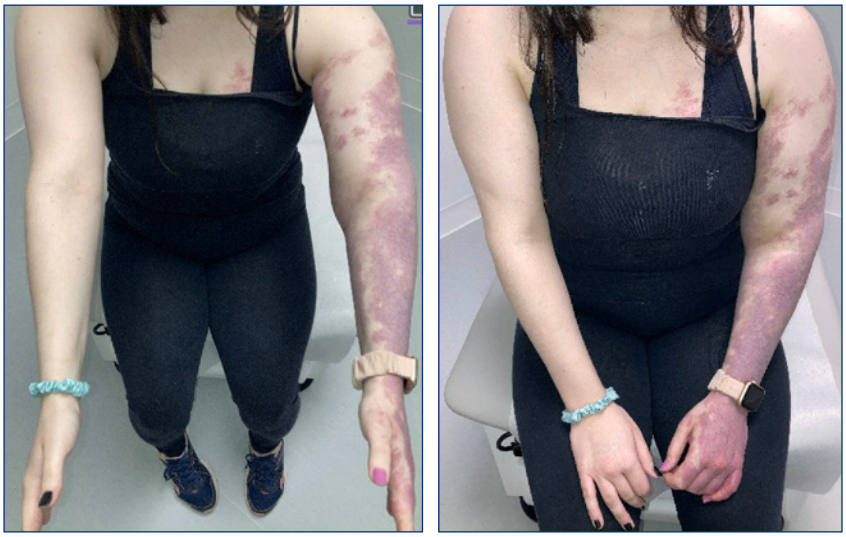
Upper-Extremity Klippel-Trenaunay Syndrome

SYED BUKHARI, MD; AMMAR SAATI, MD

A 26-year-old woman presented for evaluation of cutaneous pigmentation involving the left upper extremity, left breast, and left upper back since birth. She had developed chronic swelling of her left upper extremity during childhood, and began to notice visible veins. She was asymptomatic due to which medical attention was not sought in the past, but now she was curious to know about it. Physical examination revealed massive lymphedema of the left upper extremity, extensive vascular hemangioma of 'port-wine' variety and varicose veins (**Figures 1A, B**). Based on the clinical presentation, as well as the triad of cutaneous port-wine capillary malformations, hemihypertrophy of bone and soft tissues, and varicose veins, the diagnosis of Klippel-Trenaunay syndrome (KTS) was established.

Figures 1A,B. Port-wine stain in the left upper extremity, extending from upper arm to the posterior aspect of the hand. Additionally, left upper extremity is more swollen compared with the contralateral limb, suggestive of hemihypertrophy of the bone and/or soft tissue.



KTS is a complex congenital anomaly that has three main components: cutaneous port-wine capillary malformations, hemihypertrophy of bone and soft tissues, and venous malformations.[1] KTS is a clinical diagnosis, and while it is a very rare condition, upper-extremity KTS is even more unusual. It is usually sporadic with an estimated incidence of 2–5 per 100,000 without any gender predilection.[2] KTS is considered a part of PIK3CA-Related Overgrowth Spectrum (PROS) – a group of clinically overlapping disorders.[3] Although the exact etiology of this spectrum remains unclear, it is thought to be secondary to abnormality of mesodermal tissues in embryologic development, caused by somatic mutations in the phosphatidylinositol-4-5-bisphosphate 3 kinase, catalytic subunit (PIK3CA) gene.[3] This results in the activation of phosphatidylinositol-3-kinase (PI3K)/protein kinase and cell overgrowth through dysregulation of the mTORC2 pathway.[3] While patients may be asymptomatic in the first few decades of their lives, rectal bleeding and/or intermittent painless hematuria are often the first clinical manifestation, and hemangiomas and varicose veins are primarily the cause of bleeding. Ironically, extensive varicosities make these patients more prone to the development of venous thromboembolism as well, and IVC filter implantation is appropriate when recurrent bleeding precludes anticoagulation use.

A multidisciplinary approach is the key for management of these patients. Although symptomatic care remains the mainstay treatment, low-dose sirolimus can provide some benefit by inhibiting growth-promoting actions of PI3K, resulting in modest reduction in overgrowth.[4] Finally, the emergence of novel targeted therapies including the recently FDA-approved PI3K pathway inhibitor, Alpelisib, has further underscored the importance of genetic testing in KTS.[5]

References

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Authors

Syed Bukhari, MD, Department of Cardiovascular Medicine, Section of Vascular Medicine, Cleveland Clinic, Ohio.

Ammar Saati, MD, Department of Cardiovascular Medicine, Section of Vascular Medicine, Cleveland Clinic, Cleveland, Ohio.

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Correspondence

Syed Bukhari, MD
Section of Vascular Medicine
Cleveland Clinic
9500 Euclid Avenue, J 3-5
Cleveland, Ohio, 44195
718-674-5378
bukhars6@ccf.org