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Deep Vein Thrombosis and Staphylococcal Sepsis in a Child: A Case Report

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Abstract

Background

Deep vein thrombosis is a rare condition in the paediatric population, and it tends to overlap with musculoskeletal infections such as cellulitis, myositis or osteomyelitis. When associated with Staphylococcal infection, it is linked to poor prognosis. It should be strongly suspected in any child presenting with unilateral lower limb pain and swelling, limited mobility and fever. This is a case report of a pediatric patient who presented to our centre with deep vein thrombosis secondary to an underlying *Staphylococcus aureus* sepsis.

Case presentation

We present a case of a previously healthy seven-year-old boy, Chagga by tribe, who presented with a two-day history of right lower limb pain and swelling, which began eight days after falling from a tree. Three days later, the boy became weak and was unable to walk. He was initially admitted to the surgical ward, where abdominal visceral and limb trauma was ruled out. Clinically, he was ill-looking, tachypnoeic, tachycardic and febrile. The affected limb was swollen, tender, warm on touch and had limited range of motion at the hip and knee joints. Doppler ultrasound of the right leg revealed deep vein thrombosis of the distal femoral and popliteal veins, and blood culture revealed *Staphylococcus aureus* infection. Treatment was started in pediatric ICU, where, unfortunately, the boy's condition continued to deteriorate, and three days later, the patient succumbed.

Conclusion

Deep vein thrombosis is relatively rare in the pediatric population. The occurrence has been shown to carry significantly high mortality if diagnosis and treatment are not done promptly. *Staphylococcus aureus* infection is very aggressive and has a unique propensity to cause venous thrombosis in association with cellulitis. The rapid evolution of septic emboli in DVT associated with Staphylococcal infection may complicate the management.

Keywords: *Pediatric deep vein thrombosis, Pulmonary septic emboli, Staphylococcus aureus, Staphylococcus sepsis.*

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Background

Venous thromboembolism is the development of a blood clot in veins. They are a major cause of morbidity and mortality in adults and rarely occur in the pediatric population. When they do occur, they are associated with significant mortality. There are three important factors in the development of a thromboemboli that Virchow described in 1845. These include impairment of blood flow, vascular injury and a hypercoagulability state (1).

Venous thromboembolism commonly occurs in the lower extremities, mainly in the iliac, femoral or popliteal veins and may present as unilateral leg, buttock or inguinal pain associated with the classic signs of inflammation (2). It is important to thoroughly examine the affected limb, measure the calf diameter in the affected leg and compare it with the contralateral leg. In the case of sepsis, the systemic inflammatory response mediates coagulation and endothelial cell activation (3). Platelet dysfunction decreased aggregation and complex alterations in platelet function predispose the patient to bleed. The derangement of the coagulation system is due to the generation of thrombin mediated by tissue factor and the dysfunction of the normal physiological anticoagulants and fibrinolytic agents. The inflammatory mediators, namely, tissue factor activation and micro-particles mainly derived from platelets, activate the intrinsic and extrinsic pathways leading to thrombin generation within the micro-vascular system. This predisposes the patient to form a thrombus (3).

Pulmonary embolism is a complication of deep vein thrombosis (DVT) and may present as sudden severe respiratory distress, tachycardia, dyspnoea, and hypoxia. It must be considered in cases of sudden cardiorespiratory deterioration in patients with DVT. Prompt diagnosis and treatment are vital so as to avoid any short- or long-term complications. Treatment of the underlying condition predisposing the patient to a DVT is essentially the hallmark of management. Specific DVT treatment involves antithrombotic therapy with unfractionated heparin (UFH), low molecular weight heparin (LMWH) or vitamin-K antagonists (Warfarin) (4). We present the case of a seven-year-old boy who was diagnosed with deep vein thrombosis secondary to Staphylococcal septicaemia with suspected pulmonary emboli.

Case Presentation

A previously healthy seven-year-old boy, Chagga by tribe, presented to our centre with a two-day history of right lower limb pain and swelling, which began eight days after falling

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from a tree. According to the father, the boy had climbed up the tree and was playing when he accidentally fell, landing on his right leg. There was no history of loss of consciousness. Three days later, the boy became weak and was unable to walk unsupported. He was then admitted to the surgical ward, where examination and investigations ruled out any fractures or visceral injuries.

Clinically, the boy was ill-looking, tachypnoeic with a respiratory rate of 50 breaths/minute, tachycardic with a pulse rate of 142 beats per minute, temperature of 38.2˚C, blood pressure of 100/60 mmHg and was saturating at 92% in room air and 98% on 4L/minute of oxygen therapy. The right lower limb at the thigh and calf area was swollen, tender, warm on touch, with calf circumference measuring 25.5 centimetres (Vs 25.0 cm on the left limb) with limited range of motion at the hip and knee joints. Chest examination revealed he had bilateral basal crepitations, a pericardial rub, and a pansystolic Grade-4 murmur heard best at the lower left sternal border.

His initial laboratory work-up showed a normal leukocyte count of 10.30 with a predominance of neutrophils (8.37 x 10^9/L), normal haemoglobin of 11.7g/dL and platelets of 180 x 10^9/L. He had a prolonged prothrombin time of 19.8 seconds and partial thromboplastin time of 73.2 seconds with a raised INR of 1.60. Doppler ultrasound of the right leg revealed deep vein thrombosis of the distal femoral and popliteal veins. ECG showed supraventricular tachycardia. A blood culture sample was taken and revealed *Staphylococcus aureus infection*. He was initiated on unfractionated heparin 750 units STAT then 1500 units TDS, Paracetamol 250mg TDS, IV Ceftriaxone 1g BD for seven days.

Two days post-admission, the boy's condition suddenly changed. He developed severe difficulty in breathing, persistent high-grade fevers and chest pain. Upon review, he was found to be desaturating with SPO_2 of 80% on room air, tachycardic with PR-157 beats/min, blood pressure of 100/70 mmHg, tachypnoiec with RR-60 breaths/minute and temperature ranging between 38.9^0C – 40.2^0C. Further examination found he had nasal flaring, grunting, severe intercostal indrawing, bilateral coarse crepitations and per abdomen; he had hepatomegaly of 3cm below the costal margin. He developed a small blister on his right knee, which burst, discharging a small amount of pus. His right lower limb was swollen, tender and warm.

Based on the respiratory findings, we had a suspicion of pulmonary septic embolism secondary to DVT with staphylococcal pneumonia and Staphylococcal septicaemia. A repeated blood work-up showed leukocytosis of 26 x 10^9/L, with a predominance of

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neutrophils of 25.09 x 10^9/L, a haemoglobin level of 8.7g/dL, normal serum creatinine of 87µmol/L, elevated serum urea of 10.12 mmol/L, hyponatremia of 126.60mmol/L, hyperkalemia of 5.36mmol/L, elevated lactate of 4.4mmol/L, lactate dehydrogenase of 600 U/L, AST of 220 U/L and ALT of 107 U/L. He had raised INR of 1.69, prolonged prothrombin time of 20.3 seconds and partial thromboplastin time (aPTT) was 84.7 seconds. A chest x-ray was ordered, and it showed diffuse bilateral infiltrates suggestive of multi-lobar pneumonia (Figure 1). This suggested renal and liver failure due to severe septicemia. His antibiotics were then switched to Vancomycin 300mg IV TDS and was also initiated on LMWH - Enoxaparin and Lasix.

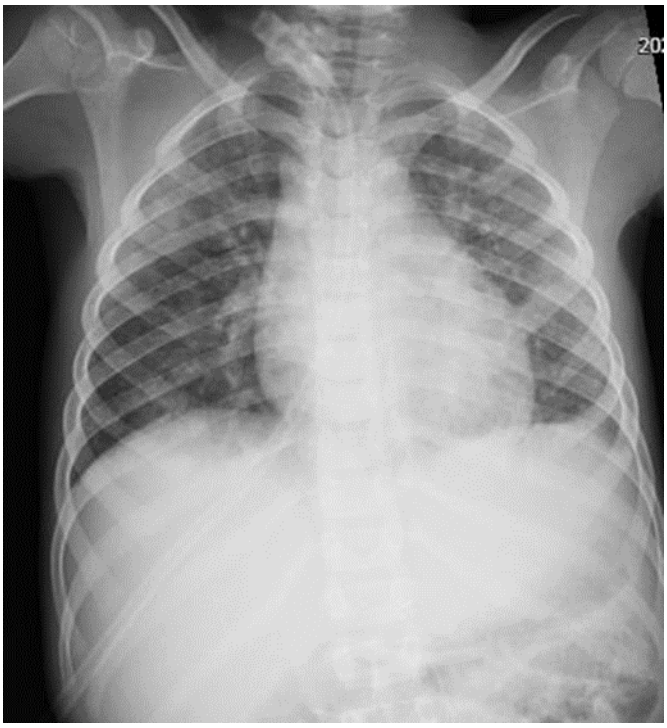

Figure 1. Plain chest x-ray showing multilobar pneumonia

During hospitalization, the boy's condition worsened, and three days later, the boy sustained a cardio-respiratory arrest with unsuccessful resuscitation. Unfortunately, the blood culture results were received after his demise revealed growth of *Staphylococcus aureus* sensitive to Clindamycin and Imipenem. The pus swab culture results also showed *Staphyloccocus aureus* sensitive only to Imipenem. The father also denied any features and family history of bleeding disorders (i.e., Haemophilia, Lupus) upon further investigating.

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Discussion

The incidence of DVT in children is relatively low, ranging from 0.14 to 0.21 per 10,000 children in the general population and 20 to 60 per 10,000 admissions among hospitalized children (2,5). The incidence of DVT in children seems to be on the rise (6). There are several risk factors known to predispose one to DVT. They include the presence of a central venous catheter, inherited hypercoagulable state, sepsis, trauma, heart disease, malignancy, immobility and chronic inflammatory illnesses (7). In the paediatric population, the major risk factors are the presence of a central venous catheter (CVC), trauma, congenital heart disease, malignancy, sepsis, inherited thrombophilia and protein C and S deficiancies (8). In children, it is commonly seen in infancy and teenage years, with the median age of occurrence being eight years (8). In our index case, trauma from the fall as well as the ensuing sepsis seem to be the trigger for the DVT. Though resources did not allow further testing to be done like G20210A mutation or other proteins and clotting Factors. Our patient's age (seven years) also put him close to the median for peak incidence.

Community-acquired methicillin resistant *Staphylococcus aureus* (MRSA) has especially been noted to be associated with DVT (8,9). Unfortunately, in our case, MRSA was not tested due to the lack of facilities at that time.

The occurrence of pulmonary embolism in children is stated to be low, but the mortality is as high as 30% (9). Resource constraints meant we were unable to do fibrinogen levels and D-dimer, which might have helped in early detection of the pulmonary emboli. Although not clearly indicated in children with sepsis, placement of intravascular filters might have also been beneficial. Unfortunately, this was beyond the resources available at our facility.

In a study by Maher et al., the authors found out that about 50% of their study participants had complete resolution of DVT by the end of treatment with LMWH, and only 12.5% had persistent thrombus at six months (10). Since Staphylococcal infections (particularly MRSA) increase the risk of DVT in children, there are recommendations for prophylactic anticoagulation in children with Staphylococcal infections (10). A study by Folsom et al. stated that liver enzymes raise due to liver failure and/or cirrhosis and increase the risk of VTE, hence they hypothesized that elevated liver enzymes associated positively with VTE incidence due to increased cytokines and coagulation factors leading to thrombotic diathesis. They found that high levels of AST and GGT preceded VTE onset (11).

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Conclusion

The systemic inflammatory response in severe sepsis has been shown to cause significant derangement in the normal physiological coagulation system by mediating the formation of a thrombus. *Staphylococcus aureus* has been found to have a very unique propensity to cause venous thrombosis in association with cellulitis, and the management may be complicated by the rapid evolution of a septic emboli. Deep vein thrombosis in correlation with septic pulmonary embolism (PE) is known to be relatively rare in the pediatric population. The occurrence of both DVT and PE in a child has been shown to carry a significantly high mortality if diagnosis and treatment is not done promptly, and even then, they have been associated with significant morbidity if the child survives. This case report highlights the burden and difficulties encountered in the management of severe sepsis and DVT in a resource-limited setting, the importance of escalating broad spectrum antimicrobial agents and initiating VTE prophylaxis earlier. Elevated liver enzymes can also be used as a predictor for VTE onset.

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from the patient's father for participation in this case report. A copy of the consent is available on record. Approval to publish was obtained from relevant authorities.

Consent for publication

Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

FM, JL and RP conceptualised and drafted the manuscript. MM, RM and BM reviewed the patient's medical records. All authors have read and approved the final manuscript.

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Abbreviations

CVC	Central Venous Catheter
DVT	Deep Vein Thrombosis
ICU	Intensive Care Unit
MRSA	Methicillin-Resistant Staphylococcal Aureus
PE	Pulmonary Embolism
VTE	Venous Thromboembolism

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