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Case studies

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COMPLEX THERAPY OF KAPOSIFORM HEMANGIOENDOTHELIOMA COMPLICATED BY KASABACH-MERRITT SYNDROME: A CASE REPORT AND LITERATURE REVIEW

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A – study design, **B** – data collection, **C** – statistical analysis, **D** – interpretation of data, **E** – manuscript preparation, **F** – literature review, **G** – sourcing of funding

ABSTRACT

Background: Kasabach-Merritt syndrome is an infrequent complication of large hemangiomas that could be life-threatening. Ninety percent of this phenomenon is associated with kaposiform hemangioendothelioma.

Aim of the study: To present the therapeutic process of a child with kaposiform hemangioendothelioma complicated by this rare syndrome.

Case report: The patient was admitted to the hospital during the first month of life due to a lesion on the head and neck. After many attempts with pharmacological treatment, surgery was the only effective treatment.

Conclusions: We want to emphasize that operative management of these tumors should be considered in cases of treatment resistance or rapidly progressive growth of the hemangioendothelioma.

KEYWORDS: child, hemangioendothelioma, infant, Kasabach-Merritt Syndrome, thrombocytopenia

Background

Kaposiform hemangioendothelioma (KHE) belongs to a group of extremely rare vascular tumors that mainly occur during infancy and early childhood [1,2]. According to Croteau et al., the prevalence of KHE has been estimated at 0.91 per 100,000 children per year [2]. About 50% of them have a fully formed lesion at birth [3]. It is characterized by locally aggressive growth and affects multiple tissue planes [1,4]. The tumor develops typically as an enlarging cutaneous lesion on the extremities especially over joints and on the trunk [2]. The cervicofacial region is a less common localization.

These neoplasms have high morbidity rates caused by compression of surrounding structures, locally invasive traits, and the Kasabach-Merritt phenomenon (KMP). It is described to present only with vascular neoplasms – KHE and tufted angioma (TA). A TA, as described by Yi Ji et al., belongs to the same neoplastic spectrum and can be found in biopsy specimens of patients with KHE. KMP presents as profound thrombocytopenia, consumptive coagulopathy, and hypofibrinogenemia [1]. It occurs in approximately

70% of KHE cases, and only 11% of them appear after initial presentation.

Aim of the study

To present management of KHE in a newborn complicated by the KMP. Development of the phenomenon was observed after treatment initiation, which is an untypical time for its presentation. Because of the lesion's clinical traits, surgical management had to be considered.

Material and methods

Study design and setting

The patient was admitted to the Department of Pediatric Surgery, Traumatology, and Urology in Poznan during the first month of life due to a lesion on the head and neck area. The data was acquired through the analysis of medical records, interviews, physical examinations, and observations of the patient throughout their hospitalization and surgery. The patient's parents were informed about every step of the treatment plan.

Participant

A one-month-old patient was born as a first child, with Apgar scores of 10 and a body weight of 3040 g. During pregnancy, oligohydramnios was diagnosed. No familial history of vascular abnormalities was reported. The lesion appeared 2 weeks after birth. The mother of the boy noticed that the changes would enlarge when he was crying.

During the physical examination, a soft, tumor-like change in the region of the left cheek and left side of the neck was observed. It was displaceable, localized under the skin, and about 6×5 centimeters in size. Clinically and on ultrasound examination, the lesion was defined as a vascular tumor.

Data sources/measurements

As a first-line treatment, propranolol was administered. According to the treatment plan, magnetic resonance imaging was performed, and pharmacological treatment was continued (Figure 1).

The lesion progressed despite treatment. The patient started to show aggravated signs of respiratory distress. A tracheostomy was performed to prevent further airway obstruction and respiratory failure. During hospitalization, the KMP resulted in thrombocytopenia purpura with a platelet count of 50×10^3/mcl. Steroid therapy was introduced, but the patient's clinical condition required transfusion of blood products. In addition, aspirin, ticlopidine, and vincristine were included in the treatment regimen. Red blood cell as well as platelet transfusions

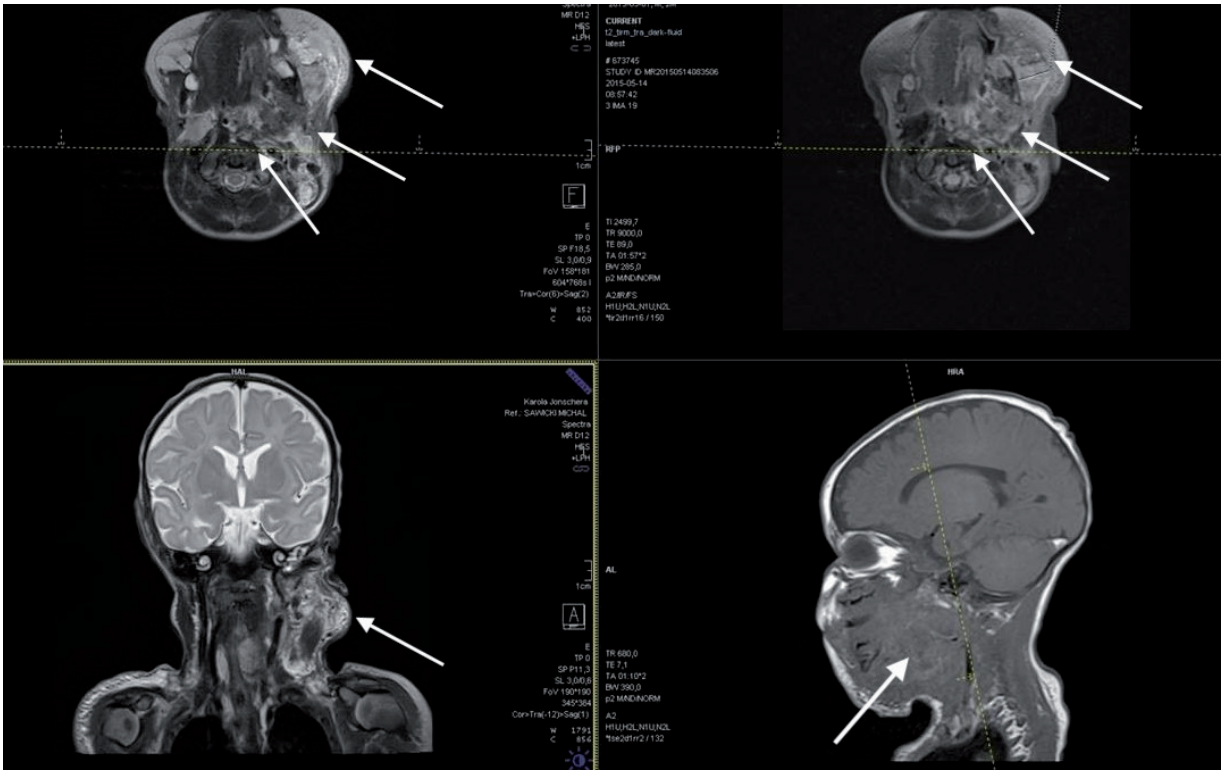

Figure 1. Magnetic resonance imaging of the head and neck shows a left-sided lesion in these areas. The tumor infiltrated the base of the tongue, a piriform sinus, and the left and medial-right part of the parapharyngeal space

were performed multiple times during the hospitalization. The patient had no clinical improvement.

The multi-specialist team, composed of a pediatric surgeon, oncologist, hematologist, radiologist, anesthesiologist, and laryngologist, decided to embolize the tumor. This was performed twice, and both attempts at closing the main lesion's vessel were insufficient. Because of the tumor's vascular structure, full closure was impossible. The team succeeded in partially closing the tumor's vessels, which decreased the risk of major bleeding during surgery.

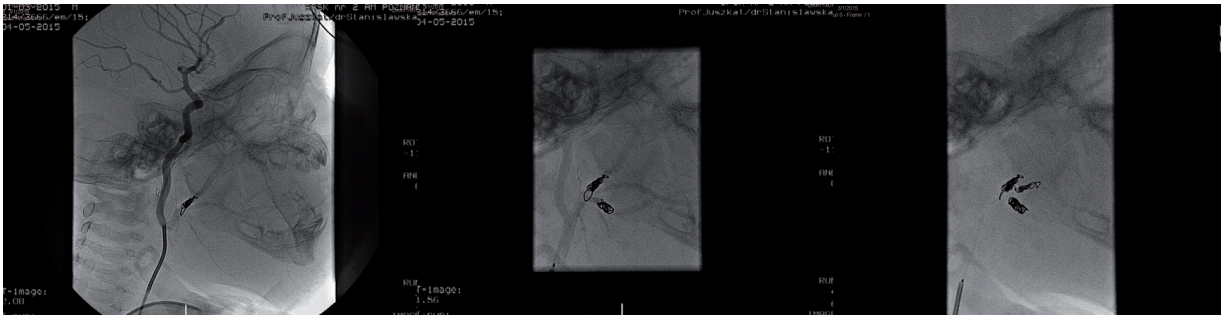

Figure 2. The images show the first embolization attempt of the vascular lesion on the left side of the head and neck

Due to a lack of improvement in the patient's condition, in the fourth month of the child's life, the decision to perform surgery was made.

During the surgery, hemostasis was obtained with the use of a thermostapler and vessel clips. Total resection was impossible, which was due to the infiltration of important anatomical structures. Intraoperative neurophysiological examination of the facial nerve revealed that it was affected by the lesion. The surgical attempt to release the nerve branches from the tumor mass was unsuccessful. A partial parotidectomy, a left sternocleidomastoid muscle removal, and a left jugular vein reconstruction took place during the surgery (Figure 3). The histopathological results were consistent with KHE.

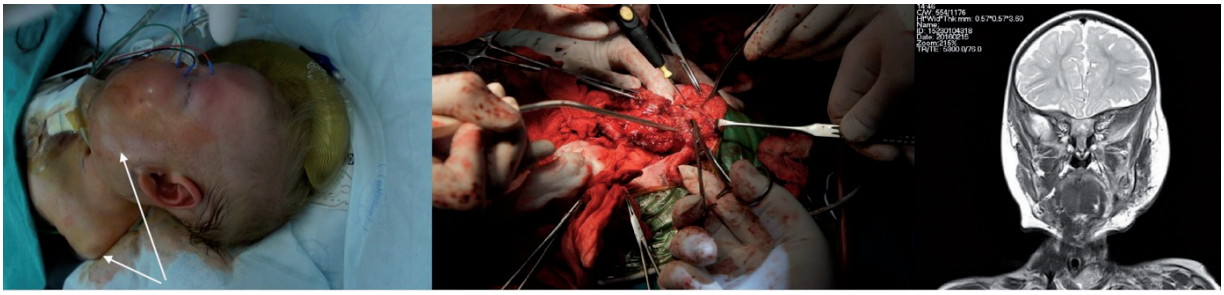

Figure 3. The figures show connected neuromonitoring before the surgery, an intraoperative picture during the preparation of the tumor, and magnetic resonance imaging in the frontal plane after surgical treatment

Results

After the surgery, a partial facial nerve palsy was observed. The boy presented with an inability to frown and close the eyelids completely, mouth drooping, hyperacusis, impairment of taste on the anterior tongue, and pain behind the ear. Lacrimation and saliva production were decreased. The patient also presented with symptoms of dysphagia, which was caused by the tumor's infiltration of the vagus nerve. The child was fed parenterally. Gastric akinesia required an alimentary jejunostomy.

Finally, the surgery stabilized the patient's condition. Chemotherapy with vincristine was continued. In total, the child received 13 courses. He completed all other pharmacological treatments.

One year after surgery, the tracheostomy was closed. The stomach function returned to normal, and the jejunostomy was removed. The boy's development is age-appropriate, and he is still under multidisciplinary medical care.

Discussion

Key results

The operative management of KHE appears to be an effective approach in cases with treatment resistance or rapidly progressive growth.

Interpretation

The KMP is associated with high mortality rates if not treated appropriately. This highlights the significance of a prompt diagnosis and immediate initiation of therapy [5]. Due to the rarity of KHE, which is the main cause of the KMP, the management is based on expert opinions and clinical cases. Consensus-Derived Practice Standards were published in 2013 by Drolet et al. to uniform the approach to unusual vascular tumors [6]. Many factors should be considered in the prognosis for tumor progression, but especially age (less than 6 months), large size, facial localization, and segmental morphology might be associated with complications, among which is KMP, which needs intensive treatment [3].

In general etiology of KHE is unknown but is constantly investigated. It is believed to be multifactorial with genetic factors being important triggers. The mutations are more likely sporadic than germline. Studies have shown GNA14 mutations to be present in KHEs and TAs. However, they are present in only 1/3 of KHE cases. They are not specific for KHE nor TA and can be found in other vascular tumors and malformations like lobular capillary hemangiomas, congenital hemangiomas, anastomosing hemangiomas, and hepatic small vessel neoplasms as well as solid tumors [1,7]. Roel W T Broek et al. found RAD50 mutations in one case of KHE [7]. The histopathology of KHE consists of confluent nodules of neoplastic spindled endothelial cells [4].

The pharmacological treatment includes vincristine, corticosteroids, sirolimus, ticlopidine, propranolol, and interferon-a. The combination of vincristine and corticosteroids or vincristine and ticlopidine/aspirin is recommended for severe cases of KMP, and that is why we administered corticosteroids, vincristine, ticlopidine, and aspirin. Due to the KMP, the patient needed multiple life-saving transfusions, therefore, transfusions should be carefully planned and performed only in life-threatening situations [6].

Non-surgical therapy protocols include interferon therapy but, in patients aged less than 1 year, should only be considered when other therapies are ineffective, and the condition is life-threatening [8]. In this case, interferon was not administrated to avoid complications in such a young child.

A surgical approach is necessary when non-surgical methods prove unsuccessful, progressive tumor enlargement needs to be stopped, or when the severity of the KMP demands immediate surgical intervention [9]. KHE is characterized by infiltrative growth affecting large neurovascular structures and muscles. In children, the nerve branches are delicate, and the compression of a bleeding tumor mass complicates the anatomy. Despite neurophysiological monitoring, there is a risk of temporary or permanent nerve damage [1,4]. Infiltration of the facial and vagus nerve was visible intraoperatively in our patient.

KMP is characterized by an intravascular coagulopathy secondary to platelet trapping, which was directly illustrated using positive immunohistochemistry for CD61, a marker of platelets, within the vascular lumen [5]. Signs of severe coagulopathy and a high risk of intraoperative and cerebral bleeding indicated embolization. Eseonu et al. suggest neoadjuvant treatment with steroids and/or embolization to be performed prior to surgery. Embolization of the tumor's vessels should be considered as an introduction to surgical procedures, though sometimes this method is recommended as palliative therapy [10]. In our patient's case, the first embolization took place in the fourth month because the equipment was not adjusted for such small children. The second was performed a short time later, before the surgical treatment.

There are medical problems associated with the tumor's anatomical location as a possibility of compression of anatomical structures, obstruction of the airway, or visual disturbances [1]. In this case, the tumor affected the left side of the head and neck, causing airway obstruction, feeding problems, and an after-surgery symptomatic facial nerve palsy. Large vascular abnormalities may also lead to cardiac compromise, which in this case was excluded after cardiological evaluation.

Generalizability

KHE is rare but is commonly complicated by KMP, which can be identified even before the diagnosis of a tumor mass. Hematological disturbances, especially thrombocytopenia, may indicate KMP and should be quickly recognized [3]. Furthermore, KMP can promote rapid growth of the tumor mass, leading to life-threatening complications.

Study limitations

The study was limited to one patient only. Larger studies are necessary to certify the effectiveness of the surgical approach.

Recommendations:

Due to the rarity of this life-threatening phenomenon, it is significant to create prospective studies to evaluate potential predictive factors for KMP development and identify effective management plans for KHE with KMP [3, 11].

Conclusions

KHE can potentially cause morbidity and mortality among children and, less often among adults. However, it can be successfully treated, and thus it is important to consider it in the differential diagnosis of unusual vessel tumors, acknowledging their common complications and risk factors. When KHE is complicated by the KMP, which can lead to the aggressive growth of a KHE and vital structure compression, operative management with pre-surgical tumor vessel embolization should be considered.

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