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RESEARCH ARTICLE

Twisted Vessels with Twisted Circuits

Dr. Navami S Rao[1], Dr. Rajkumar M[2], Dr. Bhargavi M V[3], Dr. Suresh Kumar R[4]
[1]Third year Junior Resident, Department of General Medicine, Sri Ramachandra Medical College, Chennai, Tamil Nadu, India.
[2]Professor, Department of General Medicine, Sri Ramachandra Medical College, Chennai, Tamil Nadu, India.
[3]Assistant Professor, Department of General Medicine, Sri Ramachandra Medical College, Chennai, Tamil Nadu, India.
[4]Assistant Professor, Department of General Medicine, Sri Ramachandra Medical College, Chennai, Tamil Nadu, India.

*Corresponding Author
Dr. Navami S Rao

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Abstract: Klippel–Trénaunay Syndrome (KTS) is a rare congenital vascular malformation disorder characterized by capillary malformations, venous anomalies, and limb hypertrophy. Though it is mostly peripheral in its manifestation, neurological involvement can and may happen, especially epilepsy, which can be difficult to diagnose. A 45-year-old male presented with a 5-month history of recurrent brief episodes of staring and unresponsiveness, with recent escalation to multiple daily events. He had a history of longstanding, untreated hypertension and remote seizure-like episodes. Examination revealed extensive right-sided capillary malformations with soft-tissue hypertrophy and measurable limb asymmetry. Neuroimaging showed diffuse cerebral atrophy without intracranial arteriovenous malformations. Routine EEG was normal, but long-term video-EEG captured habitual events with epileptiform discharges arising from the left frontotemporal region. Findings were consistent with structural focal epilepsy exacerbated by antiepileptic drug non-adherence. The patient responded to intravenous levetiracetam during an ictal desaturation episode and was subsequently stabilized on levetiracetam and clobazam. No further seizures occurred during hospitalization, and he was discharged with counseling on strict medication adherence. This case underscores the intersection of vascular malformations and chronic cortical dysfunction in KTS. The combination of characteristic peripheral findings and electroclinical evidence of focal epilepsy highlights the need for comprehensive neurological evaluation and sustained antiepileptic therapy in patients with extensive vascular involvement.

Keywords: Klippel–Trénaunay Syndrome, capillary malformation, focal epilepsy, video-EEG monitoring, limb hypertrophy

INTRODUCTION

The Klippel -Trénaunay Syndrome (KTS) is a rare type of vascular malformation disorder that presents with a unique triad of capillary malforms, improper development of venous anatomy, and hypertrophy of the surrounding soft tissue or bones of the affected limb. The genetic disease is the result of aberrant mesodermal differentiation, and currently, the condition is considered to be a part of the PIK3CA-related overgrowth spectrum due to the underlying somatic mutational cause [1]. Despite its traditional rarity, prevalence is estimated to range between 1:27,500 and 1:100,000 live births. Recent large-cohort studies have given a better epidemiological understanding and emphasized the extensive burden of cutaneous and vascular morbidity of the syndrome [2].

Classical triad is the basis of diagnosis: malformations of the capillary, e.g., port-wine stain, varicose veins, or persistent embryonic vein, limb hypertrophy of soft tissue and bone. These characteristics are frequently accompanied by lymphatic malformations and can differ significantly in severity and location, which adds to the heterogeneity in the clinical manifestation presented in the modern reviews [3, 4]. Although KTS is mostly known to have a peripheral vascular presentation, it has neurological involvement, although it is rare and clinical. Intracranial and extracranial vascular anomalies, including venous angiomas, developmental venous anomalies, and in some rare cases, there is screening of arteriovenous shunts, all of which indicate the possibility of central nervous system issues [5].

The connection between vascular malformations and seizure activity is getting more accepted. The presence of cerebral venous abnormalities may disrupt cortical perfusion, promote gliosis, or disrupt the normal organization of neurons, which may precondition the development of epileptogenesis in those people [6]. The identification of the epileptogenic focus will become crucial in such patients, as the seizures can be caused by inherent vascular regulation, related structural pathology, or secondary neurodegeneration [7, 8].

This has been an issue of great concern with regard to prolonged multimodal assessment of structural epilepsy due to this diagnostic complexity. Normal EEG has limited ability to detect intermittent or deep-seated abnormalities, and the combination of long-term electroencephalographic monitoring with high-tech neuroimaging considers, such as MRI, PET, and SPECT, is order to improve localization and increase the diagnostic confidence [9]. It is of great significance, especially in syndromic conditions where there are overlapping lesions, multifocal breaks, or vascular anomalies that might hide the main focus of the seizure. This case study aims to detail an adult patient who is exhibiting recurring focal seizures in KlippelTrénaunay Syndrome, which shows the interaction between vascular pathology and epileptogenesis. This report

highlights the importance of careful assessment and individualized treatment of patients with complicated neurovascular syndromes through the combination of clinical results and multimodal neurodiagnostics.

2. CASE PRESENTATION

A 45-year-old male shopkeeper of Guindy came in with a 5-month history of periodic transient episodes of unresponsiveness and staring. He initially had 2-3 episodes per day with a duration of 5-15 seconds without any automatism, tonic-clonic activity, tongue biting, urinary incontinence, or post-ictal confusion. During the last 10 days, the frequency had risen to 67 episodes per day. During his stay in the outpatient department, he had three similar incidents with complete recovery between the incidents, requiring him to be transferred to the critical care unit.

The patient had a three-year history of hypertension that was untreated. His wife reported that he had had periodical self-limiting seizures that were like absence seizures since early adulthood. He was assessed at an external hospital in October 2022, and an MRI Brain was reported to have bilateral mesial temporal sclerosis. He was on levetiracetam 500 mg BID and clonazepam 0.5 at night, which he has since stopped in the last five months. Epileptic zone in the left anterior parieto-occipital area was reported in video-EEG, left high parietal, parieto-occipital, and temporoparietal hypometabolism was reported in FDG-PET, and SPECT. No neurosurgical assessment had been done.

In the process of admission to the CCU, he experienced a persistent seizure, which was accompanied by oxygen desaturation, and was given 2 g intravenous levetiracetam, as a result of which the seizure was reduced, and he awoke. Lactate was found to be high in the arterial blood gas analysis. He did not need to be intubated.

On general examination, vital signs were stable. A cutaneous examination showed broad vascular malformations on the right face, chest, upper limb, and lower limb in the form of port-wine stain capillary malformation. There was an increase in the girth and soft tissue fullness on the right side of the body. The measurements of the limbs established an asymmetry: the right lower limb was 82 cm (left: 79.4 cm). There was an increase in girth measurements on the right arm, 30.6 cm vs 28 cm, forearm, 27 cm vs 23 cm, thigh, 44cm vs 34cm, and calf, 33cm vs 28cm.

Due to neurological examination, higher mental functions were normal, the cranial nerves were intact, the motor power was 5/5 in all extremities, deep tendon reflexes were symmetrically excited, flexor plantar reflexes were also bilateral, sensations were intact, and coordination was present. The cardiac, respiratory, and abdominal systems were small.

He was then put on intravenous levetiracetam 500 mg 2 times a day and oral clobazam 10 mg at night during hospitalization. In the MRI brain with contrast-enhanced MRA and MRV, cerebral atrophy was diffuse. EEG routine was found to be normal, and video-EEG showed three habitual events with epileptiform discharges emanating from the left frontotemporal region, which is in line with previous studies. Follow-ups after stabilization were made outpatient by him, and he was discharged on levetiracetam and clobazam with a lesson on medication adherence.

The right-sided capillary malformations and limb hypertrophy were some of the indications that showed whether a patient had Klippel-Trénaunay Syndrome, whereas the recurring events, coupled with the non-compliance with antiepileptic drugs, were, in fact, characteristic of structural epilepsy.

MATERIAL AND METHODS

The case study was carried out on a stepwise and systematic clinical and diagnostic assessment that is in line with the standard neurological and vascular assessment procedures. All data were obtained using the clinical experiences of the patient during his hospital stay, bedside examination, and research conducted.

3.1 Clinical Evaluation

The patient and his primary caregiver were interviewed on a more detailed history with an emphasis on the characteristics of seizures, how they have progressed throughout time, any neurological events that have occurred previously, medication compliance, and previous medical history. General and systematic examination was conducted in a complete form with a special focus on dermatological features, limb morphology, and the neurological condition. Asymmetry was noted by recording limb length and girth measurements through standardized techniques of measuring tapes.

3.2 Neurological Assessment

Neurological examination involved higher mental function, cranial nerves, muscle strength, deep tendon reflexes, sensory modalities, coordination, and gait, where necessary. The outpatient and critical care settings were directly observed by clinical staff, and the characteristics of the seizure were directly recorded in real-time.

3.3 Neurophysiological Testing

To assess the cortical activity in the baseline, routine electroencephalography (EEG) was carried out. This was followed by long-term video-electroencephalographic (VEEG) so as to record habitual events, so as to be able to correlate clinical episodes with electrographic changes. EEG Epileptiform discharges were analyzed to find out the lateralization and regional localization.

3.4 Neuroimaging

The magnetic resonance imaging (MRI) of the brain with contrast-enhanced magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) was carried out to evaluate structural abnormalities and intracranial vascular malformations. The epileptogenic zone was reviewed and longitudinally evaluated through previous neuroimaging findings that were attained elsewhere, i.e., MRI, FDG-PET, and SPECT.

3.5 Acute Management and Monitoring

Continuous clinical observation during hospitalization was performed, including vital signs, neurological status, and frequency of seizures. An ictal event was used to conduct an arterial blood gas analysis to determine the level of metabolic stress, including lactate. Appropriated antiepileptic drugs were also reported in the CCU, and their effect on the patient was observed.

3.6 Data Integration and Diagnostic Synthesis

The relationship between the vascular malformations and the seizure activity of the patient was determined using findings provided by history, physical examination, neurophysiology, and neuroimaging. The severity of the cutaneous and musculoskeletal involvement was recorded using clinical photographs and anthropometric measurements. The management decisions and diagnostic conclusions had been made on the basis of purely compiled clinical and investigation data.

RESULTS AND OBSERVATIONS:

Participant clinical assessment showed widespread unilateral soft-tissue and vascular defects that were typical of Klippel-Trénaunay Syndrome. There were several capillary malformations over the right half of the body, as illustrated in Figure 1(A-E), where Figure 1A shows a diffuse reddish-brown discoloration over the right face and upper chest. In Figure 1B, hypertrophy and mottled vascular staining in the right upper arm are indicated. Figure 1C points to the ankle enlargement of soft tissues and dark coloration on the right. The right upper limb is presented in Figure 1D in the frontal position, where the girth is larger with irregular vascular markings. Figure 1E demonstrates the mottling of the vascularity on the right anterior chest wall.

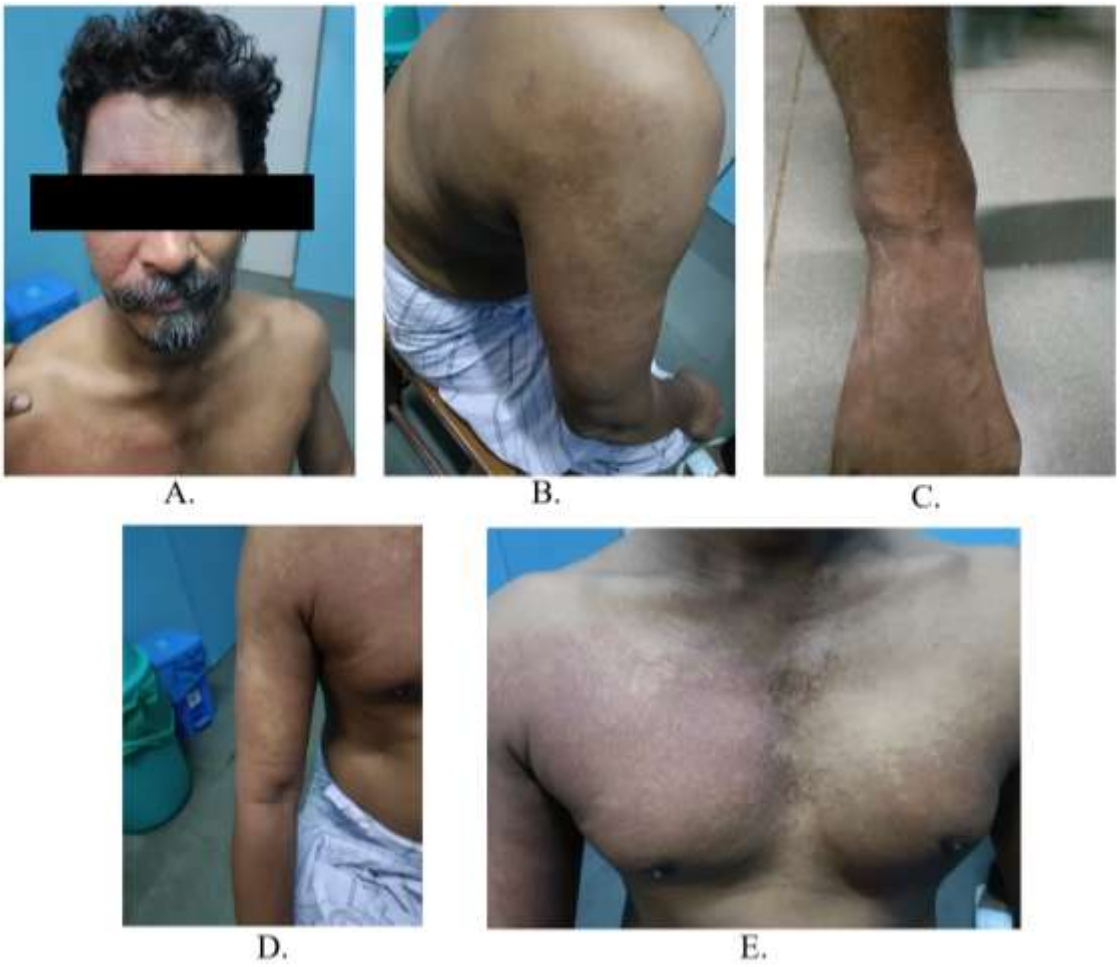

Figure 1. Clinical photographs **(**A.) Right facial capillary malformation. (B.) Right upper arm hypertrophy with vascular discoloration. (C.) Enlarged and discolored right ankle. (D.) Right upper limb hypertrophy (front view) (E.) Vascular malformations of the right anterior chest wall.

The clinical manifestations all corresponded well to the classical triad of port-wine stain, varicose/venous malformations, and hypertrophy of the limbs, as shown in Figure 2.

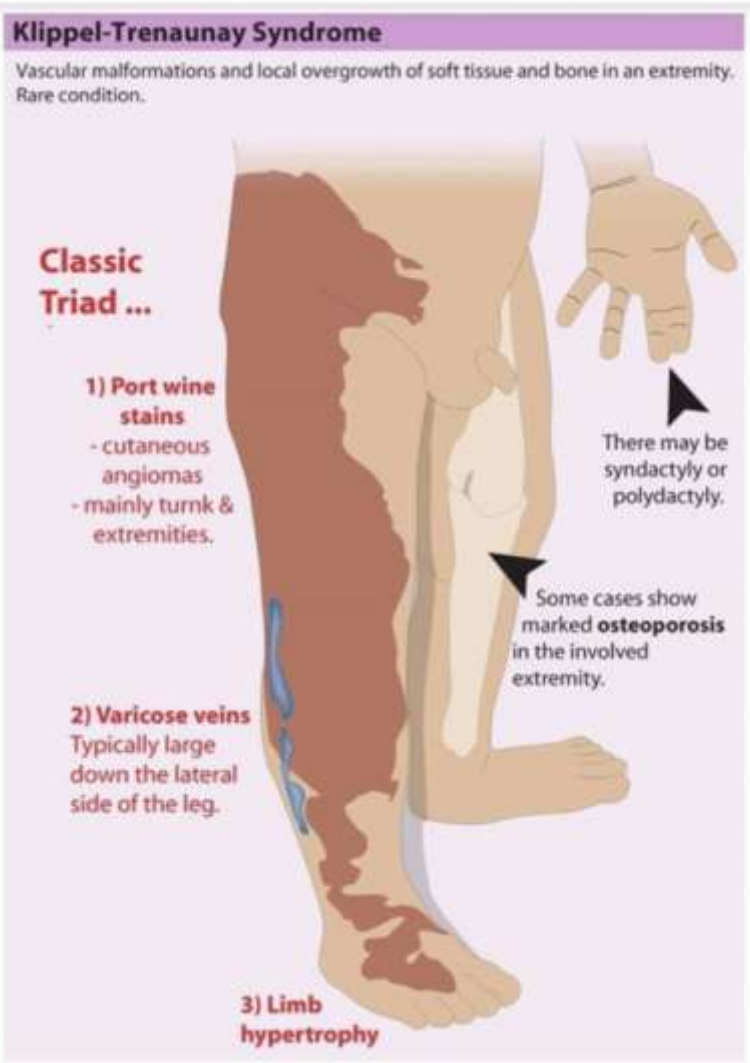

Figure 2. Classical triad of Klippel–Trénaunay Syndrome showing port-wine stains, varicose veins, and limb hypertrophy.

Anthropometric measurements showed that there was considerable overgrowth on the right side. The right lower limb had a length of 82 cm, and the left had 79.4 cm, indicating an actual difference in length. The unilateral hypertrophy was also observed in girth measurements: the right arm was 30.6 cm (left: 28 cm), the right forearm was 27 cm (left: 23 cm), the right thigh was 44 cm (left: 34 cm), and the right calf was 33 cm (left: 28 cm). Such measurements are directly related to the asymmetry that can be observed in Figures 1B through 1D, and the results are summarized in Table 1.

Table 1. Limb Girth Measurements

Region	Right (cm)	Left (cm)
Arm	30.6	28
Forearm	27	23
Thigh	44	34
Calf	33	28

Neurological assessment revealed intact higher mental status, intact cranial nerves, and full motor strength (5 /5) in all extremities. The deep tendon reflexes were bilaterally symmetrical, and the biceps, triceps, supinator, and knee jerks were rated as + on either side. Weak ankle jerks were present (+/+), and flexor bilaterally on the plantar responses. Table 2 provides a summary of these findings.

Table 2. Deep Tendon Reflexes

Reflex	Right	Left
Biceps	++	++
Triceps	++	++
Supinator	++	++
Knee	++	++
Ankle	+	+
Plantar	Flexor	Flexor

Normal EEG did not show any interictal epileptiform discharges. Conversely, three episodes of behavioral arrest and unresponsiveness that were habitual and each linked to epileptiform discharges focalized to the left frontotemporal region were assessed using long-term video-EEG, similar to previous VEEG, PET, and SPECT results in an external hospital. MRI, MRA, and MRV neuroimaging revealed diffuse atrophy of the brain without acute infarction, mass effect, or intracranial arteriovenous malformation. No aneurysmal or venous thrombosis changes were detected.

In the hospital, the patient had an instance of persistent seizure activity associated with oxygen desaturation that was responsive to intravenous levetiracetam. Blood gas analysis of the arteries showed high levels of lactic acid, which were in line with the current ictal activity. No further seizures were noted after the administration of scheduled intravenous levetiracetam and oral clobazam was started.

Right-sided capillary malformations, Unilateral limb hypertrophy, and left hemisphere epileptiform discharges findings favour the diagnosis of Klippel Trenaunay Syndrome, accompanied by structural focal epilepsy. The syndromic nature of the presentation of the patient is supported by the cutaneous and structural abnormalities compared with the classic triad.

DISCUSSION

KlippelTrénaunay Syndrome (KTS) is a vascular malformation disorder that is characterized by the three conditions of capillary malformations, venous abnormalities, and hypertrophy of the limbs. The peripheral pattern of capillary malformations and unilateral overgrowth of limbs of the patient in the case are typical and clearly delineated, as per the typical slow-flow vascular profile of the cohort studies [10]. The limb-length discrepancy and the prominent disparity in girth of the limbs, greatest in the thigh and calf, are similar to the asymmetric hypertrophy, which is noted in patients with combined venous and lymphatic malformations [11].

KTS is rarely involved with neurological involvement, although it is gradually becoming known. The reported signs include cortical malformations, developmental venous anomalies, Chiari I malformation, and, in a few cases, complex epileptic syndromes [12, 13]. The patient in this instance showed repeated focal impaired-awareness seizures that were electrophysiologically localized to the left frontotemporal part. It is worth noting that these results were realized without intracranial high-flow vascular malformations or thrombosis on MRI, MRA, and MRV. This contributes to the new idea that it is possible that smooth venous malregulation or imperceptible imbalance in perfusion, but not overt arteriovenous shunt, triggers epileptogenesis in some KTS patients [13].

The major strength of the case is that the cutaneous and musculoskeletal signs of Klippel -Trenaunay Syndrome were properly documented by precise measurements and clinical imaging. Also, the electroclinical correlation that came out after the use of video-EEG shows a good indication in localizing seizures in the patient.

The long-standing episodes that the patient presents (apparently since early adulthood), and the presence of hypometabolism with PET/SPECT in the past, indicate that it must be a chronic structural epileptogenic network, and not an acute provocation. The recent rise in the frequency of seizures was in tandem with the non-compliance with antiepileptic drugs. The observation underscores a clinical implication which is practical: although KTS is congenital, seizure control in syndromic epilepsies is most reliant on regular pharmacologic therapy. In asymptomatic cases of intracranial malformations, a predisposed area of the cortex can result in subsequent or aggravation of the seizures when the patients discontinue taking their medication.

The patient did not have any systemic manifestations, as compared to more serious KTS presentations, such as gastrointestinal bleeding, genitourinary, or skeletal complications [14, 15]. However, a wide range of phenotype variability of the syndrome is highlighted by the widespread cutaneous lesions and pronounced musculoskeletal asymmetry. In the given case, the management was right in its focus on seizure control and the need to counsel on the importance of strict medication adherence, since interventional or endovascular intervention is used in patients with symptomatic venous obstructiveness, pain, or bleeding [10].

It is noted that this case represents the overlap of noninfection and birth-related vascular malformations and chronic cortical disability in KTS. The presence of typical cutaneous signs, objectively registered

hypertrophy, and focal hyperirritability of the epileptic seizures highlights the significance of neurological examination in patients with a large extent of peripheral vascular disease. The case contributes to the paucity of literature but the growing body of literature on the description of epilepsy in KTS and supports the importance of clinical vigilance in the long-term.

CONCLUSION

The case demonstrates the crucial overlap between the presence of malformation of the vascular system congenitally and the persistent neurological impairment in the Klippel-Trénaunay Syndrome. There was a classical peripheral triad of capillary malformations, venous abnormality, and limb abnormality in the patient based on objective anthropometric measurements and apparent clinical imaging. Although there was no intracranial arteriovenous shunting, the progression of diffuse cerebral atrophy and a stable left frontotemporal epileptiform activity are significant indicators that epileptogenesis in KTS might be based on the subtle and chronic changes in cortical perfusion and not on overt vascular malformation. The long-term history of seizure disorder with recent non-adherence to medications in the patient shows the susceptibility of the structurally predisposed cortical networks and supports the idea of the significance of long-term antiepileptic treatment. Multistage assessment, such as a close clinical observation, thorough records of limb asymmetry, and chronic video-EEG records, was central to the description of the epileptic focus and elucidating the neurological impact of this vascular overgrowth syndrome. The case adds to the small yet increasing body of literature on the clinical importance of neurological manifestations in KTS, even where the vascular damage seems to have been peripheral. Early detection of seizure activity, systematic neurodiagnostic evaluation, and continuous compliance with medication still continue to play a crucial role in the prevention of worsening and enhancement of long-term results.

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