CASE REPORT
MARKED ACANTHOCYTOSIS ASSOCIATED WITH KLIPPLE-TRENAUNAY SYNDROME

Syeda Mah Ali[1], Naila Raza[1], Eraj Aftab, Mahnoor Faisal Mohammad[2]
[1]Liaquat National Hospital, Karachi, [2]Liaquat National Medical College, Karachi-Pakistan

Klipple-Trenaunay syndrome (KTS) is an extremely rare congenital vascular disorder with poorly defined incidence and prevalence. We report a case of a patient who presented after road traffic accident with primary complaints of poor wound healing and persistent bleeding from wound site. Discernible presence of arteriovenous malformation and skin hypertrophy since birth lead to the diagnosis of Klipple-Trenaunay syndrome (KTS). There was an incidental finding of acanthocytosis on peripheral film of blood which remained elevated even after clinical improvement of the patient. This case report highlights a close association of marked acanthocytosis of red blood cells and Klipple-Trenaunay syndrome.

Keywords: Klipple-Trenaunay syndrome; Acanthocytosis; Arteriovenous malformation

Citation: Ali SM, Raza N, Aftab E, Mohammad MF. Marked acanthocytosis associated with Klipple-Trenaunay syndrome. J Ayub Med Coll Abbottabad 2023;35(1).182–5.

DOI: 10.55519/JAMC-01-11307

INTRODUCTION

Klipple-Trenaunay syndrome is a benign and an extremely rare condition. It is a congenital vascular disorder typically presenting with a triad of capillary malformations, venous malformations and hypertrophy of soft tissues or bones.[1] The syndrome has a variable clinical presentation of capillary and lymphatic malformations, varicose veins and limb discrepancy, i.e., hypertrophic soft tissue or bones.[2] It usually manifests with haemorrhagic and thrombotic complications.[3,4] The haemorrhagic tendency is due to consumptive coagulopathy. Decreased fibrinogen levels and platelets with increase in D-dimers is a helpful tool in diagnosing localized intravascular coagulopathy (LIC) seen in these patients.[5,6]

The International Council for Standardization in haematology explains acanthocytes or spur cells as "hyperchromic red cells with irregularly spaced projections of variable length and thickness".[7] The standard grading system defined for acanthocytosis is "2+ or moderate" for 5–20 acanthocytes /100 RBCs and "3+ or many acanthocytes" for >20 acanthocytes/ 100 RBCs.[7] Common conditions associated with Acanthocytosis include liver and renal diseases, post-splenectomy status, Vitamin E deficiency, McLeod RBC phenotype, Abetalipoproteinemia and others.[8,9] Here we report the case of a young man with KTS who presented with intravascular coagulopathy and marked acanthocytosis.

CASE PRESENTATION

A 23-year-old man, resident of Karachi, Pakistan, presented in the Emergency Room with profuse bleeding from a wound site on left thigh following road traffic accident one week ago. Physical examination revealed a deep laceration on his left thigh and few scratches on forehead. He also had gross arteriovenous malformation with skin hypertrophy present on left upper arm, left hand, right leg and torso from birth which grew in size with age. (Figure-1A,1B). The patient was admitted for wound exploration after optimizing haemoglobin by Packed Red Blood Cells (PRBCs) transfusion. Injection tranexamic acid was also initiated. Past, personal and family history of delayed or spontaneous bleeding were negative. Baseline laboratory investigations revealed normochromic anaemia with ~~of~~ haemoglobin level of 7.8 g/dL showing 40% acanthocytes. Figure-2 Coagulation workup was deranged significantly and suggestive of Disseminated intravascular coagulopathy Table-1. To rule out possible causes of DIC, workup for infection was sent which included serum Procalcitonin levels, C-reactive protein and blood culture. No evidence of infection was found. Patient was transfused multiple PRBCs and Cryoprecipitate to arrest bleeding. After 48 hours, haemostasis was secured and wound developed healthy granulation tissues Figure-3. Later on due to persistently low levels of fibrinogen we assumed that it was being consumed in arteriovenous malformation. A detailed workup included MRI and peripheral angiography for the arteriovenous malformation was performed which

showed a classical triad of capillary malformation, venous malformation and limb overgrowth. Peripheral angiography or venogram showed diffuse left upper limb venous malformation with multiple arterial involvements predominantly at scapular and forearm region which most likely represented haemangioma. So, the final diagnosis of Klipple-Trenaunay Syndrome (KTS) was made. However, the finding that kept us engaged in this case was the presence of marked acanthocytosis (3+). To rule out the possible common causes of acanthocytosis, extensive laboratory tests were conducted but they all came out to be negative Table-2. Patient was discharged and kept on regular follow-up in OPD. His CBC report after 1 month of discharge showed Hb of 13.2g/dl and persistently elevated acanthocytes accounting for more than 40% of red cells (3+).

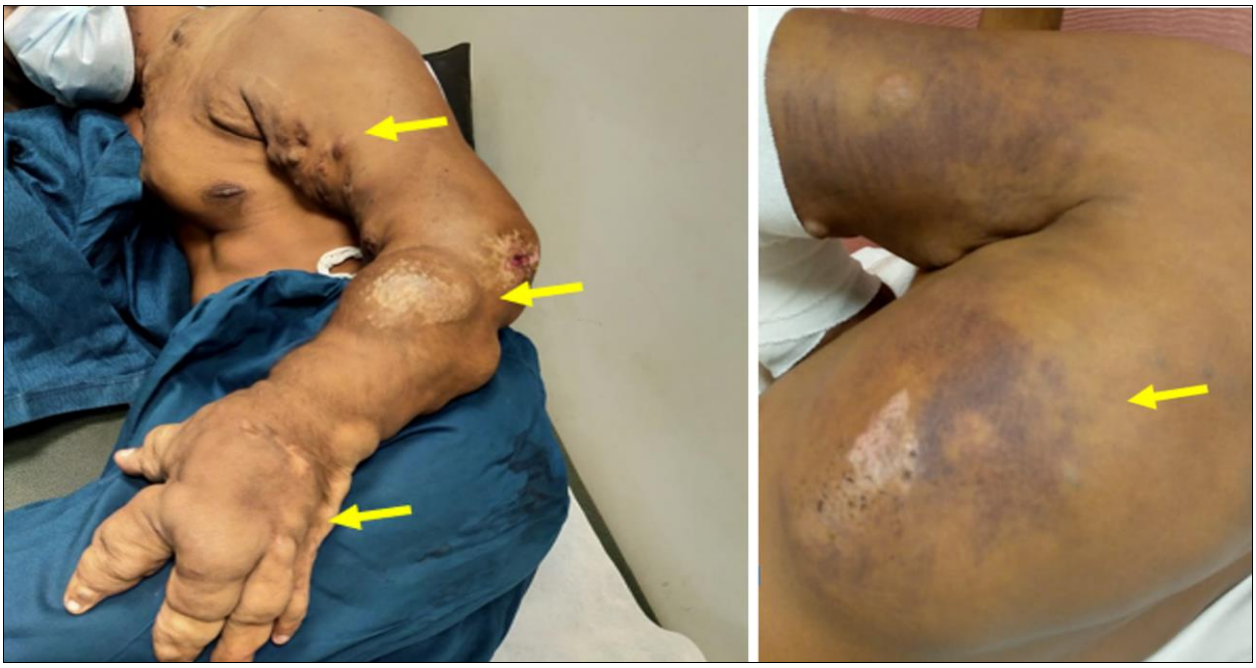

Figure-1(A): Right arm and right hand showing arteriovenous malformation with skin hypertrophy. (B): Right side of the back showing arteriovenous malformation with skin hypertrophy

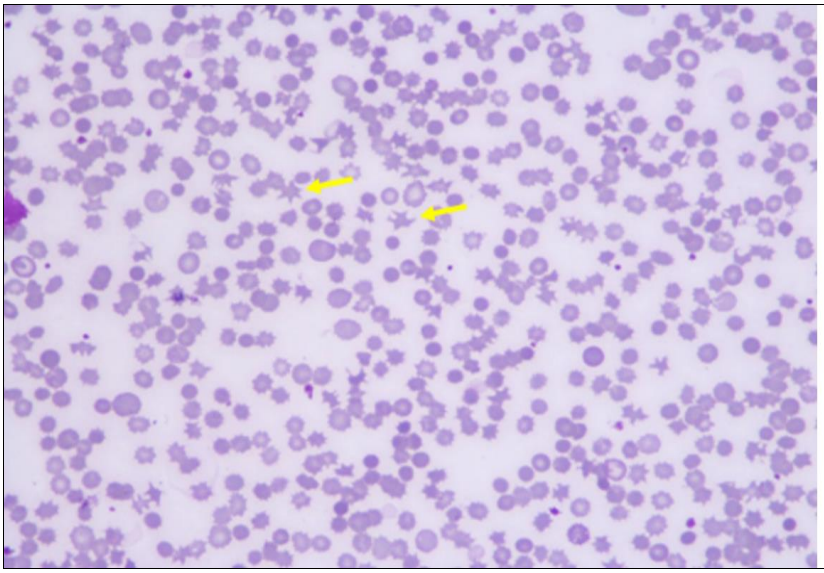

Figure-2: Peripheral smear showing acanthocytosis.

Figure-3: Haemangioma is evident in recovering wound on left thigh.

Table-1: (Abbreviations) MCV=Mean Corpuscular Volume, MCH=Mean Corpuscular Haemoglobin, TLC=Total Leucocytes Count, PT=Prothrombin Time, aPTT=activated Partial Thromboplastin Time, FDP=Fibrin Degradation Product.

Baseline laboratory Investigations
CBC
Hemoglobin 7.8 g/dl (Normal range: 11.3–17.5g/dl)
Hematocrit 28% (Normal range: 36–50%)
MCV 79.2fl (Normal range: 76–96fl)
MCH 34pg (Normal range: 27–34pg)
TLC 15.7 $x10^9$/L (Normal range :4–11 $x10^9$/L)
Platelets 80 $x10^9$/L (Normal range :150–400 $x10^9$/L)
Coagulation profile
PT 13.8 (Control: 10 seconds)
aPTT 32.6 (Control: 25 seconds)
FDP >20kg/mi (Normal range: <0.5)
D-Dimer >35 mg/di (Normal range: <0.5)
Fibrinogen 89mg/di (Normal range: 200–400mg/di)

Table-2: (Abbreviations) LFTs = Liver Function Tests, TSH = Thyroid Stimulating Hormone LDL = Low Density Lipoprotein, HDL = High Density Lipoprotein

Baseline laboratory Investigation
LFTs
Total bilirubin 2.88 mg/dL (Normal range <1)
Direct bilirubin 1.89 mg/dL (Normal range <3.4)
Aspartate aminotransferase 24 U/L (Normal range <50)
Alanine aminotransferase 18 U/L (Normal range <41)
Alkaline phosphatase 60 U/L (Normal range <129)
Renal Function Test
Urea 23mg/dl (Normal range < 50 mg/dl)
Creatinine 0.72mg/dl (Normal range 0.6-1.3 mg/dl)
Thyroid Profile
TSH 7.09 p.lU/L (0.27–4.2)
Free T4 9.67 ng/ml (5.1–14.1)
Free T3 0.98 ng/ml (0.8-2)
Lipid Profile
Serum Cholesterol 132 mg/dL (<240)
LDL 81 mg/dL (<160)
HDL 28 mg/dL (>45)
Serum Triglycerides 120 mg/dL (<150)
Serum Albumin 3.98g/dL (3.4–-4.8)

DISCUSSION

Klipple-Trenaunay syndrome (KTS) is a vascular malformation syndrome comprising of varying involvement of cutaneous capillaries, veins, and lymphatics with hypertrophy of soft tissue and bones of the affected limb[10] with multiple clinical manifestations. Although a benign condition, it can present with life threatening bleeding or thrombosis due to irregular and chronically activated coagulation cascade leading to consumptive coagulopathy as witnessed in our patient who presented with deranged coagulation profile and excessive bleeding.[3] The occurrence of acanthocytosis in the setting of KTS is a rare finding and has not been very well reported. Few cases have been published so far which showed the association of KTS and acanthocytosis but underlying pathophysiology of this rare manifestation is not clearly established.[11,12] Extensive investigation is always needed to rule out other relatively common causes of spur cells in peripheral smear. Since Klipple-Trenaunay syndrome is an abnormality in mesodermal development and removal of the spleen is sometimes known to help in cases of extensive acanthocytosis.[11] Further studies on this unique association of acanthocytosis and KTS helps in making diagnosis of Klipple-Trenaunay syndrome without going for extensive workup for acanthocytosis and could also provide a plausible explanation of the abnormal morphology of RBCs in this rare disorder.

CONCLUSION

Our patient presented as an undiagnosed case of KTS with poor wound healing following a road traffic accident. On further investigation he was found to have marked acanthocytosis in red blood cell morphology, a finding that is rare and not well documented. Our extensive investigations failed to provide a cause for this abnormal red cell finding. Further studies on the mesodermal pathology of Klipple-Trenaunay Syndrome could provide an explanation for the rare finding of marked acanthocytosisseen in Klipple-Trenaunay syndrome.

Consent

An informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent can be shown by corresponding author upon request.

Conflict of interest

There is no conflict of interest.

REFERENCES

1. Müller-Wille R, Wildgruber M, Sadick M, Wohlgemuth WA. Vascular anomalies (part II): interventional therapy of peripheral vascular malformations. RöFo 2018;190(10):927–37.
2. Karunamurthy A, Pantanowitz L, Lepe JG, Reyes-Múgica M. Lethal outcomes in Klippel-Trenaunay syndrome. Pediatr Dev Pathol 2013;16(5):337–42.
3. Oduber C, Van Beers E, Bresser P, Van der Horst C, Meijers J, Gerdes V. Venous thromboembolism and prothrombotic parameters in Klippel-Trenaunay syndrome. Neth J Med 2013;71(5):246–52.
4. Horbach S, Lokhorst M, Oduber C, Middeldorp S, van der Post J, van der Horst C. Complications of pregnancy and labour in women with Klippel–Trénaunay syndrome: a nationwide cross-sectional study. BJOG 2017;124(11):1780–8.
5. Yasumoto A, Ishiura R, Narushima M, Yatomi Y. Successful treatment with dabigatran for consumptive coagulopathy associated with extensive vascular malformations. Blood Coagul Fibrinolysis 2017;28(8):670–4.

6. Dompmartin A, Acher A, Thibon P, Tourbach S, Hermans C, Deneys V, *et al*. Association of localized intravascular coagulopathy with venous malformations. Arch Dermatol 2008;144(7):873–7.
7. Palmer L, Briggs C, McFadden S, Zini G, Burthem J, Rozenberg G, *et al*. ICSH recommendations for the standardization of nomenclature and grading of peripheral blood cell morphological features. Int J Lab Hematol 2015;37(3):287–303.
8. Salvioli G, Rioli G, Lugli R, Salati R. Membrane lipid composition of red blood cells in liver disease: regression of spur cell anaemia after infusion of polyunsaturated phosphatidylcholine. Gut 1978;19(9):844–50.
9. Storch A, Kornhass M, Schwarz J. Testing for acanthocytosis A prospective reader-blinded study in movement disorder patients. J Neurol 2005;252(1):84–90.
10. Naganathan S, Tadi P. Klippel Trenaunay Weber Syndrome. 2022 Jul 19. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.
11. Withana M, Rodrigo C, Shivanthan MC, Warnakulasooriya S, Wimalachandra M, Gooneratne L, *et al*. Klippel-Trenaunay syndrome presenting with acanthocytosis and splenic and retroperitoneal lymphangioma: a case report. J Med Case Rep 2014;8:390.
12. Cruz H, Ferreira AM, Costa E, Barbot J, Freitas MI. Marked acanthocytosis in the setting of Klippel-Trenaunay syndrome: A case report. Int J Lab Hematol 2019;41(1):e10–2.

Submitted: 14-09-2022	*Revised: 24-10-2022*	*Accepted: 24-10-2022*

Address for Correspondence:

Dr. Syeda Mah Ali, Liaquat National Hospital, Karachi-Pakistan
Cell: +92 333 374 8606
Email: dr.mah92@gmail.com