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Research article

Clinical and imaging features of Kaposiform hemangioendothelioma in infants

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ABSTRACT

Objective: Kaposiform hemangioendothelioma (KHE) is a locally aggressive tumor of vascular origin. This study investigated the clinical and imaging features of KHE to provide a reference for its early diagnosis.

Methods: The clinical and imaging findings of 27 clinically confirmed KHE cases (including 21 with focal lesions and 6 with diffuse lesions) between January 2016 and December 2021 were retrospectively analyzed.

Results: The mean age of the 27 patients was 105 ± 80.27 days. Twenty-two (81.5%) of these patients had Kasabach–Merritt phenomenon. Most KHEs were located in the trunk and/or extremities (22/27). Ultrasonography showed heterogeneous echogenicity and/or striated hypoechoic bands with abundant or patchy blood flow within the tumor. On plain computed tomography (CT), they appeared as heterogeneous lesions isodense with the muscles, with a CT value of 29.58 ± 11.53 HU. In the arterial phase, the KHEs showed striated or lamellar heterogeneous enhancement, with a CT value of 153.91 ± 52.11 HU after enhancement. All KHEs showed uneven and high signal intensity on T2-weighted imaging, mixed high and low signal intensity on fat-saturated images, and no significant diffusion restriction on diffusion-weighted imaging.

Conclusion: KHEs can occur in various locations and present as highly infiltrative and heterogeneous masses that can invade the skin, adjacent muscles, and bones. A vascularized mass with purpuric skin changes, with uneven and high T2WI signal is highly suggestive of the diagnosis of KHE.

1. Introduction

Kaposiform hemangioendothelioma (KHE) is a locally aggressive tumor of vascular origin. KHE is often associated with the

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Kasabach–Merritt phenomenon (KMP), which is characterized by rapid tumor growth and severe platelet consumption, further leading to consumptive coagulopathy, hypofibrinogenemia, and microangiopathic hemolytic anemia [1]. The mortality rate can reach 12–30% due to bleeding, high-output cardiac failure, and infiltration of vital organs [2,3]. Therefore, early diagnosis and treatment are crucial to saving the life of the child. Currently, the literature on KHE is mainly case reports, with limited information on the features of KHE on ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI). Thus, this study retrospectively analyzed the clinical and imaging features of KHE to improve the understanding of the disease by physicians and radiologists and to provide a reference for its early diagnosis.

2. Materials and Methods

2.1. General information

The data of 33 children with KHE admitted to Jinan Children's Hospital (Children's Hospital Affiliated to Shandong University) between January 2016 and December 2021 were retrospectively analyzed. Six patients were excluded from analysis, including five who were admitted for the second time and one with missing clinical data and imaging examination findings. This study retrospectively analyzed the clinical characteristics, including sex, age at onset, medical history, symptoms, anatomical location, lesion extent, and laboratory tests, of 27 children with KHE. Lesion location was categorized as the head and neck, trunk, and extremities. According to lesion extent, the lesions were classified into two subtypes as follows: focal type, defined as a solitary lesion with surrounding infiltration, and infiltrative type, defined as a diffuse lesion with ill-defined borders of the solid component. The diagnosis of KMP was made when the child developed thrombocytopenia with or without hypofibrinogenemia and elevated D-dimer levels. This study was approved by the Ethics Committee of the hospital. Informed consent was obtained from all individual participants included in the study.

2.2. Imaging findings

Of the enrolled children with KHE, 27 underwent ultrasonography, 12 underwent CT scans (11 of whom underwent enhanced CT), and 4 underwent MRI (2 of whom underwent enhanced MRI). Two children underwent both CT and MRI scans. All children underwent scans after sedation with chloral hydrate. The lesion location, size, shape, extent, internal structure, homogeneity, and borders were independently assessed by two radiologists with more than 5 years of experience in diagnostic radiology.

Compared with those of the muscles, the echo intensity, CT density, and signal intensity of KHE were recorded as low, moderate, and high, respectively. The degree of enhancement was determined by comparing it with that of the muscles and blood vessels. Enhancement comparable to that of the muscles was defined as mild enhancement; enhancement between that of the muscles and blood vessels was defined as moderate; and enhancement similar to that of the blood vessels was defined as significant. The flow void areas on T2-weighted imaging (T2WI) with significant enhancement on enhanced CT and MRI were recorded as vessels for blood supply and drainage. All images were reviewed by two radiologists, and the results were recorded after they had reached a consensus.

3. Results

3.1. General clinical findings

This study included a total of 27 patients with KHE (Table 1). The mean age of the patients was 105 ± 80.27 days, including 16 males with onset ages ranging from 1 day to 10 months. The main symptoms were tough masses (22/27), purpuric skin changes (12/27), and swelling of the extremities (2/27). One patient developed cerebral hemorrhage due to platelet depletion caused by the tumor,

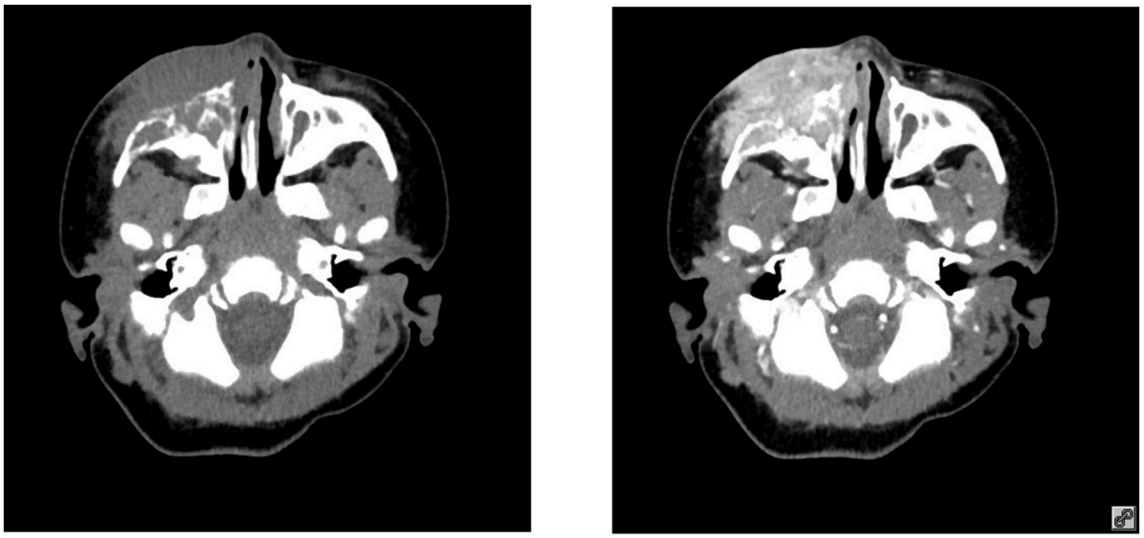
Table 1
Clinical information.

Gender	
Male	16
Female	11
Age	105 ± 80.27 d
Location	
Limbs	17
Trunk	7
Head and Neck	5
Size[a]	7.1 ± 2.57 cm
Type	
Focal	21
Diffuse	6
KMP	22

KMP , Kasabach–Merritt phenomenon.
[a] One patient only showed thickening of the diaphragm, which was not included in the statistics.

and one developed pericardial effusion and pleural effusion, which was considered to be caused by the lesion invading the pleura and pericardium. Treatment was delayed in five children due to unknown diagnoses at admission, and one was given up for treatment due to multiple organ failure and pulmonary hemorrhage. The laboratory tests showed that many of the children developed thrombocytopenia (22/27), elevated D-dimer levels (21/25), hypofibrinogenemia (20/25), and anemia (19/27).

A total of 26 children were full-term, and 1 was born prematurely. The lesion locations included the extremities (17 cases), trunk (7 cases), and head and neck (5 cases), with 1 case involving both the left upper limb and chest wall and 1 involving the pelvis, perineum, and left lower limb simultaneously. The lesions were diffusely infiltrative in 6 cases and focal in 21, with an average diameter of 7.1 $\pm$ 2.57 cm. The lesions invaded both the skin and deep tissues in 26 cases, with no obvious tumor-like structure observed in 1 with only thickening of the diaphragm.



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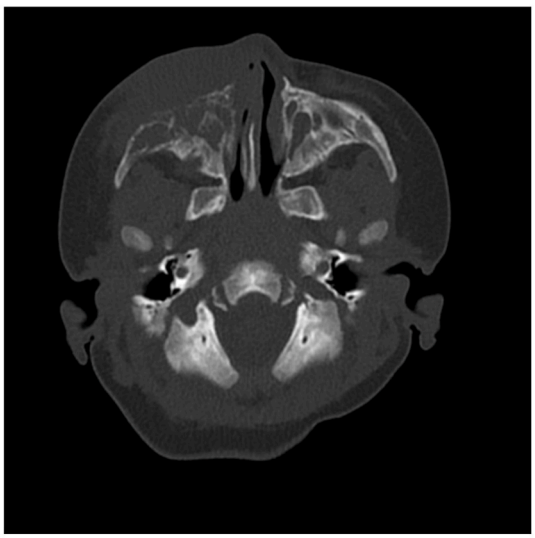

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Fig. 1. A female baby, 1 month 15 days, (A) CT scan showed irregular mass soft tissue density in the right maxillofacial region, CT value 29HU; (B) Inhomogeneous enhancement on enhanced scan, CT value 166HU; (C) Multiple bone involvement was seen in the bone window.

3.2. Imaging features

3.2.1. Ultrasound features

The lesions presented as moderately echoic masses in 13 cases, hypoechoic masses in 9, and hyperechoic masses in 4. The lesions also involved the deep anatomical structures in five cases. One patient presented with a diffuse mediastinal lesion only with thickening of the diaphragm with no obvious mass observed on ultrasound. The tumor-like lesions in 26 cases were all ill-defined, 19 of which had abundant blood flow signal, 7 showed patchy blood flow signal, 7 showed striated hypoechoic bands, 10 presented tortuous vessels, 9 had punctate hyperechoic foci, and 8 showed soft tissue thickening. Due to tumor infiltration, head and neck lesions were complicated with parotid gland invasion (2/5). Lesions in the extremities often involved the spatium intermusculare (5/17), while trunk lesions could involve the visceral pleura or diaphragm simultaneously.

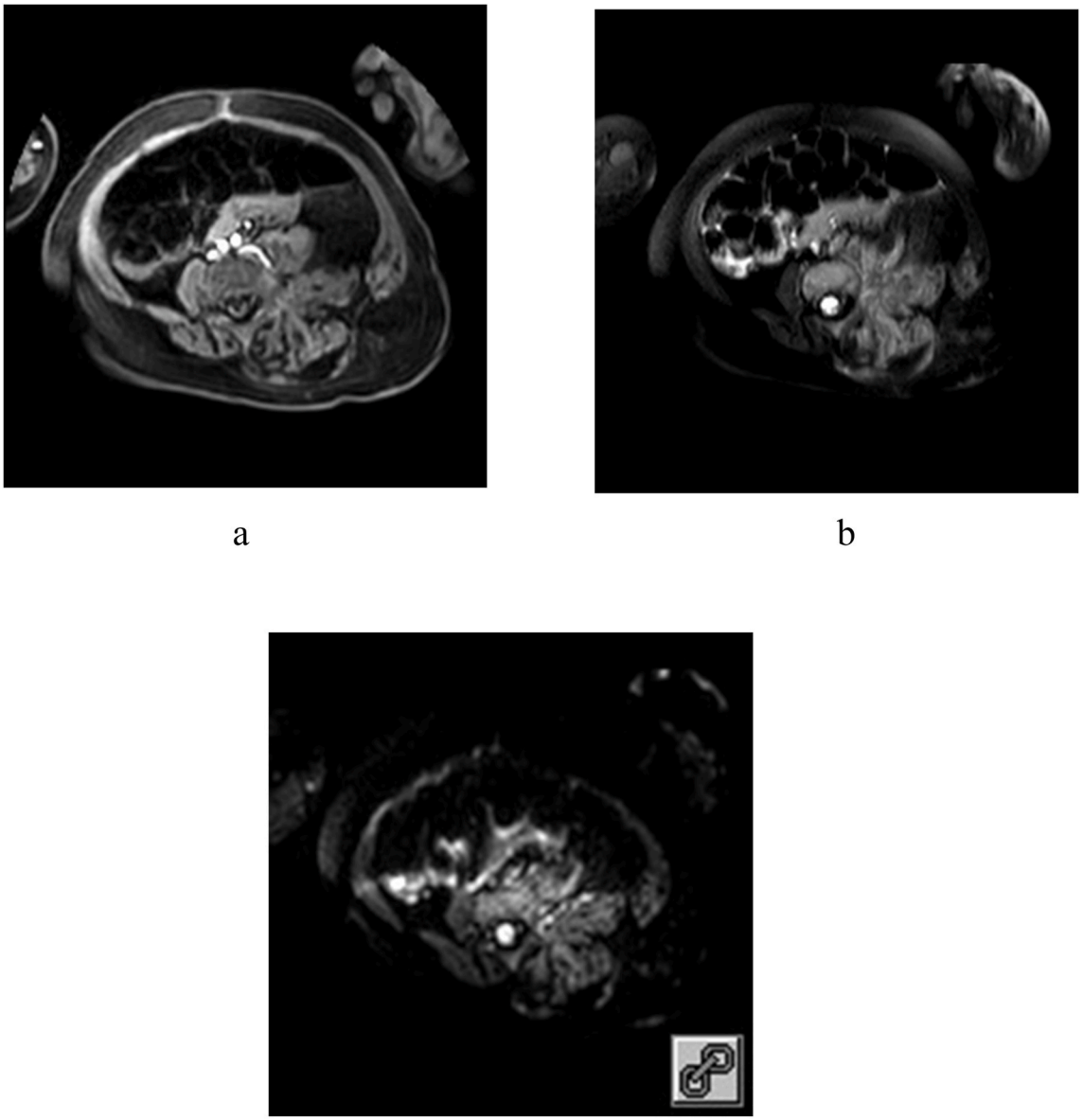

Fig. 2. A male baby, 9 months, (A) T1-weighted image showed local soft tissue thickening and irregular mass-like mass, and surrounding muscle tissue was involved; (B) T2-weighted image showed high and low mixed signals; (C) DWI showed no obvious diffusion limitation.

3.2.2. CT features

Among 12 patients who underwent CT scans, 9 and 3 showed focal and diffuse lesions, respectively. The involved tissues showed skin thickening (9/12), striated or flocculent soft-tissue shadow (11/12), involvement of the spatium intermusculare (8/12), and bone invasion (3/12) (Fig. 1A–C), with a CT value of 29.58 ± 11.53 HU. After contrast administration, the lesions showed striated or flocculent heterogeneous enhancement (10/11) in the arterial phase, with a CT value of 153.91 ± 52.11 HU. No obvious mass lesion was observed in one patient who presented only with thickening of the diaphragm, with a CT value of 171 HU after contrast enhancement.

3.2.3. MRI features

Four patients underwent MRI scans (Fig. 2A–C). Compared with the muscles, KHEs showed heterogeneous and high signal intensity on T2WI, mixed high and low signal intensities on fat-saturated T2WI, and no significant diffusion restriction on diffusion-weighted imaging. The KHE showed heterogeneous enhancement in one case. Adjacent fat adhesion and muscle invasion were observed in four cases. Obvious flow void signal was observed in two cases. Bone changes, such as bone destruction or invasion, were observed in one case. Grid-like lymphedema was observed in two cases. No significant calcification, hemorrhage, or hemosiderosis was observed.

4. Discussion

KHE, first described by Zukerberg et al., in 1993, is a rare vascular tumor that occurs most frequently in the deep soft tissues of the extremities [4,5]. The overall incidence is low, and KHE predominantly occurs in infants and children, with most of the lesions located in the soft tissues of the extremities and trunk and a few diffuse lesions involving the mediastinum, retroperitoneal tissues, intracranial tissues, and spine [3,6–8]. In their study of 165 patients, Fernandez et al. showed that most patients were children under 12 years of age and that 60 patients had lesions located in the extremities, with the remaining patients showing involvement in multiple sites [9]. In this study, 26 of the 27 patients had lesions detected at birth and all were under 1 year of age at first presentation to the hospital. Among these, 17 cases had lesions in the extremities and 7 had lesions in the trunk, consistent with that reported in the literature. Unlike babies, KHE is mostly located in the head and neck in toddlers (1–5 years) [10].

KHE is often associated with skin involvement, manifesting as purpura-like or purplish-red skin changes, localized palpable tough masses with ill-defined margins, or diffuse limb swelling. Nearly 75% of patients with KHE show skin involvement, predominantly in infants and children, and only 11% of patients lacked skin changes [3]. In this study, 12 patients showed purpura-like skin changes and 14 had red or purplish skin changes, with 4 showing extensive skin lesions presenting as diffuse masses or swelling of the limbs, which suggested local infiltrative growth. Interestingly, Kaposiform hemangioendothelioma (KHE) and tufted hemangioma (TA) have overlapping clinical and histopathological features [11]. Therefore, hematological tests and imageological examinations should be performed in infants and children with the abovementioned symptoms.

KMP includes a series of coagulation abnormalities associated with KHE [12] that present as severe platelet depletion and consumption of coagulation factors. The incidence is 42–71% [13] and is positively correlated with tumor volume, especially when the diameter of the tumor is $>$ 8 cm [14]. Second, a correlation has also been reported between the lesion location and KMP. KHE that infiltrates muscles or deeper tissues is 6.3 times more likely to manifest as KMP than superficial lesions and 18 times more likely if it is a retroperitoneal or intrathoracic lesion [3]. Hu et al. [15] reported a mean diameter of 9 cm (range 2–20 cm) among lesions in 25 cases of KHE; all cases had deep tissues involvement, and 20 (80%) developed KMP. In this study, 22 patients were complicated with thrombocytopenia and all 7 patients with KHE lesions in the trunk developed KMP. The incidence of KMP mostly decreases with age [10]. In clinical practice, the identification of the risk factors most associated with KMP will be of great help to the physicians.

Color Doppler ultrasonography is the first choice for assessing superficial masses, in which KHE mostly appears as a heterogeneous mass with striated hypoechoic bands and abundant/patchy blood flow signals [16], which may be related to its pathological features. Qiuyu et al. [17] reported that KHE mostly appeared as infiltrative lobulated nodules under a light microscope; these nodules comprised a clustered proliferation of spindle-shaped endothelial cells with epithelioid morphology and irregular crescent-shaped or lacunar vessels around the nodules. Although ultrasonography can suggest the possibility of a tumor of vascular origin, it cannot clearly reveal the infiltrating part of KHE, making it difficult to accurately assess the extent of KHE by ultrasonography. Thus, although ultrasonography is the first choice for assessing KHE, it has limitations compared with CT or MRI.

On CT scans, KHE also presents as striated soft-tissue shadows with enhancement after contrast administration. Moreover, CT is more advantageous in revealing osteolytic destruction, bone erosion, and remodeling [15,18]. In their report of seven patients with KHE who underwent CT scans, Hu et al. [15] observed one case with osteolytic destruction and three with bone erosion or remodeling. The infiltrative and destructive growth pattern of KHE causes skeletal and muscle involvement leading to functional limitations, thereby affecting the patient's ability to perform daily activities and, ultimately, quality of life [19]. In contrast, most infantile hemangiomas present enhanced homogeneously with clear boundaries [20]. In this study, seven patients developed spatium intermusculare involvement and significant localized pain. The CT scans revealed morphological abnormalities of the involved muscles with internal punctate or flocculent enhancement. Unlike that observed in previous studies, one patient in this study only showed morphological abnormalities of the rib without significant bone erosion.

The reported MRI features of KHE typically include heterogeneous and high signal intensity on T2WI, with speckled or striated low signal intensities [16,21]. It is helpful to differentiate KHE from other vascular tumors, especially infantile hemangioma. On MRI, infantile hemangioma appears as a regular and well-defined lesion with significant homogeneous high signal intensity on T2WI, without significant destruction of the adjacent bone [1,22]. However, in addition to the infiltrative morphologic findings, MRI can help detect hemorrhage within the lesions, hemosiderosis, and grid-like lymphedema [15,23,24]. Both CT and MR are good methods for

detecting vascular lesions, and CT has the added benefit of being less time-consuming, enabling a comprehensive assessment of vessels and identification of typical musculoskeletal abnormalities, which may be helpful in the initial diagnosis and subsequent treatment of KHE.

In conclusion, the results of this study showed that KHE mostly occurred in infants at different body locations. The imaging findings revealed significantly heterogeneous and ill-defined lesions, most of which infiltrated the surrounding tissues. In clinical practice, attention should be paid to differentiate infantile masses with the abovementioned features from KHE.

Declarations

Author contribution statement

Yuanjun Hu; Dan Song: Conceived and designed the experiments; Performed the experiments.
Changhua Wu: Analyzed and interpreted the data; Wrote the paper.
Liang Wang; Jing Li; Lei Guo: Contributed reagents, materials, analysis tools or data.

Data availability statement

No data was used for the research described in the article.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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