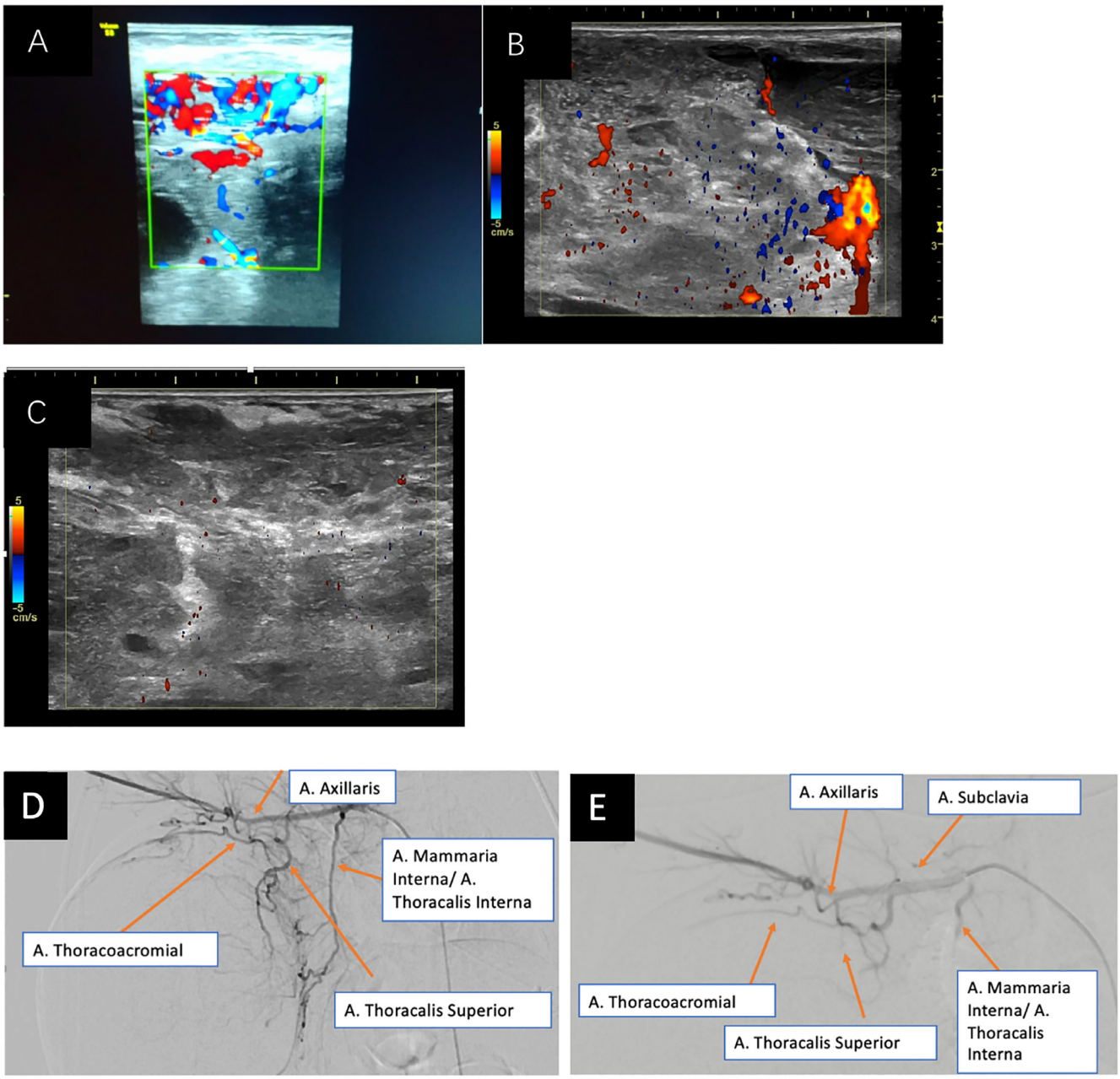

Fig. 3 – (A) Initial Doppler examination showed a hypervascularity lesion, (B) after first embolization showed a reduced vascularity lesion, (C) after second embolization showed no vascularity ln the mass.
(D)() Pre-embolization and (E) post first embolization.

cal examination results, showed proliferation of the vascular and anastomotic appearance, ultimately confirmed by CD 34 was positive and D240 which was positive in lymphatics, but negative in large lumens and positive in solid areas (Fig. 9). This may have been caused by sporadic somatic mutations which occurred due to vascular malformations. These findings show that the diagnosis of the disease cannot be based on one positive or negative finding on Immunohistochemistry examination [11]. Options for therapy in KHE are systemic or intralesional steroids, low dose radiotherapy, excisional surgery, and chemotherapy with vincristine, cyclophosphamide, and sirolimus. Monotherapy with steroids can give varying outcomes on patients, and failure is common in pediatric patients causing relapse of disease. Side effects of steroid treatment are hypertension, obesity, acne, growth and developmental disorders, Cushingoid appearance, and higher risk of opportunistic infection caused by its anti-proliferative and anti-angiogenic effects. Steroids cannot be given to children under one year of age due to the increased risk of spastic diplegia [12].

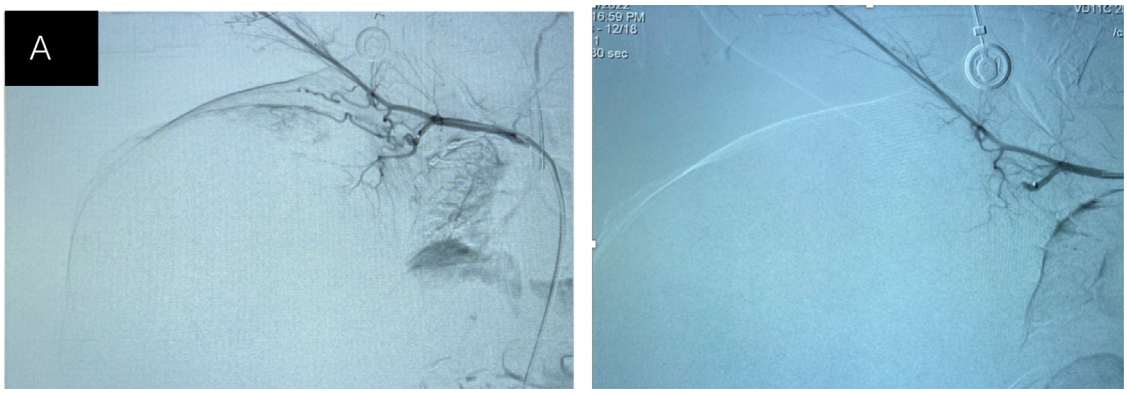

Fig. 4 – (A) Pre-embolization and (B) post second embolization on right superior thoracic artery.

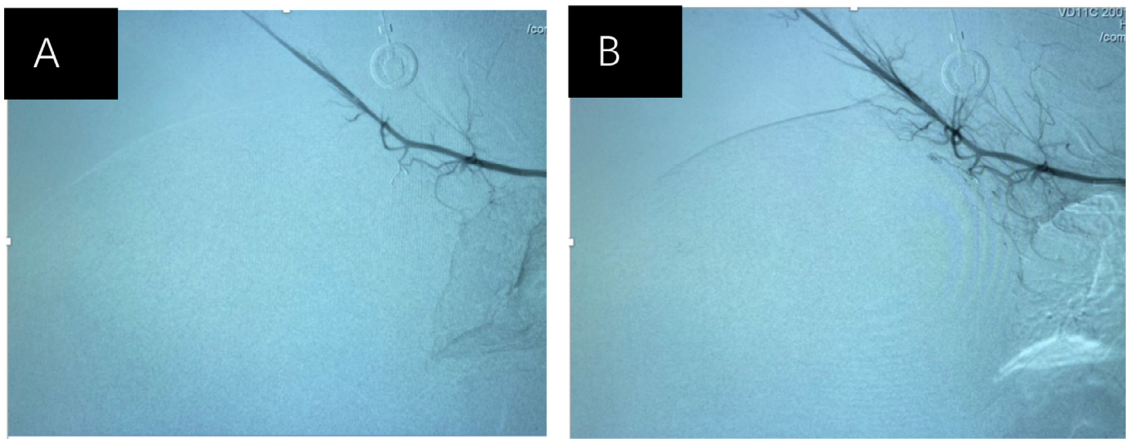

Fig. 5 – (A) Pre-embolization and (B) post second embolization on right thoracoacromial artery.

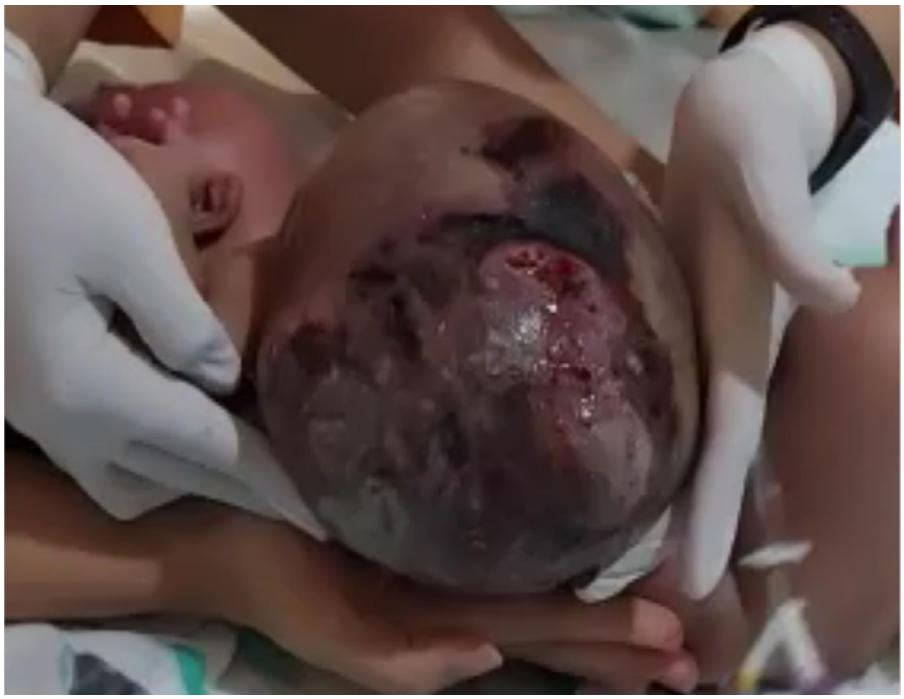

Fig. 6 – Tumor mass on the third day after second embolization.

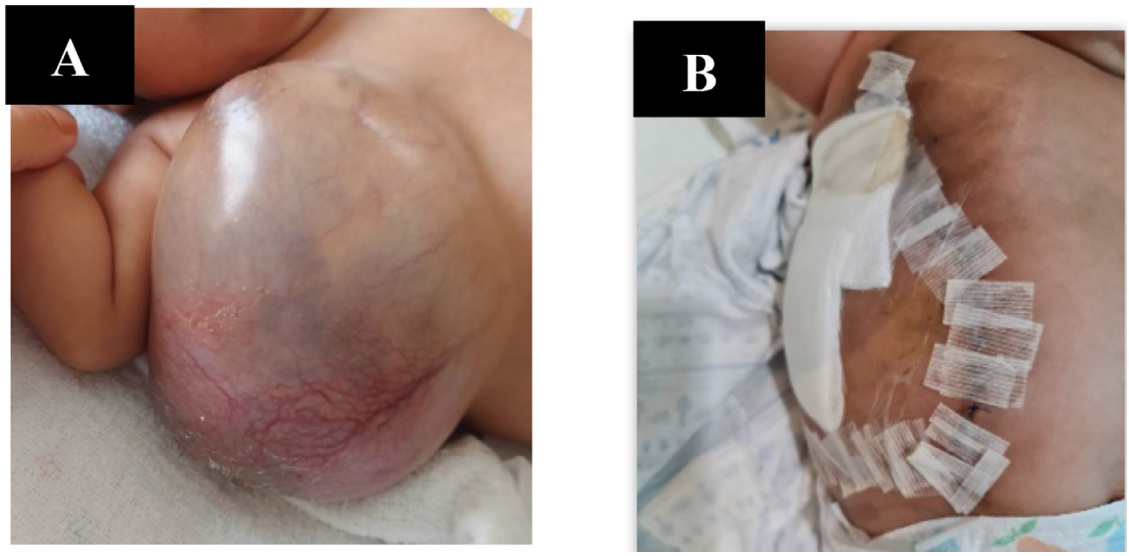

Fig. 7 – (A) Before tumor removal surgery (B) After tumor removal surgery with skin graft technique.

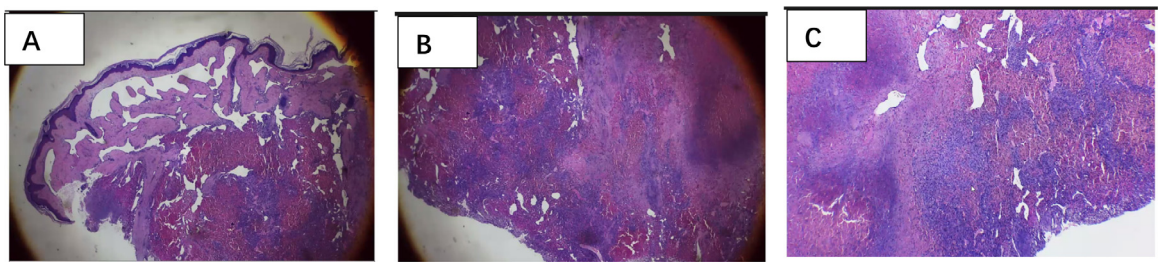

Fig. 8 – (A, B, and C). Histopathology examination showed proliferation of spindle cells with the formation of slit-like chambers.
Figure A with HE staining 25x magnification, with ortokeratotic and atropic epidermis
Figure B with HE staining 25x magnification, and Figure C with HE staining 40x magnification.

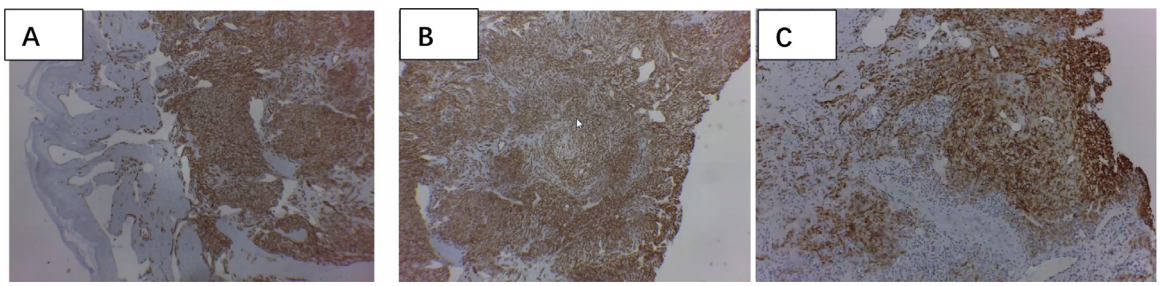

Fig. 9 – (A, B, and C). Immunohistochemistry staining result
Figure A and B with 40x magnification. Positive for CD 34
Figure C with 100x magnification. Positive for D240 in lymph and solid area whereas it was negative on large lumen.

Excisional surgery is the first choice for small local lesions that can be extirpated. If the blood vessels involved are larger and has a higher hemorrhage risk, preoperative embolization should be performed. To prevent regrowth of collateral blood vessels, the surgery must be performed in 24-48 hours after embolization. In this case, patient was delayed to 6 days after first embolization due to blood transfusion process for preoperative preparation. Local excision of tumors cannot be performed in tumors that have infiltrated important structures such as neurovascular structures, muscle, or fascia. This type of infiltration is commonly found on lesions located on the head. The severe coagulopathy caused by KMP may also be a complicating factor in performing surgical methods. There is a rather high risk of surgical mortality in neonate and pediatric patients. Embolization also carries a risk of causing cerebral infarcts and loss of function of both extremities [12].

Chemotherapy with vincristine, vinca alkaloids is not only given in KHE, but also in other lymphoproliferative disorders. This chemotherapy agent works by inhibiting the proliferation of endothelial cells and has been proven to treat KHE with KMP complication in children who are resistant to steroid use. A study by Wang et al. showed that this chemotherapy agent is relatively safe and a good option in cases of KHE with KMP. Side effects to be aware of are abdominal pain, constipation, ileus, nausea and vomiting, autonomic neuropathy, and hyponatremia. Other than vincristine, there is also another chemotherapy agent which is Sirolimus. Sirolimus inhibits the proliferation of cells, metabolism, lymphongiogenesis, and angiogenesis. This chemotherapy agent has also been found to be safe and effective in cases of KHE with KMP. The appropriate dose given is 0.5 mg twice a day daily for 12 months. In younger patients, the agent can be administered orally. Sirolimus also causes fewer side effects compared to vincristine, without recurrence in the first year [12].

For the patient in this case, there were no signs of KMP, thus the first choice of treatment was excisional surgery. Embolization was performed to reduce the size of the mass, but the effect is only temporary [13]. This therapeutic approach is appropriate with a previous study done by Schimd et al. [14]. The choice of excisional surgery was also made considering age, duration of treatment, tumor proliferative activity, compression effect, and invasion. Excisional surgery is also preferred in patients with coagulopathies [10].

Conclusion

The choice of therapy of transarterial embolization prior to excisional surgery has been proven to be safe and effective in cases of Kaposiform Hemanigoendothelioma with characteristics of large mass size and progressivity such as in this case.

Patient consent

Purpose of the study: The purpose of this study is to add insight based on a real case of a patient suspected with intratumor hemorrhage to prevent massive hemorrhage of Kaposiform hemangioendothelioma by digital subtraction angiography and transarterial embolization. Also provide the latest data sources related to the management since the absence of consensus.

Confidentiality: All personal data obtained is confidential which is guaranteed by the author. The author will not publish personal information of subjects that is not related to research interests.

Participation: Subject participation in this study is voluntary. Subject will not be compensated for the participation in this study. Subject may withdraw his/her participation at any time. Subject may also choose not to participate in this study.

Risks: Subject will not be compensated for his/her participation. However, subject will have the satisfaction of contributing to our knowledge and understanding of Kaposiform hemangioendothelioma. If Subject would like to receive one, Author will provide Subject with a preliminary report of my findings.

Informed consent: Subjects voluntarily participate in this study. Subject agree that Subject have given the opportunity to ask questions and have them answered to Subject satisfaction. Subject have received a copy of this consent form signed by the researcher.

Consent statement: Written informed consent for the publication of this case report was obtained from the patient's parents.

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