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Neonatal Intestinal Obstruction and Thrombocytopenia: Sepsis or Otherwise? Neonatal Intestinal Kaposiform Haemangioendothelioma: A Case Report and Literature Review

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Abstract A two-day-old full-term baby presented with vomiting and distended abdomen with a right-lower-quadrant mass. He had severe thrombocytopenia without sepsis. Radiograph showed dilated bowels displaced to the left side. Contrast enema showed micro-colon. Sonogram revealed a vascular lesion involving bowels. Laparotomy proceeded on day three for persistent obstruction: a large angiomatous lesion was found encroaching on distal ileum. Profuse haemorrhage forbade dissection; temporising ileostomy was performed. Obtruction was relieved but thrombocytopenia persisted. After ten days of supportive treatment and follow-up vascular imaging, the second operation proceeded; the intestine and mesentery bearing the lesion were resected. The baby recovered and thrived well; ileostomy was soon closed before discharging home. Histology revealed mesenteric Kaposiform haemangioendothelioma. This is a rare report of such lesion with extensive intestinal involvement causing life-threatening intestinal obstruction and coagulopathy in a newborn, necessitating urgent surgical resection. Although the baby recovered from operation, significant intestinal length was resected and resection margins were involved: post operative surveillance is needed to monitor nutrition and possible tumour recurrence.

Key words Kasabach-Merritt syndrome; Mesenteric Kaposiform haemangioendothelioma; Neonatal intestinal obstruction

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Introduction

Haemangioendothelioma is a vascular neoplasm with biological and histological features in between benign haemangioma and angiosarcoma. Variants include infantile, spindle cell, retiform, epithelioid, and kaposiform type.[1,2] Kaposiform haemangioendothelioma (KHE) is a rare vascular lesion of infancy and childhood. Having distinctive features of infiltrative growth and consumptive thrombocytopenia (Kasabach-Merritt phenomenon),[3] KHE can be life-threatening. Common locations include extremities, head and neck, chest, retro-peritoneum and scrotum, but visceral involvement in newborn has not been documented. We hereby report a case of KHE presenting in a neonate with coagulopathy and intestinal obstruction.

Case Report

1. Presentation

A full term Chinese baby boy of normal delivery

presented with bilious vomiting and abdominal distension from day one of life. At initial examination, his abdomen was grossly distended with a palpable right sided abdominal mass and visible bowel loops. He was thrombocytopenic with deranged coagulation profile, although he was clinically not severely septic. Radiograph showed multiple distended bowel loops. Contrast enema revealed small colon caliber. Empirical antibiotics were given. Coagulopathy persisted despite platelet and cryoprecipitate transfusions. Urgent sonogram disclosed a right-sided undetermined hypervascular abdominal mass, differential diagnosis being vascular flows in a mass of compressed bowels (Figure 1).

2. The First Operation

In view of persistent bowel obstruction and deteriorating clinical condition, the baby was taken to emergency theatre on day three. At operation, proximal small bowel was grossly distended with tight encroachment by an indurated mesenteric vascular mass extending from the superior mesenteric artery origin just below the third part of duodenum down to the terminal ileum and caecum. The distal one third of the small intestine was thick-walled and coiled around the mesentery mass. The obstructing mass measured 5 cm by 3 cm by 2 cm (Figure 2). He remained thrombocytopenic with continued bleeding from raw

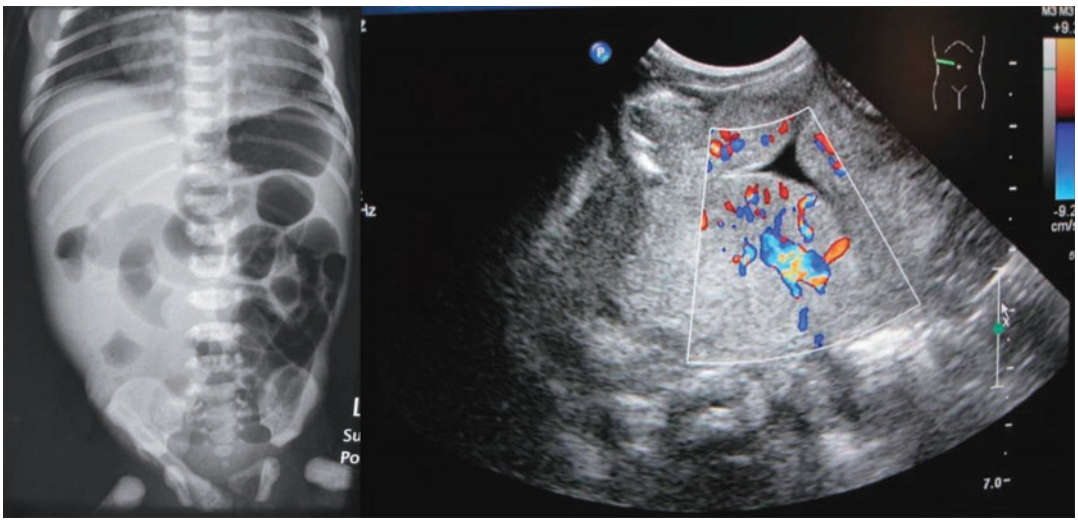

Figure 1 Pre-operative abdominal radiograph and sonogram suggesting a right sided abdominal mass of coiled intestine loops with compressed mesenteric vessels.

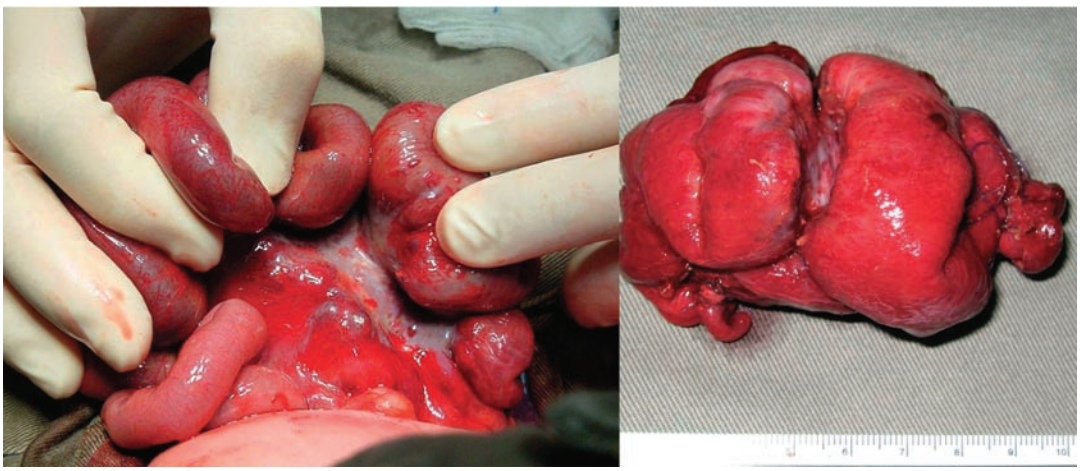

Figure 2 Operative photos: thickened and indurated distal ileal loops around an extensive vascular mesenteric angioma and resected specimen at the end of the second operation consisting of distal ileum, appendix, caecum and mesenteric angioma.

surfaces during attempted dissection of the mass. The extent of the mesenteric vascular supply involved by the lesion was uncertain. For these adverse reasons, further surgical manipulation was abandoned. The abdomen was closed after a temporising ileostomy was fashioned for decompression.

Post operatively, the stoma worked well to relieve the obstruction, but the baby remained coagulopathic in spite of blood product support. Follow-up vascular assessment with duplex-sonogram and contrast computerised tomogram were performed to assess the resectability of the lesion or feasibility for angiographic embolization otherwise. The celiac trunk and superior mesenteric artery coursed adjacent but away from the mass which, although hypervascular, had no discernible feeding vessels. Findings were suggestive of an infiltrative type haemangioma of the intestine and mesentery, and that surgical resection might be feasible while angiographic treatment was not.

3. The Second Operation

The second operation was performed on day twelve of life with intent for curative resection. Two apparent feeding vessels from pelvis were ligated. The distal ileum, caecum and the mesenteric haemangioma were *en bloc* resected by painstaking dissection to achieve gross tumour clearance and major vessel preservation (Figure 2). Stoma had to be revised. Peri-operative blood loss was significant. Adequate and timely blood product transfusions were necessary to achieve haemostasis before closing the abdomen. 30 cm of distal ileum with caecum was removed and 60 cm of proximal healthy small intestine remained.

4. Post-operation and Outcome

His general condition stabilised after transient ventilatory and inotropic support. Oral feeds were resumed and tolerated. Platelet count rose to normal range without further platelet transfusion (260 x 10^9 platelets/L). Stoma was closed at two month. He thrived well to be discharged home at three months old.

5. Histology

Microscopic examination of the mesenteric tumour shows a Kaposiform haemangioendothelioma composed of lobules of spindle tumour cells (Figure 3A) separated by fibrous septa. The tumour cells were arranged in sieve-like pattern and fascicles with slit-like spaces containing red blood cells resembling Kaposi sarcoma (Figure 3B). Focally, there were capillary haemangioma-like areas with the tumour cells forming tiny capillary channel (Figure 3C). Glomeruloid structures (Figure 3D) were also present with the tumour cells forming whorls punctuated by tiny holes containing red blood cells. Immunostaining showed that the tumour cells were positive for vascular endothelial marker CD31 and CD34. D2-40 (a lymphatic marker) was focally positive, suggestive of focal lymphatic differentiation. HHV-8 immunostaining was negative, which ruled out Kaposi sarcoma.

Microscopically tumour cells involved the posterior mesenteric resections margins.

Discussion

KHE, a term first coined by Zukerberg et al in 1993,[4] is a clinical entity distinct from juvenile haemangioma. It is a rare aggressive tumour of childhood and adolescent, often associated with Kasabach-Merritt phenomenon (KMP). Literature to-date has documented sixty odd cases of KHE describing the lesion as behaving clinically and histologically intermediate between juvenile haemangiomas and Kaposi's sarcomas. However, it is difficult to determine the precise number

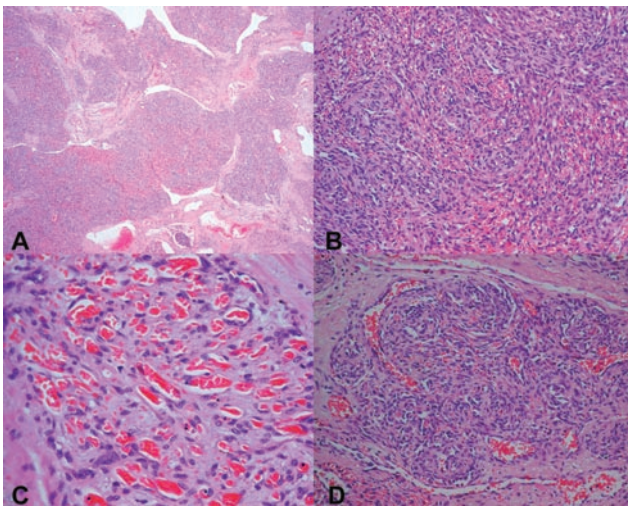

Figure 3 (A) Lobules of spindle tumour cells are separated by fibrous septa. (B) In Kaposi sarcoma-like area, the spindle tumour cells arrange in sieve-like pattern and fascicles with slit-like spaces containing red blood cells. (C) Focally there are capillary haemangioma-like areas with the tumour cells forming tiny capillary channels. (D) Glomeruloid structures are present with the spindle tumour cells forming whorls punctuated by tiny holes containing red blood cells.

of cases as diagnosis and documentation were not always accurate.[3-6] Most of the KHE present during early childhood, as superficial or deep blue-red soft tissue lesions on extremities, head and neck, mediastinum and retroperitoneum. Bone lesions may also occur. A KHE of the mesentery and intestine in the newborn however has not previously been reported.

KHE, once developed, shows little tendency to involute spontaneously, in contrast to juvenile haemangioma that displays a dramatic proliferative phase in the first year of life and then regresses. KHE carries significant morbidity and even mortality because of its biological and clinical characteristics:

(i) Cutaneous plaques may cause ulcerations, pain, and sepsis. (ii) Mass effect on neighbouring vital structures; (iii) extensive visceral involvement may encroach on intestine and vascular pedicle to produce obstruction and risks short-gut syndrome after resection; (iv) there may be functional limitation of musculo-skeletal system and bone lesions may require amputation; (v) residual disease with recurrent symptoms. (vi) KMP may cause life threatening bleeding. (vii) Tumour behaviour relates to its location, size and presence of KMP where extensive unresectable retroperitoneal lesions associated with KMP usually have the worst prognosis. (viii) Bone invasion may occur although distant metastasis has not been reported.[2,4,5]

Kasabach-Merritt Phenomenon

Large series have concluded that at least 90% of KMP are secondary to KHE.[5,6] Even the original case documented by Kasabach and Merritt may have fitted in with the picture of KHE.[4] It is postulated that the distinctive endothelial architecture in KHE lesions create turbulence flow inducing platelet aggregation, but not in juvenile haemangiomas, resulting in thrombocytopenia. KMP does not develop in other vascular lesions and the term had been misapplied to the consumptive coagulopathy of slow flow vascular lesions in which the platelet count is minimally depressed.[4,5]

Immunohistochemical Profile: KHE vs Haemangioma vs Kaposi Sarcoma

KHE displays strong expression of vascular growth factor receptor-3 and von Willebrand factor vWf. The endothelial cells express CD31, CD34, and Friend leukaemia virus integration 1, but not GLUT-1 and Lewis Y antigen LeY, which are positive in capillary haemangiomas. Both KHE and Kaposi sarcomas express CD34, but human herpes simplex virus 8 HHV- 8 is found in Kaposi sarcoma only. KHEs have histopathological features shared by capillary haemangiomas and Kaposi's sarcoma. Some nodules possess vessels with round, oval lumens similar to capillary haemangiomas. Other nodules within the same tumour possess spindled endothelial cells with attenuated nuclei and crescent vascular spaces, the intra-cellular and extra-cellular hyaline globules all bearing resemblances to Kaposi's sarcoma. Kaposi sarcoma typically possesses uniformly spindled cells, slit-like blood vessels and a marked peripheral inflammatory infiltrate not seen in KHE.[2,5]

Other Differential Diagnosis

The differential diagnosis of KHE also includes tufted angioma, appearing as pink macules or indurated nodular plaques and sometimes associated with KMP. The clinical features of pain, hyperhydrosis, spontaneous regression, and the histological picture of cannonball distribution of cellular tufts of capillaries and endothelial cells with an overall benign appearance are distinguishing features.[6]

On Magnetic Resonance Image

Haemangioma has diffuse contrast enhancement, increased signal on T2 weighted images, and dilated feeding and draining vessels, whereas KHE has ill-defined margin and has small feeding and draining vessels. Signal voids are consistent with haemosiderin, blood products or fibrosis. T1-weighted and T2-weighted hyper-intense signals are suggestive of tumour extension via lymphatics. Osteolysis may be apparent.[7]

Definitive Treatment

KHE behaves aggressively and carries significant morbidity and mortality despite trials of multimodal |therapy including with corticosteroids, interferon-alpha, epsilon-aminocaproic acid, tranexamic acid, ticlopidine with aspirin, chemotherapy with vincristine and cyclophosphamide, and radiotherapy, but none are effective when used singularly.[8-10] Arterial ligation and pneumatic compression of limb, surgical excision, partial resection and limb amputation had been instituted to control any bleeding.[11]

In this case report, the presentation was an obstructing tumour which mandated early surgical decompression. The first operation was confounded by coagulopathy and uncertainty of tumour anatomy. Subsequent vascular imaging was necessary to delineate tumour resectability. Possible involvement of distal duodenum and superior

mesenteric artery and its territory, i.e. the risk of massive gut resection, were the main surgical dilemmas. Fortunately this baby lost no more than 30% of small intestine, and sufficient gross resection could be achieved to eradicate platelet consumption. Surgical cure without short-gut syndrome was attained, at least temporarily. With mesenteric margin focally involved by KHE, long term surveillance for disease recurrence is paramount. Significant loss of small intestinal still requires nutritional monitoring.

In retrospect, had the differential diagnosis of a vascular tumour of intestine been considered more likely than that of a newborn with life-threatening signs of septic intestinal obstruction displaying initial radiological signs masquerading as vascular flow amongst compressed intestinal loops, then more detailed pre-operative imaging studies might have been arranged for anatomical/ pathological delineations, e.g. CT contrast scans, and the first operation likely spared.

Literature on the treatment of KHE involving intestine and mesentery is lacking. To-date, there have been only isolated reports of definitive surgical treatment for KHE of viscera in infancy or childhood.[12,13]

Conclusion

Kaposiform haemangioendothelioma is a rare aggressive vascular proliferation in infancy and childhood distinct from infantile haemangioma both clinically and histologically. It is associated with Kasabach-Merritt phenomenon and displays infiltrative biological behaviour. Multimodal pharmacological agent may be helpful but the best treatment option is surgical resection unless vital organs are involved. This paper is to report a rare, extensive visceral lesion causing neonatal intestinal obstruction and life-threatening coagulopathy. Early surgical resection appeared mandatory and was feasible after appropriate radiological workup and peri-operative optimization.

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