



Lower Gastrointestinal Bleeding Because of Kasabach-Merritt Syndrome Showing an Impressive Response to Sirolimus

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ABSTRACT

Kasabach-Merritt syndrome is a rare but life-threatening disease in which a rapidly growing vascular tumor induces localized intravascular coagulation, causing thrombocytopenia, microangiopathic hemolytic anemia, and consumption coagulopathy. It presents mainly in infants and young children. We present an adult with recurrent and severe lower gastrointestinal bleeding due to Kasabach-Merritt syndrome, treated successfully with sirolimus after multiple other failed interventions.

INTRODUCTION

Kasabach-Merritt syndrome (KMS) is a syndrome of intravascular coagulation that occurs in the setting of rapidly growing vascular tumors. The aberrant anatomy, and the endothelial dysfunction of the intratumoral vessels, causes abnormal activation of the coagulation pathway leading to thrombocytopenia, microangiopathic hemolytic anemia, and consumption coagulopathy. The vascular tumors primarily associated with KMS are the Kaposiform hemangioendothelioma and the tufted angioma.¹⁻⁴ It was first described in 1940 in a male infant; only approximately 200 cases have been reported in the literature, most of which (80%) are diagnosed within the first year of life.^{5,6} The mortality rate of KMS is 20%–40%, mainly because of intractable bleeding caused by the consumption coagulopathy.^{4,7} The lack of consensus to guide therapy makes the management much more challenging.

CASE REPORT

A 21-year-old woman with a presumptive diagnosis of Klippel-Trenaunay syndrome was transferred from another institution because of severe lower gastrointestinal bleeding (LGIB). She was born with a large capillary and venous malformation extending from the gluteus maximus and pelvis to the right foot, accompanied by congenital right lower limb overgrowth and numerous intestinal vascular tumors, causing multiple episodes of LGIB over the years (Figure 1). At the age of 4, an effort to debulk the limb tumor was unsuccessful because of severe intraoperative bleeding. Previous attempts with treatments such as propranolol, corticosteroids, interferon-gamma, vincristine, aminocaproic acid, and embolization and partial elective jejunocolic colectomy at 10 and 17 years old, respectively, were ineffective. The patient had no pediatric follow-up since, and at 20 years old, she had a severe episode of bleeding and underwent terminal ileum and ceco-ascending colon resection (20 cm), with partial jejunal resection (9.5 cm): Both surgical specimens revealed the presence of capillary type vascular malformations.



Figure 1. Patient at 4 years of age. Congenital vascular malformation before first surgical intervention.

After 1 year without bleeding, she went to another institution complaining of a 3-week history of bright red blood mixed with brown stool, associated with pallor, palpitations, and exertional dyspnea. Laboratory test results revealed a hemoglobin of 5.9 g/dL, physical therapy: 23.2 seconds, partial thromboplastin time: 30 seconds, international normalized ratio: 2.02, severe hypofibrinogenemia (<50 mg/dL), and thrombocytopenia (59 k/uL). The patient was admitted to the intensive care unit with symptomatic anemia due to LGIB and a clinical diagnosis of KMS.

During hospitalization, the patient received multiple units of packed red blood cells, fresh frozen plasma, and cryoprecipitate. A colonoscopy was advanced to the ileotransverse anastomosis, revealing vascular tumors; no hemostasis was attempted, given the



Figure 2. Colonoscopy: Scant congealed blood noted on colon without active bleed; however, it stopped at anastomosis with view suggesting vascular malformation at small intestine.

patient's coagulopathic state and especially because it was not considered to be the etiology of the bleeding (Figure 2). An upper endoscopy and a gastrointestinal bleeding scan also failed to reveal the bleeding site. Abdominopelvic computed tomography enterography was pertinent for at least 2 intraluminal vascular blushes within the small bowel loops of the right lumbar region of the abdomen, most probably representing additional intraluminal vascular malformations (Figure 3).

An intraoperative enteroscopy was considered. However, a multidisciplinary team recommended against embolization and further surgeries, given the previous history of recurrence and the risk of short bowel syndrome. The patient improved with administration of anti-inhibitor coagulant complex; however, after discontinuation of coagulation factor replacement, and each time enteral feeding was restarted, the LGIB reoccurred.

Given the severe clinical presentation refractory to all forms of standard treatment, we decided to administer sirolimus, at a dose of 0.8 mg/m². The patient was informed of risks and benefits, and she consented to treatment. Complete resolution of bleeding was observed within 48 hours of the first dose. In addition, hemoglobin improved (10.6 g/dL) and platelet count (205 k/uL), and fibrinogen levels (98 mg/dL). After 48 days of hospitalization, the patient was discharged home. One year later, the patient continues taking the sirolimus and has maintained an appropriate hemoglobin level without evidence of new bleeding or coagulopathy (Table 1).

DISCUSSION

KMS involves activation and consumption of platelets and clotting factors inside vascular malformations, giving rise to

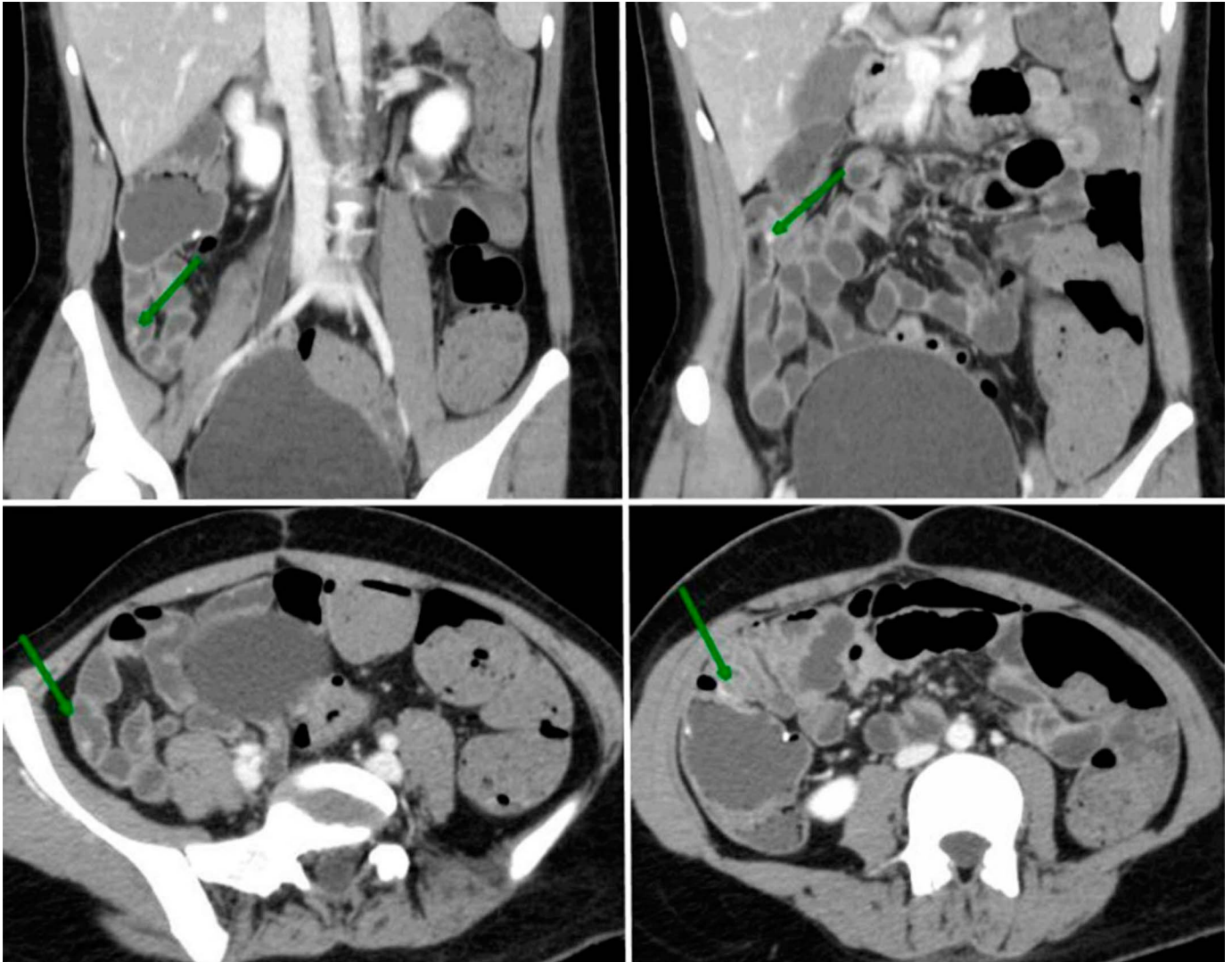


Figure 3. Computed tomography enterography: Pertinent for at least 2 intraluminal vascular blushes within the small bowel loops of the right lumbar region of the abdomen.

consumption coagulopathy and bleeding. Its management primarily should be directed to hastening vascular lesion regression, responsible for the coagulopathy, and supportive measures to maintain hemostasis.⁸ Several treatments have been used, including surgery, radiotherapy, vascular embolization, and pharmacology with variable rates of effectiveness, and as a result, standard and definitive guidelines for the treatment of KMS have not yet been established.⁹

Surgical intervention is rarely feasible, given the infiltrative nature of the associated tumor and existing coagulopathy, as evidenced in this case. It is the treatment of choice for small, localized tumors and is usually followed by the resolution of thrombocytopenia and coagulopathy. If a lesion is inoperable, an interventional radiologic procedure to embolize the tumor or local administration of sclerosing agents may be attempted. In our case, radiological embolization was not attempted because of critical location and extensive limb involvement.

Several pharmacological options reported in the literature have demonstrated some benefits but are not approved by the US Food and Drug Administration. For large, nonresectable tumors, 2 alternatives are the administration of vincristine 0.05 mg/kg intravenous weekly plus prednisone 2 mg/kg orally daily or sirolimus 0.8 mg/m² orally every 12 hours with or without prednisone.

Sirolimus is believed to exert its beneficial effect by blocking the mammalian target of rapamycin signaling pathway, which is activated in response to vascular endothelial growth factor receptor attaching to its ligand. This pathway is essential for the proliferation of endothelial cells of vascular tumors, and blocking it using sirolimus may promote shrinkage of the lesion and improvement of coagulopathy.

Owing to its oral administration and growing literature attesting to the safety and effectiveness of sirolimus, including a more rapid resolution of the coagulopathy of KMS, most physicians

Table 1. Comparative of laboratory results before and after sirolimus

Laboratory tests	Results			References
	At admission	At discharge (after sirolimus)	One year after sirolimus	
WBC	6.7	8.5	7.12	$4-11 \times 10^3/\mu\text{L}$
Hgb	5.9L	10.6L	13.2	12–14.5 g/dL
Htc	17.3L	33.6L	40.0	35%–45%
Platelets	5 L	205	222	$150-450 \times 10^9/\text{L}$
PT	23.2H	12.1	10.4	10.0–13.9 s
INR	2.02H	1.0	0.99	0.86–1.20
PTT	30.0	30.0	28	25.3–32.8 s
Fibrinogen	<50	98L	117L	174–343 mg/dL

Hgb, hemoglobin; INR, international normalized ratio; PTT, partial thromboplastin time; WBC, white blood cell.

are using sirolimus as the first-line treatment for KMS. It is essential that sirolimus through serum levels be monitored regularly and must not exceed 10–13 ng/mL. However, how long the patient should be under treatment is not yet established in the literature. This is the first case of KMS successfully treated with sirolimus in the largest supratertiary hospital in Puerto Rico. This experience demonstrated the efficacy of sirolimus and could contribute to developing appropriate guidelines for the management of these patients.

DISCLOSURES

Author contributions: All authors contributed equally to this manuscript. JS Pérez is the article guarantor.

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Informed consent was obtained for this case report.

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