Lethal prognosis of an infant with intraperitoneal large venous malformation

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ABSTRACT

Intraperitoneal venous malformations are uncommon. Therefore, the prognosis of patients has not been determined, and appropriate treatments have not been established. We have reported the case of a neonate with an extensive intraperitoneal venous malformation. She did not have a developmental disorder nor a functional disability; thus, she was observed without treatment. However, the patient died suddenly of obstructive venous return disorder due to thrombosis in a vein draining from the venous malformation, followed by blood pooling in the expanding venous malformation. Extensive intraperitoneal venous malformations can be associated with a lethal prognosis owing to thrombosis. Anticoagulation therapy should be considered proactively for prophylaxis of thrombotic dysfunction. (J Vasc Surg Cases and Innovative Techniques 2021;7:512-5.)

Keywords: Anticoagulant therapy; Large intraperitoneal venous malformation; Localized intravascular coagulation; Neonate

Venous malformations (VMs) are slow-flow vascular malformations that account for two thirds of all congenital vascular malformations.[1] VMs are commonly distributed in the skin, muscle, and subcutaneous tissues,[2] and the therapeutic strategy and prognosis for these types of VMs have been well discussed.[3,4] However, intraperitoneal VMs are rare; therefore, appropriate treatments have not been established, and the prognosis remains unknown. We have reported the case of a neonate with an extensive intraperitoneal VM who died of sudden failure of venous return due to VM thrombosis. The patient's parents provided written informed consent for the report of their infant's case details and images.

CASE REPORT

A newborn girl was referred to the pediatric department on her day of birth for evaluation of an abdominal cystic mass that was identified on routine fetal ultrasound examination at 25 weeks' gestational age. She had large, soft, compressible purple nodules on the skin of her right lower abdomen without a VM in her extremities (Fig 1). Her hemoglobin and platelet

Fig 1. External identification of intraperitoneal venous malformation (VM).

counts were stable. Her D-dimer concentration was elevated (32.5 μg/mL); however, the fibrinogen and coagulation test results were normal.

Ultrasound scanning demonstrated slow-flow vascular structures, some consisting of round lesions (Fig 2). Magnetic resonance imaging showed extensive lesion distribution with multiple abdominal nodules (Fig 3, A). The maximum lesion diameter was 110 mm, and the lesion occupied approximately one half of the peritoneal cavity. The lesion had compressed and deviated the gastrointestinal tract and bladder (Fig 3, A) to the left. However, the renal pelvises were not dilated. The early phases of contrast-enhanced T1-weighted axial sequences showed enhancement of part of the large malformation (Fig 3, B), and the late phases of contrast-enhanced T1-weighted axial sequences showed

Fig 2. Ultrasound scan of intraperitoneal venous malformation (VM) showing a slow-flow vascular structure and a round lesion.

homogeneous enhancement of the malformation (Fig 3, *C*), indicating that the malformation had a venous component. The lesion was connected to a femoral vessel (Fig 3, *B*); however, we could not clearly identify any feeding or draining vessels using magnetic resonance imaging. We diagnosed the lesion as a VM with phleboliths, and we attributed the increased D-dimer concentration to the formation of the phleboliths. Venography was considered but was not performed because of the risk of intraperitoneal bleeding owing to the large VM size.

At this point, we discussed the indications for anticoagulation therapy, surgical intervention, and sclerotherapy with pediatric surgeons and radiologists. The patient's growth and development were acceptable during the neonatal period, and she had no symptoms of pain, gastrointestinal obstruction, or urinary tract obstruction. Therefore, she was observed without treatment, considering the potential adverse effects. We monitored her with serial measurements of the D-dimer concentration, which did not demonstrate an increasing trend. Venography or surgical resection when she was 3 years old, when the risk of intervention would be lower, was planned. However, when she was 2 months old, she became transiently ill after crying. The D-dimer concentration was 16.2 μg/dL, which was lower than the value at diagnosis. No imaging studies were performed. We considered that physiologically, the crying had resulted in increased intrapleural pressure after transient blood pooling in the VM and a decrease of systemic venous return to the heart. Therefore, we instructed her parents to place a diaper tightly such that the VM would not expand or retain venous blood. When she was 3 months old, the patient presented with sudden cardiopulmonary arrest. Cardiopulmonary resuscitation was performed for ~10 minutes. After the return of spontaneous circulation, we initiated a continuous intravenous infusion of dopamine. The hemoglobin concentration was 6.6 g/dl, lower than the normal level for a 3-month-old infant (normal range, 9.5-13.5 g/dL). Whole-body computed tomography showed no signs of internal bleeding. A red blood cell concentrate transfusion and intensive intravenous administration of extracellular fluids made the abdominal nodule more protrusive and incompressible and did not improve the patient's circulation. She died 1 day after onset, despite intensive therapy.

Autopsy confirmed the diagnosis of a VM. The VM contained ~610 mL of blood, and the right external iliac vein was identified as the draining vein (Fig 4, *A*); the vein contained a thrombus (Fig 4, *B*). The VM was too large to excise completely, identify the connection to the inferior vena cava or other vein, or reveal its origin. Histopathologic examination of the VM demonstrated dilated vessels with irregular elastic fiber walls. The endothelial cells were positive for CD34 (Fig 4, *C*) and negative for D2-40 (Fig 4, *D*). The thrombus in the draining vein was both calcified and organized (Fig 4, *E* and *F*), indicating chronicity.

DISCUSSION

The present patient's course has provided two important clinical suggestions. First, extensive VMs can develop in the neonatal abdomen. VMs will usually occur in the skin, muscle, and subcutaneous tissues[2]; however, intraperitoneal VMs have also been reported.[2,5,6] Unlike VMs in the skin, muscle, and subcutaneous tissues, which will be noted at birth from the medical history and physical examination, intraperitoneal VMs often remain unnoticed until they manifest with symptoms, such as chronic bleeding and anemia.[2] Most previously reported cases were diagnosed after 2 years of age, with the exception of two neonatal cases of Klippel-Trenaunay syndrome.[2,6,7] In contrast, in our patient, the VM was obvious at birth owing to its large size, despite the lack of signs of Klippel-Trenaunay syndrome.

Fig 3. A, T2-weighted magnetic resonance imaging (MRI) scan demonstrating extensive lesion distribution with multiple phleboliths (*clear arrowheads*). *White arrow* indicates the bladder, which was compressed and deviated to the left. **B,** Contrast-enhanced, early-phase, T1-weighted MRI scan showing heterogeneous contrast enhancement of the lesion in the early phase. *White arrowhead* indicates the connection between the lesion and a femoral vessel; and *clear arrowhead,* a phlebolith. **C,** Contrast-enhanced, late-phase, T1-weighted MRI scan showing homogeneous contrast enhancement. *Clear arrowhead* indicates a phlebolith.

VMs can be classified into four types according to the hemodynamic anatomy of the lesion and adjacent veins. Type I is an isolated VM without peripheral drainage. Type II is a VM that drains into normal veins. Type III is a VM that drains into dilated veins. Finally, type IV is a VM that represents dysplastic venous ectasia.[8] Autopsy of our patient revealed that the VM drained into a normal right external iliac vein, indicating a type II VM.

Second, intraperitoneal VMs carry the risk of a lethal prognosis resulting from the development of thrombosis in a draining vein. Extensive VMs can be highly associated with localized intravascular coagulation (LIC) owing to the relatively slow flow within the lesion.[9] Additionally, patients exhibiting chronic LIC have an increased risk of systemic complications, including venous thrombosis.[10] Therefore, the International Union of Phlebology has recommended anticoagulation therapy with low-molecular-weight heparin for patients with a VM and thrombophilia.[3] Moreover, prophylactic anticoagulation has been recommended for patients with hypercoagulability or coexisting malformations.[3] However, no evidence-based guidelines are available for the management of children with LIC-associated VMs because few reports have described the natural history of this condition. Our patient had had multiple phleboliths and elevated D-dimer concentrations; however, these findings were not associated with pain, developmental dysfunction, or decreased fibrinogen levels. In addition, prophylactic anticoagulation carries the risk of hemorrhagic

diathesis, as an adverse effect. Hence, our patient was observed without anticoagulation therapy. However, she died of a sudden systemic circulation disorder. The chronic thrombosis in a draining vein, which was revealed by autopsy, suggested that the thrombosis had finally led to obstruction of the draining vein and a large volume of blood pooling in the expanding VM. This was followed by obstructive venous return disorder. Specifically, the 610 mL of blood in the VM, which was revealed during autopsy, was equivalent to the patient's estimated entire circulating blood volume. In a cohort study, intraperitoneal ectatic rectal VM was highly complicated by portomesenteric venous thrombosis, leading to venous return disorder.[2] Our observations suggest that an extensive intraperitoneal VM is a risk factor for LIC and subsequent thrombosis. Therefore, when an intraperitoneal VM occupies approximately one half of the peritoneal cavity, therapeutic anticoagulation should be considered proactively for prophylaxis of thrombotic dysfunction, even if the VM is asymptomatic.

Sclerotherapy or surgical resection is a therapeutic option for symptomatic VMs. For our patient, these options were avoided because the lesion was asymptomatic.[11] Recently, embolization with n-butyl cyanoacrylate was reported as an alternative option.[6,11,12] Embolization will better define the lesion's margins and decrease the risk of bleeding after surgical resection.[12] If venography had been performed and the thrombus formation in the draining vein had been found, preoperative embolization
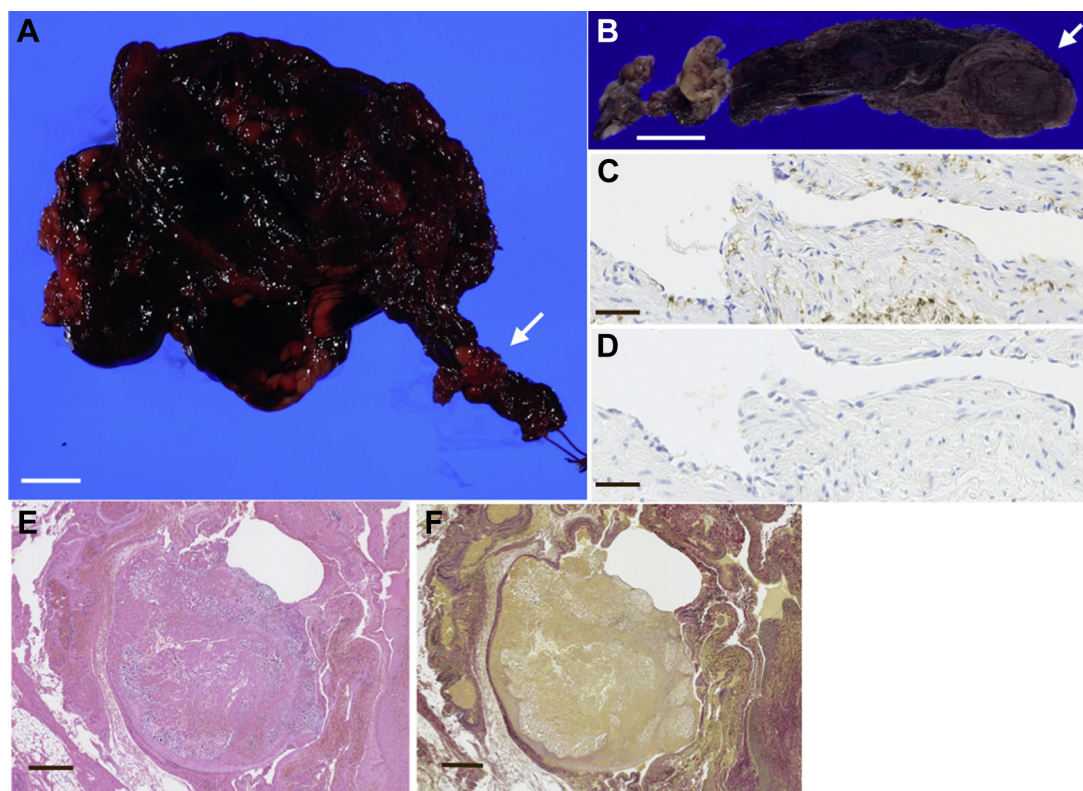
Fig 4. Autopsy findings. **A,** Macroscopic evaluation of the excised venous malformation (VM) revealing the right external iliac vein as a drainage vein (*white arrow*). Scale bar = 10 mm. **B,** The right external iliac vein was obstructed by a thrombus (*white arrow*). Scale bar = 10 mm. **C,** Positive immunostaining for CD34 in vessel endothelial cells. Scale bar = 50 μm. **D,** Negative immunostaining for D2-40 in vessel endothelial cells. Scale bar = 50 μm. **E,** Hematoxylin and eosin staining of the thrombus in the right external iliac vein showing calcification and fibrin. Scale bar = 500 μm. **F,** Elastica van Gieson staining of the thrombus in the right external iliac vein showing calcification and fibrin. Scale bar = 500 μm.

and surgical resection would have been alternative management options for our patient.

CONCLUSIONS

Antithrombotic therapy should be considered for large intraperitoneal VMs because it could prevent catastrophic thrombosis and hemodynamic collapse. Further studies are needed to clarify the effect of anticoagulant therapy on preventing LIC in patients with large intraperitoneal VMs.

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