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Klippel-Trénaunay syndrome, pregnancy and the liver: an unusual interplay

Dimitrios N. Samonakis[a,b], Pantelis Oustamanolakis[b], Penelope Manousou[a], Elias A. Kouroumalis[b], Andrew K. Burroughs[a]

Royal Free Hospital Hampstead, London, UK; University Hospital of Heraklion, Crete, Greece

Abstract

Klippel-Trénaunay syndrome is a rare congenital syndrome characterized by capillary malformations, soft tissue and bone hypertrophy, and varicose veins. There is a well-established risk for thrombotic complications in these patients. A case of a young patient diagnosed post partum with the very rare liver involvement is presented. The complex clinical course, the multidisciplinary management and the long-term outcome are discussed.

Keywords Klippel-Trénaunay syndrome, portal vein thrombosis, varicose veins, pregnancy

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Introduction

Klippel-Trénaunay syndrome (KTS) is a congenital malformation involving blood and lymph vessels, with disturbed growth of bone and soft tissues. The triad of varicose veins, cutaneous capillary malformation, and hypertrophy of bone soft tissue is characteristic [1]. These vascular malformations may involve areas other than the affected extremity and may vary in depth of involvement; they may be limited to the skin, muscles or bones whereas some affect visceral organs [2]. The risk of thrombophlebitis, venous thrombosis and pulmonary thromboembolism is high among KTS patients.

Women with KTS have been reported to have normal pregnancies and the risk to deliver an abnormal child is low, with complications being proportional to the severity of the disease [3]. It is recommended therefore to adopt careful monitoring with serial ultrasounds. The presence of vulval, vaginal, or cervical varicosities demand attention as lacerations may cause massive blood loss [4].

Gastrointestinal tract involvement is variable and may be more common than previously believed [5] while the liver involvement is extremely rare in the context of KTS. We report a case of a lady who was diagnosed only after her third delivery and presented with a thrombotic complication related to KTS and a combination of additional factors. A written informed consent was obtained from the patient for publishing the case and the relevant photos.

[a]The Royal Free Sheila Sherlock Liver Centre and University Department of Surgery, Royal Free Hospital Hampstead, London UK (Dimitrios N. Samonakis, Penelope Manousou, Andrew K. Burroughs); [b]Department of Gastroenterology and Hepatology, University Hospital of Heraklion, Crete, Greece (Dimitrios N. Samonakis, Pantelis Oustamanolakis, Elias A. Kouroumalis)

Conflict of Interest: None

Correspondence to: Dimitrios N. Samonakis MD, Department of Gastroenterology & Hepatology, University Hospital of Heraklion, Heraklion 711 10, Crete, Greece, Tel: +30 2810 392356, Fax: +30 2810 392429, e-mail: dsamon@freemail.gr

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Case report

In January 2008, a 29-year-old woman was referred from the Obstetrics Unit because of fever and the development of ascites, 3 days after a Caesarian section (gravida 3) performed because of vaginal-cervical varices. She had had no previous spontaneous vaginal deliveries and bilateral stripping of varicose veins. She was a non-smoker and she abstained from alcohol.

At referral, she was normotensive without encephalopathy. Pyrexia (38.8°C), mild tachycardia and moderately distended and tender abdomen were present. There were no cutaneous markers of chronic liver disease and no cardiac, respiratory or neurological abnormalities. However, she had limb asymmetry with the right side (length 95 cm, circumference 35 cm), larger than the left (length 93 cm, circumference 29 cm) (Fig. 1), together with right sided enlargement of the face compared to the left. She had capillary (port-wine) hemangiomas in the right cervical area and right upper limb (Fig. 2). She was diagnosed with the KTS.

Hemoglobin was 8.9 g/dL, white cell count 16500 K/μL and platelet count 173000 K/μL. The liver and renal function tests were normal apart from an albumin of 2.5 mg/dL. The INR was 1.4. Viral and autoimmune markers were negative. A computed tomography (CT) scan showed hepatomegaly with arteriovenous anastomoses within

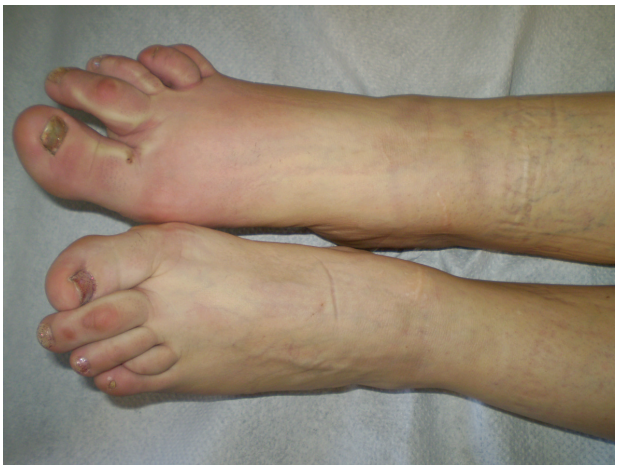

Figure 1 Limb asymmetry with right-side predominance

the liver parenchyma, splenoportal hilar varices, splenomegaly (length 15.5 cm), a moderate amount of ascites and phlebolithiasis in intra-abdominal varicose dilated veins. Smallesophageal varices were seen endoscopically. A brain magnetic resonance imaging (MRI) and echocardiography were unremarkable.

She was treated empirically with piperacillin/tazobactam and metronidazole. Subsequently bacterial cultures from the lochia isolated *Escherichia coli* and *Enterococcus faecalis*. Piperacillin/tazobactam was continued and linezolid was added according to sensitivities. She responded to these antibiotics. The ascites responded to diuretics. Prophylactic low molecular weight heparin was started and continued for 6 weeks because of persistent tachycardia and raised D-dimers.

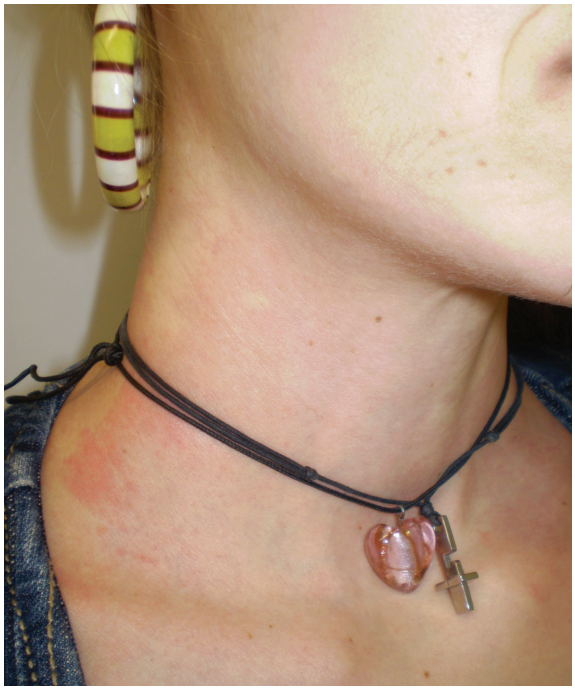

Figure 2 Cutaneous (port wine) hemangioma of the right side of the neck and face

After 3 months a percutaneous liver biopsy was performed which showed non-specific features. The ascites had resolved completely and blood biochemistry was normal. A thrombophilia screening was weakly positive for lupus anticoagulant and hyperhomocysteinemia (28.4 μmol/L, normal range 3.7-11). A chest CT was normal whilst CT of skull–cervical region showed muscle enlargement and projection of the right pharyngeal wall.

Referral for further evaluation was made at 8 months after initial presentation. A transjugular liver biopsy and hepatic venous pressure measurements were performed. Liver histology and hepatic venous pressures were essentially normal. An MRI scan revealed portal vein (PV) thrombosis with cavernoma. There was no evidence of PV aplasia. She was commenced on warfarin for PV thrombosis on a procoagulant background and she has been well for four years since the initial diagnosis.

Discussion

Although KTS is mostly sporadic, there are cases in the literature reporting an autosomal dominant pattern with incomplete penetrance. The syndrome has a wide spectrum of clinical presentation from truncular to extratruncular, from limited to infiltrating forms containing primarily three anomalous vascular elements: veins, capillaries and lymphatics. Various anomalies of the deep venous system, including absent, atretic or hypoplastic deep veins may be found [1].

The involvement of gastrointestinal tract may go unrecognized in patients without symptoms, with bleeding being the most common when symptomatic [5,6]. The most frequently reported sites are the distal colon and rectum. However, varicose veins and venous malformations can involve abdominal organs.

PV thrombosis (PVT) is caused by a combination of local (30% of the cases) and general (70%) risk factors. The leading causes for local risk factors are malignancies and cirrhosis, followed by inflammatory foci intra abdominally. General risk factors are similar in acute and chronic PVT and could be inherited or acquired, irrespective of the presence of an additional local factor. Thus, myeloproliferative disorders, antiphospholipid syndrome, paroxysmal nocturnal hemoglobinuria, protein C or S deficiency, factor V-Leiden mutation, hyperomocysteinemia, MTHFR genotype and oral contraceptive use are commonly encountered amongst thrombotic risk factors.

Very few data exist in the literature about the liver involvement in the context of KTS. There are reports of patients with a hypoplastic PV and prehepatic portal hypertension [7] as well as intrahepatic anastomoses between arteries and veins

and an association with multiple focal nodular hyperplasia (shared pathogenesis – abnormal arteriovenous flow in the liver) [8,9]. A case of a KTS patient with factor VII deficiency and Wilson's-like liver disease has been published [10]. PV thrombosis is infrequently reported despite the thrombophilic tendency of KTS patients.

Patients with this syndrome have increased risk of thromboembolic disease. Thrombotic episodes in the extremities, multiple recurrent pulmonary emboli causing pulmonary hypertension or even death may occur [2]. Avoidance of estrogen use and aggressive prophylaxis for deep vein thrombosis in patients undergoing surgery is strongly advised.

On the other hand, it is documented that women with thrombophilia are at increased risk not only for pregnancy-related venous thromboembolism but other vascular pregnancy complications. In this patient the occurrence of PVT was cardinal. Ascites was a result of the extensive PVT together increased plasma volume of pregnancy and the documented infection. Clearly, the thrombophilic tendency of KTS, hyperhomocysteinemia and the natural hypercoagulability of pregnancy, most likely contributed to the development of PV thrombosis (and ascites) in this lady's case, since liver histology was twice near normal.

In conclusion, an increased awareness is needed from the physicians for the accurate diagnosis of this syndrome, as it is related with potentially significant problems and a long-term follow up of KTS patients is mandatory.

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