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Treatment of retroperitoneal kaposiform hemangioendothelioma: 2 case reports

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ABSTRACT

Kaposiform hemangioendothelioma (KHE) is an uncommon vascular tumor that affects young children. It frequently affects the trunk, limbs, head and face, but rarely the retroperitoneal area. This retrospective study analyzed two cases of retroperitoneal KHE admitted to the Children's Hospital of Fudan University, and investigated the clinical characteristics and treatment of this disease.

1. Materials and methods

Two patients with combined retroperitoneal KHE and Kasabach-Merritt phenomenon (KMP) were admitted to the Children's Hospital of Fudan University from 2009 to 2011.

2. Case 1

A five-month-old male child was admitted with a complaint of an "accidentally discovered abdominal mass noticed a week ago." Physical examination revealed a distended, left mid-to upper abdomen. Upon palpation, it was felt as a solid mass, 7 cm in diameter, with a clear boundary and no tenderness. Ultrasonic examination revealed a giant mass comprising a mixture of solid and liquid contents in the adrenal area of upper left retroperitoneum, indicating the possibility of neuroblastoma. The mass was located adjacent to the tailof pancreas and left kidney, resulting in the compression and deformation of the spleen. Abdominal enhanced CT scan revealed a huge mass with a clear boundary and measuring 7.4 × 7.7 × 10 cm in size, located in the left abdomen, exceeding the midline. The mass appeared as isodense to slightly hypodense lesions with stripe calcification. The lesions exhibited heterogeneous enhancement, while the spleen was not clearly visualized. Computed tomography angiography (angiography or CTA) showed that the blood supply of the mass originated from the branch of splenic artery (Fig. 1A). Complete blood count (CBC) revealed a platelet count of 27×10^9/L. Pre-operative diagnosis was "retroperitoneal mass with the possibility of neuroblastoma."

After platelet transfusions, exploratory laparotomy and mass biopsy were performed. During the operation, a giant solid tumor was found originating in the retroperitonium, which elevated the spleen and pancreas. Nodular projection was detected on the surface of the mass. The mass infiltrated the spleen, and could not be separated. Due to the unique pathological manifestation, no precise, short-term diagnosis was possible. After two weeks of consultation with the Pathological Department of Fudan University Shanghai Cancer Center, we finally diagnosed the tumor as (abdominal) Kaposiform hemangioendothelioma, based on biopsy.

3. Case 2

A four-month-old female child was diagnosed as volvulus based on "darkened feces accompanied with crying and vomiting" at a local hospital. During exploratory laparotomy, hemorrhagic enteritis was diagnosed and the child did not receive any special treatment. After postoperative hormone therapy and platelet transfusions, symptoms were relieved within a short period followed by recurrence. Physical examination revealed a pale appearance and a soft and distended abdomen. No tenderness or apparent solid mass was detected. The bowel sound was weak. CBC showed a hemoglobin value of 70 g/L; platelet count,

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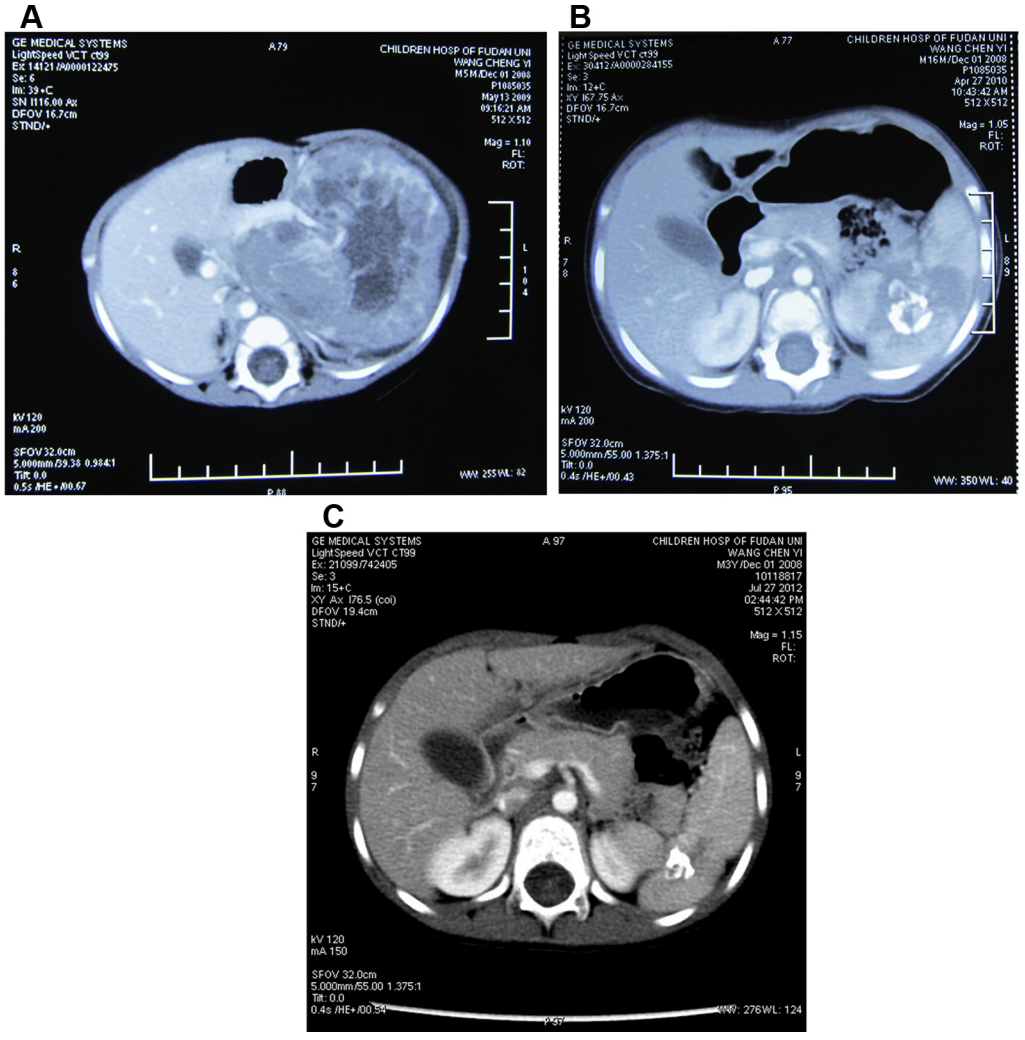

Fig. 1. A: Disease onset. A huge heterogenous mass with a clear boundary and a diameter of 7 cm, located in the left abdomen, exceeding the midline; stripe calcification can be seen. The lesions exhibited heterogeneous enhancement, while the spleen was not clearly visualized. B: One year after VCR treatment. The mass was diminished in size. Spleen was restored to normal position. C: Two years after VCR treatment. The tumor almost disappeared, with only slight calcification left.

12×10^9/L; and white blood count, 8.9×10^9/L. The child tested positive for fecal occult blood. Ultrasonic scan indicated abnormal bowel in the left abdomen. MRI revealed an abnormal crumby signal in the mesentery root. The intestine wall was thickened and swollen accompanied with a large amount of ascites (Fig. 2A). CTA revealed multiple abnormal enhancements in the head of pancreas and mesentery root. Intestine wall became thickened and swollen accompanied with a large amount of ascites and collateral vessel formation (Fig. 2B).

After consultation with multiple clinical departments, the child was diagnosed as retroperitoneal KHE combined with thrombocytopenia. Medical hemorrhagic diseases and strangulated intestinal obstruction were both excluded.

4. Results

4.1. Case 1

Due to the unique pathological manifestations, we finally certified the pathological results as retroperitoneal KHE after multidisciplinary consultation 2 weeks later. The child underwent experimental chemotherapy with cyclophosphamide (CTX), adriamycin and etoposide (VP16) on day 5, postoperatively. Persistent thrombocytopenia following chemotherapy and methylprednisolone pulse therapy was used to arrive at a definitive pathological diagnosis. After the treatment, platelet counts were rapidly elevated to 121×10^9/L. Oral drugs (5 mg/kg, qd) was then administered instead of intravenous methylprednisolone and platelet counts were maintained at 100×10^9/L. The tumor size was reduced by 25%, 1 month later. During the treatment phase, platelet counts decreased to 69×10^9/L prompting reduction of the dose of methylprednisolone and gradual substitution with vincristine (VCR) treatment comprising 10 cycles. The tumor almost disappeared although slight calcification was visible 2 years later (Fig. 1B and C).

4.2. Case 2

After consultation with multiple clinical departments, a definitive diagnosis of retroperitoneal KHE was obtained. The child received hormonal pulse therapy without any response. The child exhibited continuous bleeding and non-elevated platelet counts. VCR was used simultaneously and platelet counts were elevated immediately to 85×10^9/L, resulting in gradual hemostasis. After 4 cycles of VCR

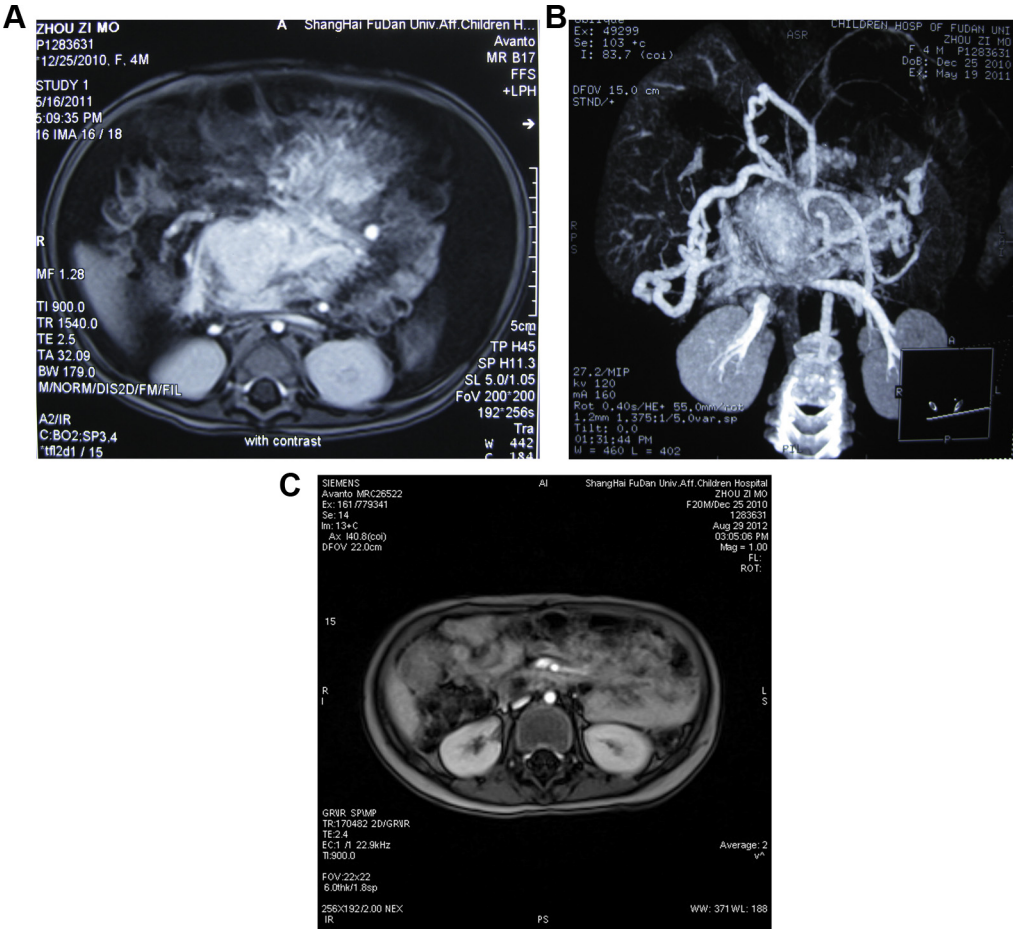

Fig. 2. A: MRI revealed abnormal crumby signals in the mesentery root, and intestine wall became thick and swollen accompanied with a large amount of ascites. B: CTA revealed multiple abnormal enhancements in the head of pancreas and mesentery root. Intestine wall became thickened and swollen accompanied with a large amount of ascites and collateral vessel formation. C: MRI revealed disappearance of previous abnormal crumby signals, with only slight intestinal wall enhancement.

treatment, the platelet counts increased to 154 $\times$ 10^9/L, and then hormone therapy was gradually discontinued. The child was provided ordinary food and showed no hemafecia. All chemotherapies were completed, hormone therapy discontinued and the child's nutritional status recovered rapidly. Follow-up MRI revealed disappearance of previous abnormal crumby signals, with only slight enhancement of intestinal wall (Fig. 2C).

5. Discussion

The morbidity of retroperitoneal KHE is relatively low. Since 2001, only nine reports of retroperitoneal KHE have been published in pediatric surgery journals worldwide [1–9], though other cases maybe reported in other specialties Due to the low incidence of this disease, therapeutic experience is limited and misdiagnosis is common. Pathological manifestations may contribute to correct diagnosis. However, considering the lack of expertise, the limited vigilance of physicians, and inadequate multidisciplinary consultation, accurate diagnosis is not easy. In this retrospective study, the two cases of retroperitoneal KHE provide valuable insights for clinical diagnosis. 1) Both surface and retroperitoneal KHE usually occur in children, especially in 2–4-month-old infants, and commonly accompanied with thrombocytopenia. Thrombocytopenia was detected during the early stage of disease onset in two children. Physicians administered repeated platelet transfusions, leading to temporal elevation of platelet and subsequent severe platelet reduction. 2) The differential diagnosis of retroperitoneal KHE [2,4] includes retroperitoneal solid tumors such as neuroblastoma, primitive neuroectodermal tumors (PNET) and other hematologic tumors, such as lymphoma, idiopathic thrombocytopenic purpura (ITP). Among the 2 children mentioned above, one was misdiagnosed as neuroblastoma and received anti-neuroblastoma chemotherapy briefly. The other case was misdiagnosed as volvulus and received exploratory laparotomy for digestive tract bleeding. Therefore, the definitive diagnosis of KHE is quiet difficult. 3) Based on experience with our 2 case studies in treating KHE, other than marked thrombocytopenia, medical imaging showed extensively vascularized, retroperitoneal regular or irregular mass. The microscopic examination revealed flake-like, continuous small nodular or lobular tumors separated by fibrous tissue. The tumor was composed of many small proliferative vessels, spindle-shaped and epithelioid endothelial cells, which resembled Kaposi sarcoma [10]. The pathological examination revealed glomerulus-like structure but was negative for GLUTl. The pathological manifestations of KHE varied and clinical experience was essential for a correct diagnosis. 4) Knowledge and therapeutic experience are crucial for the diagnosis of KHE. In the present study, one case did not manifest the typical pathology of KHE. However, our therapy resulted in good outcomes. Therefore, careful observation, comprehensive judgment, bold hypothesis, multidisciplinary consultation and discussion are important factors for accurate diagnosis.

According to literature, the therapeutic approaches and clinical outcomes of retroperitoneal KHE varied. High dose of hormone pulse therapy, low dose of VCR pulse chemotherapy or administration of interferon have been used for the treatment of retroperitoneal KHE [11–13]. Our treatment experience was as follows: 1) The two cases responded to early stage of hormone therapy, with partial relief. Nevertheless, the two cases showed tolerance or resistance to hormone therapy during the early or late stage of therapy. Finally, patients were administered intravenous injection of low-dose VCR to stabilize their condition. The tumor completely vanished two years after disease onset in one case. In the other case, after 4 cycles of VCR treatment, the platelet counts were elevated from 4×10^9/L to 154×10^9/L. Symptoms like hemafecia, abdominal distension and vomiting were diminished. Among different therapies for combined KHE and KMP (body trunks, limbs, head, face, and retroperitoneal area) in children, hormone pulse therapy was efficient in 60% of children. The efficiency of VCR therapy was as high as 90% for those resistant to hormone pulse therapy. Further, short-term VCR therapy was associated with few side-effects and quicker cessation of hormone therapy. VCR has been proposed by a few researchers as the first-line treatment for combined KHE and KMP instead of hormones. 2) During the course of therapy in children with combined KHE and KMP, platelet transfusion should be carried out based on indications. Vasogenic proteins were released by platelet degranulation, which may induce the growth of Kaposi-like hemangioendothelioma, accelerating platelet damage, and leading to severe platelet reduction [14]. On the other hand, the half-life of platelets is 1–24 h. The transfused platelets were depleted in a short period of time, resulting in limited effect on elevation of platelet counts [15]. Therefore, in children with combined KHE and KMP, platelet transfusion should be performed with caution unless obvious spontaneous bleeding occurs. Individualized therapy is recommended for the treatment of combined KHE and KMP, whereas standardized protocal should also be considered.

We retrospectively analyzed the clinical characteristics, diagnosis and treatment regimens of two cases of retroperitoneal KHE. We would like to share our experiences with other physicians interested in the management of the non-malignant vascular tumor. Additional cases and therapeutic experiences may result benefit children with retroperitoneal KHE.

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