# Klippel-Trenaunay Syndrome: Two Cases with Colon Involvement

## Klippel-Trenaunay Sendromu: Kolon Tutulumlu İki Olgu

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**ABSTRACT** Klippel-Trenaunay syndrome (KTS) is characterized by the triad of red hemangiomas, hypertrophy of bone and soft tissue and venous malformations. It is a rare, congenital malformation. Although many different types of involvement are present, these three pathologies are observed in many cases. Involvements of head and neck are rare. In addition varicose veins or venous malformations may also be found in the lung, gastrointestinal tract (colon-intestine), liver, kidney and bladder, which may result in recurrent hemorrhagie at the affected organs. Though colonic involvement is rarely observed, it may be confused with ulcerative colitis. We detected colon involvement in two cases with anaemia and hematochesia that we followed-up at our clinic. Our cases had been followed-up considering ulcerative colitis. However, one of our cases has hearing loss, involvement of fundus oculi and hypospadias. We report these two cases since they present rare involvement types of KTS and mimicking ulcerative cholitis.

**Key Words:** Klippel-Trenaunay-Weber Syndrome; congenital, hereditary, and neonatal diseases and abnormalities; colon; gastrointestinal hemorrhage; hypospadias; hearing loss

**ÖZET** Klippel-Trenaunay sendromu (KTS) kırmızı hemanjiomlar, kemik ve yumuşak doku hipertrofisi ve venöz malformasyonları içeren triad ile karakterizedir. Nadir görülen konjenital bir malformasyondur. Farklı tutulum şekilleri olsa da çoğu vakada bu üç patoloji görülür. Nadiren baş ve boyun tutulur. İlaveten variköz venler ve venöz malformasyonlar etkilediği organlarda tekrarlayan kanamalar ile sonuçlanacak şekilde akciğer, gastrointestinal alan (kolon-ince barsak), karaciğer, böbrek ve mesanede de bulunabilmektedirler. Kolon tutulumu nadir görülmekle birlikte ülseratif kolitle karışabilir. Klinikte takip ettiğimiz anemi ve hematokezyalı iki olgumuzda kolon tutulumu saptadık. Vakalarımız daha önce ülseratif kolit düşünülerek bir süre takip edilmişlerdi. Bununla beraber vakalarımızın birisinde işitme kaybı, göz dibi tutulumu ve hipospadiyas mevcuttu. KTS'nun nadir tutulum şekillerini göstermesi ve ülseratif koliti taklit etmesi bakımından bu iki vakayı sunuyoruz.

**Anahtar Kelimeler:** Klippel-Trenaunay Sendromu; konjenital, herediter, neonatal hastalıklar ve anormallikler; kolon; gastrointestinal hemoraji; hipospadias; işitme kaybı

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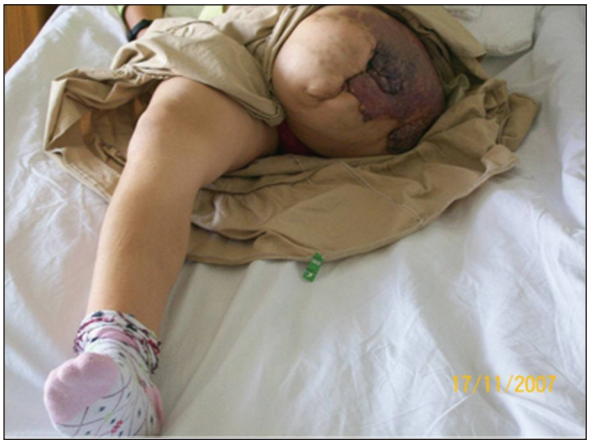
Klippel-Trenaunay Syndrome (KTS) has been first described by the French physicians Maurice Klippel and Paul Trenaunay in 1900 which was characterized by the triad of haemangiomatous lesions of the skin, soft tissue and bone hypertrophy involving one limb and varicose veins or venous malformations.[1] In the literature, it has also been called



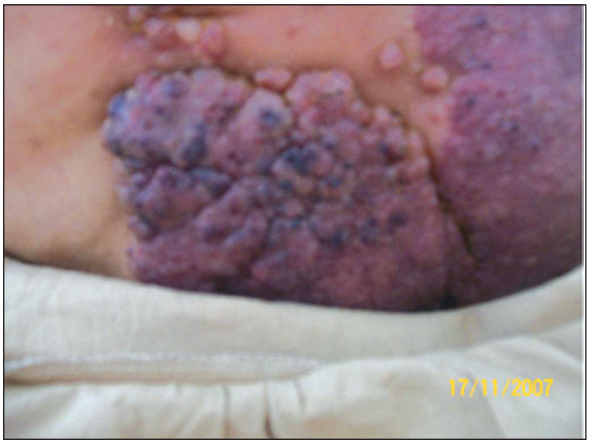




**FIGURE 1:** The image on the left shows amputed and markedly hypertrophic left leg **(A)**. The image on the right shows the vascular structures on the leg closely **(B)**.

such as angioosteohypertrophy syndrome, Parkes Weber syndrome and Klippel-Trenaunay-Weber syndrome.[2] Generally, it may involves multiple extremities and lower limb involvement is observed in 95% of cases.[3,4] Head and neck involvements are rare and commonly ipsilateral. One third of patients have hemangiomatous lesions in the lung, gastrointestinal tract, liver or bladder causing bleeding and compromise organ function. Colonic involvement has been rarely reported. Therefore this syndrome can be associated with severe lower gastrointestinal bleeding due to diffuse cavernous hemangioma of the colon. As multiple organs are frequently involved, a multidisciplinary approach for evaluation and current treatment is mandatory. Therefore, we present two cases of KTS with colon involvement and deep anemia.

**TABLE 1:** Demographic and clinical characteristics of the cases .

| | Case 1 | Case 2 |
|---|---|---|
| Gender | 31 | 24 |
| Age | Female | Male |
| Bladder involvement | None | Hematuria, venous dilatation |
| Urethra | Normal | Hypospadias |
| Fundus involvement | Venous dilatation | None |
| Limb involvement | Left leg | Right leg |
| Operation history | Left leg amputation (once) | 2 operations at the right leg |
| Hearing | Decreased hearing on the left, complete hearing loss on the right | Normal |
| Skin lesion | Giant nevus | No skin lesion |
| Anemia HCT % | 27 | 33 |
| Hematochesia | 15 years | 10 years |
| Vascular structure | Major vascular structures are normal | Tumoral appearance in the lower extremity |
| Diarrhea | Occasional | 10 years |

## CASE REPORTS

### CASE 1

31 year-old-woman presented at our clinic with the complaints of hematochesia. In her physical examination, the left leg was observed to be amputed and a red, blistered, large nevus with a cauliflower appearance was noticeable (Figures 1A and 1B). Her left leg was amputed 10 years ago due to swelling and ischemic recurrent ulcer. She also had been experiencing hematochesia occasionally for the last 15 years (Table 1). She has admitted to our clinic with these increased complaints for the last 2 years. Upper gastrointestinal endoscopy was normal. Colonoscopy revealed segmental involvement of vascular ectasia from cecum to desending colon for 5-10 cm in lenght . Involvement of rectum and sigmoid colon were diffuse (Table 2). Biopsy was performed for the lesions resembling a mass in the rectum (Figure 2A). Histopathology revealed focal goblet cell loss, diffuse vascular and lymphatic ectasia (Figure 3). Neural type hearing loss was detected partially in the left ear and completely in the

**TABLE 2:** Clinical, colonoscopic and histopathologic characteristics of cases with colonic involvement of KTS.

| | Case 1 | Case 2 |
|---|---|---|
| Symptom | Hematochesia | Hematochesia |
| | - | Chronic diarrhea |
| İnvolvement area | Segmental involvement from cecum to desending | Segmental involvement from cecum to rectum for |
| | colon for 5-10 cm in lenght | 5-10 cm in lenght |
| | Diffuse involvement of rectum and sigmoid colon | Diffuse involvement of rectum |
| İnvolvement characteristic | Mucosal edema | Mucosal edema |
| | Hyperemia | Hyperemia |
| | Fragility | Fragility |
| | Dilate venous and vasculary ektasi | Dilate venous and vasculary ektasi |
| | Rectal mass | - |
| Histopathological characteristic | Focal goblet cell loss and diffuse vascular and | Focal goblet cell loss and diffuse vascular and |
| | lymphatic ectasia | lymphatic ectasia |

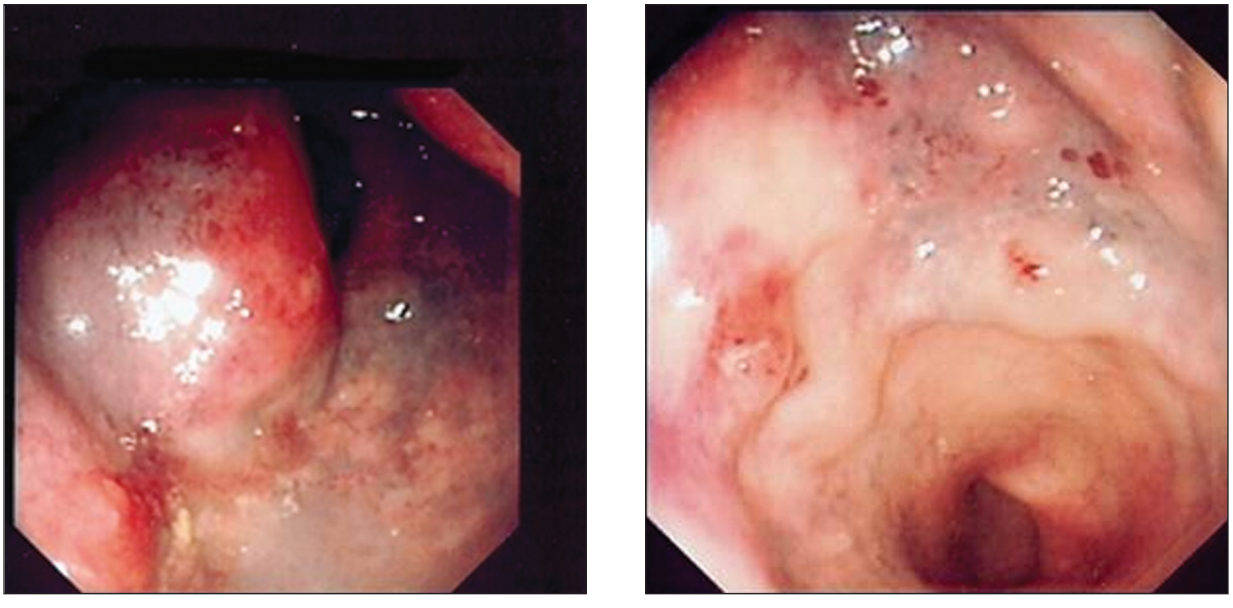


**FIGURE 2:** The image on the left shows a vascular lesion at an approximate size of 3-4 cm **(A)**, in a way resemble the rectal mass, and the surrounding venous vascular structures. The image on the right shows marked dilatation in the ascending colon and venous vascular structures **(B)**.

right ear. Thus, abdominopelvic and cerebral magnetic resonance (MR) angiography were performed. No pathology was detected in the main vascular structures. Fundus examination revealed marked dilatation in bilateral veins. Laboratory investigations revealed the following: WBC: 4700/mm$^3$, HCT: 27.3%, PLT: 456000/mm$^3$, Prothrombin Time: 14.5 sec, ferritin: 26.6 ng/ml, B12: 184, Folic Acid: 7.6, Glucose: 108, Total protein: 7.8 gr/l, Albumin: 4.5 gr/l, AST: 20U/L, ALT: 13U/L, Total bilirubin: 0.8 mg/dl, Direct bilirubin: 0.2 mg/dl, ALP: 162U/L, LDH: 496U/L, BUN: 8 mg/dl, Cr: 0.2 mg/dl.

## CASE 2

A 24-year-old-man presented to our clinic with the complaints of hematochesia and hematuria. His medical history included two operations at right leg due to hemangioma when he was 10-months and 7-years old (Table 1). Then, mass was extracted twi-

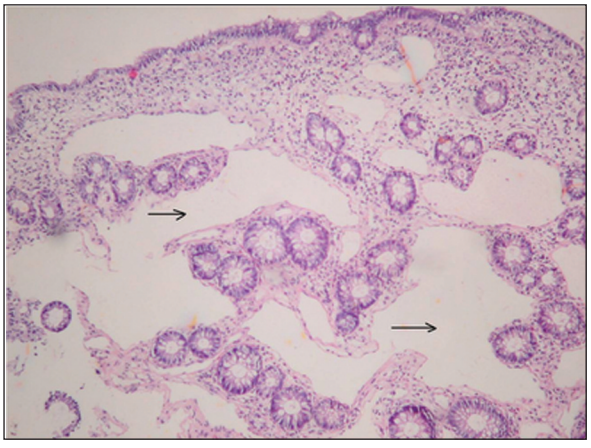


**FIGURE 3:** The biopsy sample obtained from the mass-appearance lesion colonoscopically. Hereby, highly dilated lymphatic and venous ectasias are seen (the area shown by the arrows).

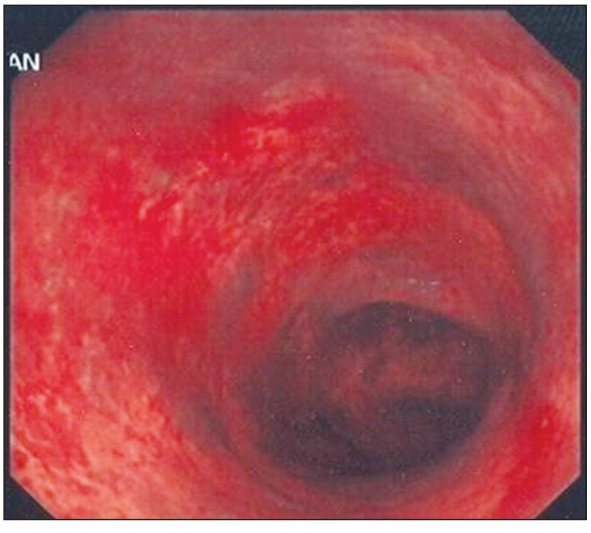


**FIGURE 4:** Vascular ectasias that mimic the colonoscopic view of the ulcerative colitis due to diffuse and highly fragile mucosa.

ce from his right leg, calf and ankle. He started to experience bleeding fistly at 7 years of age and intermittent bleeding continued. Rectal bleeding was constant for last 10 years. Rectoscopy revealed mucosal fragility and marked venous structure (Figure 4). Treatment was initiated considering ulcerative colitis since he had chronic diarrhea and hematochesia (Table 2). The patient also had a history of operations for hypospadias and hematuria. Ultrasonography (USG) revealed right peritesticular hemangioma and cysts in left epididymis. Cerebral and abdominal MR angiography were normal. MR angiography of the lower limb was normal. Colonoscopy revealed a segmental involvement from cecum to rectum for 5-10 cm in length and diffuse involvement of rectum. Terminal ileum was normal. The intermediary mucosal areas were normal. The laboratory values were as follows: Glu: 83 mg/dl, BUN: 11 mg/dl, Cr: 0.8 mg/dl, ALP: 109 U/L, Uric acid: 4 mg/dl, T prot: 8 gr/l, Alb: 4.8 gr/l, Total biluribin: 0.36 mg/dL, Direct biluribin: 0.11 mg/dL, AST:18 U/L, ALT: 17 U/L, GGT: 15 U/L, LDH: 290, WBC: 6500/mm$^3$, HCT: 33, MCV: 72, PLT: 308000/mm$^3$. Hepatitis markers were negative. Microscopic hemathuria was observed. Cystoscopy was performed and venous dilatation was detected.

## DISCUSSION

The etiology of KTS is still not known. Various theories have been suggested. It has been considered to result from vascular and soft tissue malformations during fetal development and genetic mutation or chromosome abnormality.[5,6] Overproduction of insulin growth factor (IGF2) was considered to lead to soft tissue hypertrophy.[7] The number of cases is considered to be below 1000, worldwide. There's no curative treatment for these cases, thus symptomatic therapies are administered.[8,9] It affects both males and females at an equal ratio.[10,11] KTS may affects any region of the body. Face, bladdery, rectum, lower gastrointestinal system, vagina, liver, kidneys, vertebra and lungs are rarely affected regions.[2] One of our cases had skin lesions and lower limb involvement with hypertrophy. In the literature, stasis ulcers develop in the cases with advanced vascular malformation.[3] The female patient had undergone limb amputation due to recurrent stasis ulcer. The male patient had been operated for hypospadias. At the same time, he had recurrent hematuria attacks. Vascular malformations had been detected in the bladder at the operation. In both cases, involvement of the colon and particularly rectum severely effected the patient's quality of lives. The patients had occasionally blood transfusions for bleedings (Table 1). Colonoscopic appearance of this diffuse mucosal fragility is generally a rare condition and may be confused with ulcerative colitis (Figure 4). One of our patients was administered a long-term medical treatment for ulcerative colitis

with the similar clinic and endoscopic findings such as chronic diarrhea and hematochesia. Rectum has been more affected rather than the other colon segments.[12,13] The involvement of various organs have been reported in this syndrome, whereas auditory disorder has not been described in the literature before. Although it's not a vascular pathology revealed with MR angiography, we think that this auditory disorder may be related with KTS.

This syndrome may present with different types of clinical findings. Since hemangiomatous lesions may be present at any part of the colon, it is necessary to perform colonoscopic examination for cases with Klippel-Trenaunay Syndrome. This very rare syndrome must be keep in mind for the differential diagnosis of ulceratif colitis. The clinician must be alert in the case of biopsy, since lesions are usually vascular type.

## REFERENCES


1. Garzon MC, Huang JT, Enjolras O, Frieden IJ. Vascular malformations. Part II: associated syndromes. J Am Acad Dermatol 2007;56(4): 541-64.
2. Oduber CE, van der Horst CM, Hennekam RC. Klippel-Trenaunay syndrome: diagnostic criteria and hypothesis on etiology. Ann Plast Surg 2008;60(2):217-23.
3. al-Salman MM. Klippel-Trénaunay syndrome: clinical features, complications, and management. Surg Today 1997;27(8):735-40.
4. Berry SA, Peterson C, Mize W, Bloom K, Zachary C, Blasco P, et al. Klippel-Trenaunay syndrome. Am J Med Genet 1998;79(4):319-26.
5. Nielsen JR, Tschen EH. Klippel-Trénaunay-Weber syndrome. Cutis 1987;40(1):51-3.
6. Whelan AJ, Watson MS, Porter FD, Steiner RD. Klippel-Trenaunay-Weber syndrome associated with a 5:11 balanced translocation. Am J Med Genet 1995;59(4):492-4.
7. Sperandeo MP, Ungaro P, Vernucci M, Pedone PV, Cerrato F, Perone L, et al. Relaxation of insulin-like growth factor 2 imprinting and discordant methylation at KvDMR1 in two first cousins affected by Beckwith-Wiedemann and Klippel-Trenaunay-Weber syndromes. Am J Hum Genet 2000;66(3):841-7.
8. Jacob AG, Driscoll DJ, Shaughnessy WJ, Stanson AW, Clay RP, Gloviczki P. Klippel-Trénaunay syndrome: spectrum and management. Mayo Clin Proc 1998;73(1):28-36.
9. Dökmeci Ş, Apaydın R, Bilen N, Bayramgürler D, Yıldırım G, Kesepara C, et al. [Klippel-Trenaunay syndrome]. Turkiye Klinikleri J Dermatol 2000;10(2):110-2.
10. Gianlupi A, Harper RW, Dwyre DM, Marelich GP. Recurrent pulmonary embolism associated with Klippel-Trenaunay-Weber syndrome. Chest 1999;115(4):1199-201.
11. Lisko JH, Fish F. Klippel-Trenaunay-Weber syndrome. Med J 2001;2(1): 7.
12. Mussack T, Siveke JT, Pfeifer KJ, Folwaczny C. Klippel-Trenaunay syndrome with involvement of coecum and rectum: a rare cause of lower gastrointestinal bleeding. Eur J Med Res 2004;9(11):515-7.
13. Wilson CL, Song LM, Chua H, Ferrara M, Devine RM, Dozois RR, et al. Bleeding from cavernous angiomatosis of the rectum in Klippel-Trenaunay syndrome: report of three cases and literature review. Am J Gastroenterol 2001;96(9):2783-8.