

Lower gastrointestinal bleeding, hematuria and splenic hemangiomas in Klippel-Trenaunay syndrome: A case report and literature review

Klippel-Trenaunay sendromunda alt gastrointestinal kanama, hematüri ve dalakta hemanjiomlar: Olgu sunumu ve literatürün gözden geçirilmesi

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Klippel-Trenaunay syndrome is a congenital vascular anomaly characterized by a triad of varicose veins, cutaneous capillary malformation, and hypertrophy of bone and soft tissue. Gastrointestinal and genitourinary vascular malformations in Klippel-Trenaunay syndrome may present with lower gastrointestinal bleeding and hematuria. The majority of patients with splenic hemangiomas are asymptomatic. We herein report a case admitted to the Gastroenterology Clinic with life-threatening hematochezia and symptomatic iron deficiency anemia. The patient's history was remarkable for subtotal cystectomy and enterocystoplasty in December 2002 for vascular malformation, located in the bladder, which presented with hematuria. Although the patient was also diagnosed with colonic varices and splenic hemangiomas at that time, due to the asymptomatic mild intermittent hematochezia and splenic hemangiomas, the patient did not seek any help for rectal bleeding until her admittance to our department for evaluation of massive lower gastrointestinal bleeding. Endoscopy revealed vascular malformations starting from the transitional zone in the rectum extending up to the descending colon. Due to this extensive involvement of the rectum and sigmoid colon, no interventional endoscopic procedure was attempted and she was referred to surgery. A very low anterior resection with double stapling technique was done. Postoperative follow-up has been uneventful for six months since the operation. To the best of our knowledge, this is the first Klippel-Trenaunay syndrome case presenting with lower gastrointestinal bleeding, hematuria and splenic hemangiomas. The literature on the evaluation and management of lower gastrointestinal and genitourinary bleeding in Klippel-Trenaunay syndrome is reviewed.

Key words: Hematochezia, hematuria, Klippel-Trenaunay syndrome, splenic hemangiomas

INTRODUCTION

Klippel-Trenaunay syndrome (KTS) is a rare congenital vascular malformation characterized by

Klippel-Trenaunay sendromu variköz damarlar, kutanöz kapiller malformasyonlar ile kemik ve yumuşak dokunun unilaterale hipertrofi üçlü bulgusuyla tanımlanan konjenital vasküler bir anomalidir. Gastrointestinal ve genitüriner vasküler malformasyonlar alt gastrointestinal sistem kanaması ve hematüri ile belirti verebilir. Splenik hemanjiomatozis çoğunlukla asemptomatiktir. Bu yazıda, yaşamı tehdit eden hematozezi ve semptomatik demir eksikliği anemisi nedeniyle gastroenteroloji kliniğine yatırılan bir Klippel-Trenaunay sendromu olgusu sunulmuştur. Hastanın özgeçmişinde, Aralık 2002 tarihinde hematüri ile belirti veren mesane yerleşimli vasküler malformasyon nedeniyle subtotal sistektomi ve enteroplasti hikayesi mevcuttu. Hastanın o dönemde kolonik varislerinin ve splenik hemanjiomlarının tespitine rağmen, asemptomatik, hafif, ara ara olan hematozezi ve semptomsuz splenik hemanjiomlar nedeniyle, hasta masif alt gastrointestinal sistem kanaması tanısıyla kliniğimize yatırıldığı döneme kadar doktora başvurmamıştı. Endoskopide, rektumda geçiş zonundan başlayıp inen kolona kadar uzanan vasküler malformasyonlar izlendi. Hasta, rektum ve sigmoid kolonda mevcut olan yaygın tutulumdan dolayı Genel Cerrahi Bölümü'ne sevk edildi. Hastaya "çift stapler tekniği ile aşağı anterior rezeksiyonu" operasyonu yapıldı. Operasyon sonrası 6 aylık takipte problem yaşanmadı. Bugünkü bilgilerimize göre, yazımız alt gastrointestinal kanama, hematüri ve splenik hemanjiomlarla ortaya çıkan ilk Klippel-Trenaunay sendromu olgusu olma özelliğini taşımaktadır. Sunumuzda ek olarak, Klippel-Trenaunay sendromunda alt gastrointestinal ve genitüriner sistem kanamalarına yaklaşım literatür eşliğinde gözden geçirilmiştir.

Anahtar kelimeler: Hematozezi, hematüri, Klippel-Trenaunay sendromu, splenik hemanjiomlar

the clinical triad of bony and soft tissue hypertrophy, usually affecting one extremity; hemangio-

mas and/or lymphangiomas; and varicosities or venous malformations (1). All three features were reported to be present in 63% of patients, and 37% had two of the three features, which illustrates that not all patients with KTS have all three features of the triad. Patients can, therefore, be diagnosed as KTS with only one or two features (2). Although seemingly uncommon, vascular malformations involving the gastrointestinal (GI) tract have been reported and can be a source of significant morbidity and even mortality (1). Clinical manifestations range from occult to massive, life-threatening hemorrhages. KTS patients with clinically significant hemorrhage usually require resection of the involved bowel segment (1).

Genitourinary manifestations may present as intrapelvic and retroperitoneal vascular malformations and affect the penis, scrotum, vagina or vulva, and bladder (3). Bladder lesions in KTS are mostly found at the dome and the anterior wall, whereas the trigone and the neck are rarely involved. On cystoscopy, the malformations are usually reddish-blue and may appear sessile, lobulated or flattened (4). Gross hematuria, which is recurrent and painless, is usually the first clinical sign of bladder involvement and frequently manifests early in life (3).

Visceral hemangiomas in KTS have been described involving organs such as the GI tract, liver, spleen, bladder, kidney, lung, and heart (5). Computed tomography (CT) of the abdomen and pelvis provides a simple, noninvasive means of assessing visceral hemangiomatous masses and identifying upward extension in the pelvis and abdomen (6).

We herein report the clinical presentation and surgical management of a young female patient with the diagnosis of KTS.

CASE REPORT

A 19-year-old female patient was admitted to the Gastroenterology Clinic for management of life-threatening hematochezia and symptomatic iron deficiency anemia. The patient had been frequently admitted to the emergency unit due to transfusion-dependent anemia caused by intermittent gross painless hematuria and mild intermittent hematochezia up to December 2002. A lymphovenous malformation in the bladder was detected as the etiology of hematuria and subtotal cystectomy and enterocystoplasty were performed at that time. Afterwards, the mild intermittent hematoche-

zia continued and the amount of rectal bleeding increased over time. She was admitted to our hospital for evaluation after a severe and debilitating attack of hematochezia.

Physical examination revealed generalized pallor. Laboratory evaluation showed significant anemia with hemoglobin of 6.45 g/dl, hematocrit 20.9%, iron 11 mcg/dl, total iron binding capacity 323 mcg/dl, and ferritin 9.3 ng/ml. The platelet count and coagulation parameters were normal. A retrospective evaluation of abdominopelvic CT imaging showed abnormal vascular structures in the anterior wall of the urinary bladder (Figure 1), in the mesorectum and in the subcutaneous fat tissue of the left gluteal region (Figure 2), and multiple hemangiomas (Figure 3) in the spleen. The vascular mal-

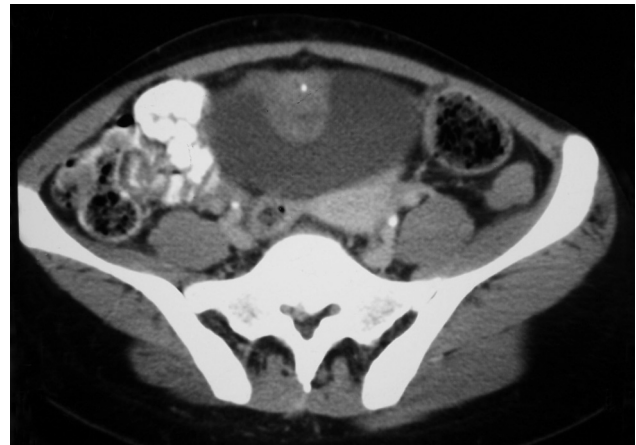


Figure 1. Contrast-enhanced pelvic CT showing a soft tissue density (lymphovenous malformation) in the anterior wall of the urinary bladder containing a small calcification.



Figure 2. Contrast-enhanced pelvic CT showing a vascular malformation in the subcutaneous fat tissue of the left gluteal region.

formations in the left gluteal subcutaneous region were not apparent on the skin. Colonoscopy revealed varices extending from the transitional zone in the rectum up to the descending colon (Figure 4). Upper GI system endoscopy and double balloon enteroscopy showed normal mucosal findings in the stomach and small intestine. During hospitalization, the patient had an attack of massive hematochezia with loss of consciousness. The endoscopic investigation after supportive treatment revealed bleeding rectal varices. Selective magnetic resonance imaging (MRI) and visceral angiograms of the mesenteric system demonstrated normal findings except for pooling of blood in multiple dilated irregular-appearing vessels in venous phase with contrast lakes in the rectum and sigmoid colon. Based on the venous malformations in the rectosigmoid region and urinary bladder, splenic hemangiomas and subcutaneous vascular malformations, the patient was diagnosed as having KTS.

Due to the severe symptomatic anemia and increased amount of lower GI bleeding over time, the patient was considered a surgical candidate. Submucosal vascular malformations in the rectosigmoid region were seen during the operation (Figure 5). A very low anterior resection with double stapling technique was done. The pathologic evaluation of the resected specimen revealed submucosal vascular malformations consistent with the rectosigmoidal involvement of KTS (Figure 6). Follow-up colonoscopy revealed no vascular malformation two months after the operation. The six-month follow-up since the operation has been uneventful without any attack of hematochezia.



Figure 3. Contrast-enhanced abdominal CT showing multiple splenic hemangiomas.



Figure 4. Varices in the colon.

DISCUSSION

Klippel–Trenaunay syndrome is a term used to describe the combination of a cutaneous capillary malformation, varicose veins, and hypertrophy of bone and soft tissue. Most cases of KTS are sporadic; the syndrome affects males and females equally, has no racial predilection, and manifests at birth or during childhood (5).

Involvement of the GI tract may be more common in KTS than previously believed (occurring in perhaps as many as 20% of patients) and may go unrecognized in patients without overt symptoms (7). Genitourinary manifestations may occur as intrapelvic and retroperitoneal vascular malformations and affect the kidney, bladder, penis, scrotum, and vagina or vulva (3).

The patients with vascular malformations in the GI tract frequently have both recto-pelvic vascular malformations. Rectal and bladder hemorrhage may complicate pelvic vascular malformations and have been reported in 1% of cases (3,8). The most common bleeding sites in the GI system are the distal colon and rectum. Jejunal hemangiomas and esophageal varices as bleeding sources caused by prehepatic portal hypertension were reported in the literature (1). The spectrum of the GI bleeding may vary from asymptomatic occult bleeding to life-threatening massive bleeding. GI hemorrhage usually begins in the first decade of life and tends to be intermittent (8).

Investigation of lower GI bleeding should begin with endoscopic examination in a patient with suspected KTS. Although endoscopy has the advantage of showing the localization and extension

of vascular malformations, it might be misleading to accuse the vascular malformations observed during the endoscopy of bleeding due to possible metachromic localizations of vascular malformations in the different parts of the GI tract. Considering this point of view, endoscopic investigation of the entire GI tract should be the routine clinical practice for true localization and effective management of GI bleeding in patients with KTS. In addition, with other findings specific for KTS, being aware of this rare diagnosis can prevent taking biopsies from ulcerated mucosal lesions overlying the vascular malformations, which might be fatal in a patient with hematochezia (9).

Radiologic studies are important in the diagnosis and ongoing evaluation of patients with KTS. Due to different managements of hemangiomas and vascular malformations, the work-up for differential diagnosis should begin with Doppler ultrasound, which has the ability to differentiate those entities (10). CT scans and MRI are useful for determining the borders of lesions, associated vascular malformations, and infiltration of deeper tissues before treatment (11). MRI may also be used for evaluating treatment response and prognosis (12). Although the role of MR angiography in imaging the vascular system in KTS has not been well defined, the modality has the potential to visualize these lesions with better accuracy. In cases of hemorrhage that require surgical intervention, preoperative angiography is required to define the anatomy and extent of intestinal involvement to guide surgical resection (7).

Management and treatment of GI and genitourinary vascular malformations in KTS depend on

the extent and severity of blood loss. Patients with good quality of life and mild anemia might be advised to take iron supplements and be followed without any invasive intervention. However, the progressive nature of KTS warrants that physicians consider invasive surgical operation or angiographic intervention such as embolization of the bleeding vessel during the ongoing follow-up when there is a patient with transfusion-dependent anemia, life-threatening bleeding episodes, and/or poor quality of life due to severe anemia (1).

Endoscopic therapy is usually preferred for localized lesions or postoperative residual disease. A literature search showed that KTS patients with colonic hemangiomas may benefit from endoscopic interventions. The neodymium: yttrium-aluminum-garnet laser for residual lesions, partial colectomy for visceral hemangiomas (13), and argon laser photocoagulation for hemangiomas involving the distal 7 cm of the anorectum (14) were found effective in patients with KTS. Both partial cystectomy and conservative treatment have been successful in the treatment of gross hematuria associated with genitourinary vascular malformations (3).

Hemangioma is the most common benign primary tumor of the spleen. Splenic hemangiomas may occur as a part of generalized angiomas as seen in KTS. Complications of the splenic hemangiomas include rupture, hypersplenism, and malignant degeneration. The exact course for a given hemangioma is difficult to predict. Larger tumors (>4 cm) are likely to be more prone to rupture than smaller ones, either spontaneously or from minor trauma, and may result in fatal hemorrhage.



Figure 5. Multiple vascular malformations in the wall of the rectosigmoid region.

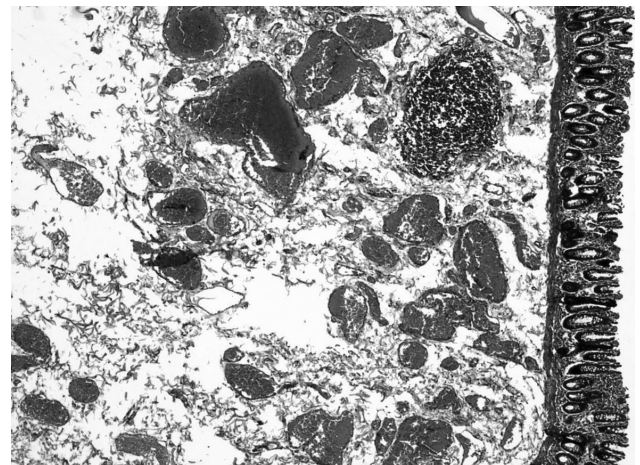


Figure 6. Vascular malformations in the submucosa (hematoxylin and eosin x40).

Spontaneous rupture has been reported as the most common complication, occurring in 25% of patients having large (>4 cm) hemangiomas (15). Recent reviews in adult patients reported that asymptomatic patients with small splenic hemangioma (<4 cm) have been managed conservatively with observation, without rupture or other complications (16). Kasabach-Merritt syndrome has been reported in patients with large hemangiomas (17). As our patient was asymptomatic with splenic hemangiomas <4 cm, a conservative approach with observation was preferred and splenectomy was not performed.

The spectrum of clinical manifestations of KTS is wide and can include additional arterial and lymphatic system abnormalities beyond the classical manifestation (18). The potential of KTS to have widespread-localization venous malformations in any part of the body implies that heterogeneous genetic mutations affecting mesodermal develop-

ment may be present in patients with KTS (19). At present, molecular diagnosis for KTS is not available.

In conclusion, KTS is a rare condition with protean manifestations. Hematochezia may be the debilitating and life-threatening finding of GI involvement in KTS. Painless hematuria with hematochezia should alert the physician about the possibility of associated vascular malformations in the genitourinary and GI systems. Due to the progressive nature and wide extension of KTS lesions, endoscopic therapies have limited value in the management. Angiographic interventions should be used preoperatively for visualizing the vascular anatomy and determining the disease extent. Resection of the involved bowel segment is usually necessary to adequately control bleeding. When vascular malformation-related hematuria is recurrent and life-threatening, the treatment of choice is subtotal cystectomy with enterocystoplasty.

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