A Patient with Klippel-Trenaunay Syndrome and Mild Ophthalmic Manifestations

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Klippel-Trenaunay syndrome (KTS) is a rare congenital complex vascular multisystem disorder characterized by bony and soft-tissue hypertrophy. It is famous for its hallmarks like port-wine stains and varicose veins. The syndrome is sporadic, although rare familial cases have been reported [1]. The most common ophthalmological alterations encountered in KTS are conjunctival telangiectasia, anterior chamber malformation, raised episcleral venous pressure with associated glaucoma, and choroidal hemangiomas [2].

The purpose of this report is to raise awareness of KTS and its diverse scale of expressions as well as complications. This study was conducted in accordance with the ethical standards set by the Declaration of Helsinki. The patient gave signed informed consent.

PATIENT DESCRIPTION

A 55-year-old man with known left port-wine stain [Figure 1A] and cutaneous hemangiomas on the right abdomen and forearm [Figure 1B] was referred to the ocular oncology service in April 2019 for evaluation. He had previously presented with glaucoma and retinal disorders. The patient was treated consistently in the left eye with Xalatan (latanoprost) eye drops once per day and maintained normal intraocular pressure. A visual field examination in June 2019 showed both eyes were normal.

On the day of presentation, a nasal hemangioma in the left eyelid and an ipsilateral port-wine stain on V2 dispersion were observed. In addition, there were conjunctival and episcleral telangiectatic vessels, without congestion, dispersed 360° [Figure 1C]. There were no abnormal iris blood vessels or iris neovascularization and the iridocorneal angle was open 360° without abnormal iris blood vessels or neovascularization.

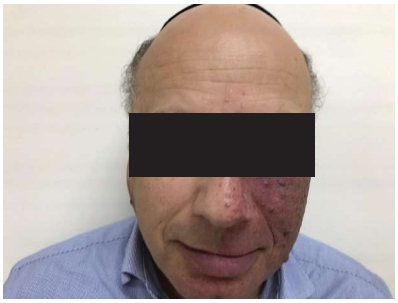
During the examination of the posterior segment of our patient, no clinical pathology was found. An ultrasound of the left eye demonstrated normal retina, choroid, and sclera without thickened areas or fluid accumulation. However, choroid measurements presented a difference in the thickness of choroid in the left eye compared to the right eye: superior 0.7 mm, nasal 0.78 mm, temporal 0.91 mm, and inferior 0.98 mm vs. superior 0.64 mm, nasal 0.58 mm, temporal 0.74 mm, and inferior 0.71 mm, respectively. All the measurements were within the normal range.

COMMENT

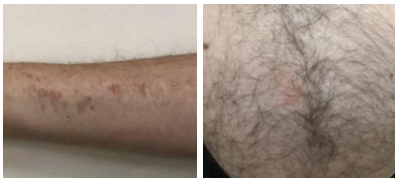
Cutaneous vascular patches involving the limb raised the suspicion for KTS, which is a complex vascular syndrome. KTS is diagnosed mainly on the basis of physical findings including a segmental anomaly

Figure 1. A 55-year-old man with known left port-wine stain

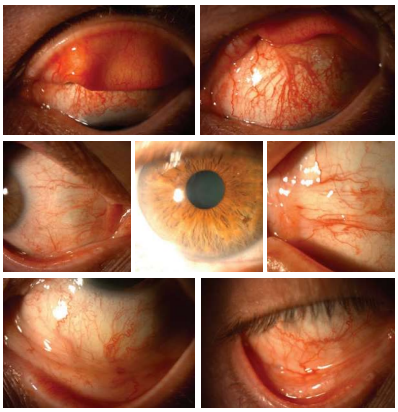
[A] A nasal hemangioma in the left eyelid and an ipsilateral port-wine stain on V2 dispersion



[B] Cutaneous hemangiomas on the right abdomen and forearm



[C] Conjunctival and episcleral telangiectatic vessels 360°, left eye



with a cutaneous port-wine stain, lymphatic and venous malformations, and soft tissue and bony overgrowth. Clinical severity varies from patient to patient. Some patients may present with severe problems, such as recurrent skin infections, thromboembolism, massive limb overgrowth, chronic pain, and life-threatening pelvic, urinary tract, or rectal bleeding, whereas others experience mild forms of cosmetic matters only.

The range of severity of ocular complications is also wide. Ophthalmic pathologies arise primarily from vascular abnormalities of the conjunctiva, episclera, retina, and choroid. When the facial vascular malformation involves mainly the upper eyelid, ocular pathologies may occur. Choroidal hemangiomas, usually of the diffuse type, and conjunctival involvement are the most common abnormalities [3]. Glaucoma, another frequent ophthalmic pathology, occurs due to anterior chamber malformation and angle dysgenesis or raised episcleral venous pressure. Treatment may be challenging as the disease can be refractory [2,4]. Other rare ophthalmic alterations include conjunctival telangiectasia, orbital varix, strabismus, oculosympathetic palsy, Marcus-Gunn pupil, iris coloboma and heterochromia, cataracts, persistent fetal vasculature, chiasmal and bilateral optic nerve gliomas, drusen of the optic disk, acquired myelination of the retinal nerve fiber layer, and retinal dysplasia with astrocytic proliferation of the nerve [2].

Because of its low prevalence, only a few cases have been reported. Olcaysu et al. [5] reported a case of a 17-year-old boy with typical systemic characteristics of KTS accompanied by unilateral mature cataract and vitreoretinopathy. Our patient presented at the age of 55 years with prominent cutaneous systemic manifestations of KTS involving the left side of his face, abdomen, and forearm, yet the diagnosis of KTS was not made. Our patient's ocular manifestations were mild and involved elevated intraocular pressure with no visual field damage or conjunctival and episcleral telangiectatic vessels. There was no retinal or choroidal involvement. His best corrected visual acuity was 6/6 in his left eye and 6/6 partial in his right eye. Due to no new complaints, stable glaucoma, and stable ophthalmic findings, the patient was invited for a 6-month follow-up.

CONCLUSIONS

The Klippel-Trenaunay syndrome is a rare congenital complex vascular multisystem disorder. Ocular involvement in KTS can present as a mild esthetic form with topically treated glaucoma. This involvement is variable. Complications can range from esthetics to glaucoma and sight threatening pathology.

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References

1. Craven N, Wright AL. Familial Klippel-Trenaunay syndrome: a case report. *Clin Exp Dermatol* 1995; 20 (1): 76-9.
2. Abdolrahimzadeh S, Scavella V, Felli L, Cruciani F, Contestabile MT, Recupero SM. Ophthalmic alterations in the sturge-weber syndrome, Klippel-Trenaunay syndrome, and the phakomatosis pigmentovascularis: an independent group of conditions? *Biomed Res Int* 2015; 2015: 786519.
3. Dorairaj S, Ritch R. Encephalotrigeminal angiomatosis (Sturge-Weber Syndrome, Klippel-Trenaunay-Weber Syndrome): a review. *Asia Pac J Ophthalmol (Phila)* 2012; 1 (4): 226-34.
4. Haidu SD, Aktas Z. Gonioscopy-assisted transluminal trabeculotomy for congenital glaucoma secondary to Klippel-Trenaunay-Weber syndrome: a case report. *Am J Ophthalmol Case Rep* 2022; 28: 101734.
5. Olcaysu OO, Altun A, Olcaysu E, Marzıoğlu Ozdemır E, Demır B. Unilateral cataract and vitreoretinopathy in a case with klippel-trenaunay syndrome. *Case Rep Ophthalmol Med* 2014; 2014: 312030.

Capsule

Antitumor T cells in head and neck cancer

Immune checkpoint blockade (ICB), for example, targeting anti-programmed cell death protein 1 (anti-PD-1), reinvigorates tumor-specific T cell responses, but the mechanisms underlying specific clinical responses remain unclear. Using single-cell transcriptomics and T cell receptor sequencing, **Oliveira** et al. analyzed tumor specimens from patients with head and neck cancer enrolled in a phase 2 clinical trial testing two doses of neoadjuvant anti-PD-1 before surgical resection. Tumors responding to anti-PD-1 contained a baseline population of T cells expressing the transcription factor *ZNF683*, as well as genes associated with T cell exhaustion, tissue resident memory, and cytotoxicity. In paired pre- and posttreatment biopsies, *ZNF683*+CD8+ T cells were clonally expanded and exhibited the strongest change in patients responding to ICB. Reinvigoration of cytotoxicity among *ZNF683*+CD8+ T cells is a likely mechanism underlying response to neoadjuvant anti–PD-1 in head and neck cancers.

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