

Deep Venous thrombosis with osteomyelitis in a child having Protein C deficiency; A case report.

Sushant Ghate¹, Kumarswami R Dussa¹, Ashish Agarwal¹

ABSTRACT:

Deep venous thrombosis is not very common in pediatric orthopedic cases, although it may present in association with other pathologies. Recent reports have shown association between osteomyelitis and deep venous thrombosis (DVT).

We report a case of osteomyelitis in a child having deep venous thrombosis who was admitted for deep venous thrombosis and then diagnosed to have osteomyelitis. On further investigations, patient had protein C deficiency which is one of the rare causes of thrombotic tendencies. Diagnosis of osteomyelitis was delayed due to overlapping clinical signs. As DVT associated with osteomyelitis is known for complications like septic emboli and their sequel, increased awareness is required in the orthopedic community in order to diagnose and treat this condition appropriately so as to prevent the morbidity. We highlight on potential difficulties in diagnosing a case of deep venous thrombosis associated with osteomyelitis and brief review of related literature.

Keywords : Osteomyelitis; deep venous thrombosis .

INTRODUCTION:

Deep venous thrombosis and pulmonary embolism are rare in children with an estimated prevalence of <0.01%.^{1, 2, 3, 4} Data regarding association of DVT and osteomyelitis is not very clear but recent reports has shown definite association between deep musculoskeletal sepsis and deep venous thrombosis in children.^{1, 2, 3, 4} Features of deep venous thrombosis may mask the features of osteomyelitis or vice a versa because clinical features such as redness, swelling and pain are common in both conditions.^{4, 5} So, a high index of suspicion is required to diagnose concomitant occurrence of

DVT & osteomyelitis. There is currently no adequate explanation why children with osteomyelitis have increased susceptibility to develop DVT. Present case illustrates good example where increased awareness can facilitate a timely intervention and can prevent the morbidity.

CASE REPORT:

A nine year male child presented with complaints of pain in left knee and leg since 7 days. His mother gave a history of high grade fever for last 4-5 days and calf swelling. There was no history of swelling around knee joint. There was no history of any bleeding or coagulation disorders in the family.

On clinical examination, there was fixed flexion deformity of 10° (Fig 1) with no limitation of further flexion. Tenderness over calf and local warmth was present. Inguinal lymph nodes were palpable. Patient was admitted in pediatric ward and was diagnosed as a case of deep venous thrombosis of popliteal and distal left superficial femoral vein as shown in MR venography (Fig 2). Patient was referred to orthopedic services for knee deformity; Radiographs of the knee including whole length of tibia was found to be normal (Fig 2). Ultrasound of the affected knee was done which was also normal. Hematological investigations showed increased total leucocyte count with predominant polymorphonuclear cells. Erythrocyte sedimentation rate and C-reactive protein were raised. In view of palpable inguinal lymph nodes; raised polymorphonuclear count and history of fever are unlikely in DVT we further investigated the patient with bone scan which showed increased uptake of radioactive tracer in proximal tibia and mid shaft of tibia (Fig 4). After 7 days we repeated the radiographs of the patient which showed osteomyelitis of proximal tibia extending to diaphysis (Fig 3). The causative organism was isolated as *S.aureus* which was methicillin resistant (MRSA). For deep venous thrombosis, patient was further evaluated in the form of all hematological investigations and he was diagnosed with a deficiency of Protein C which is a one of the rare causes of thrombotic tendencies in children due to hypercoagulable state. Patient was treated with heparin for five days followed by overlap with warfarin and then continued with warfarin treatment monitoring the International Normalized Ratio (INR). As soon as patient was diagnosed with osteomyelitis, patient was started on antibiotic therapy which was given for six weeks and patient was given long leg knee brace in complete

¹ Department of Orthopaedics, B Y L Nair hospital & T N Medical college Mumbai, India.

Address for correspondence: Dr Sushant Ghate
Dept of Ortho. R N Cooper Municipal General hospital, Juhu,
Mumbai, India.
Email- ssushantghate@gmail.com

extension. At the end of six weeks, patient got rid of flexion deformity with full range of movements at the knee joint. MR venography showed recanalization of previously occluded popliteal and femoral veins (Fig 3). At two year follow up, patient is completely asymptomatic with full range of movements of knee.

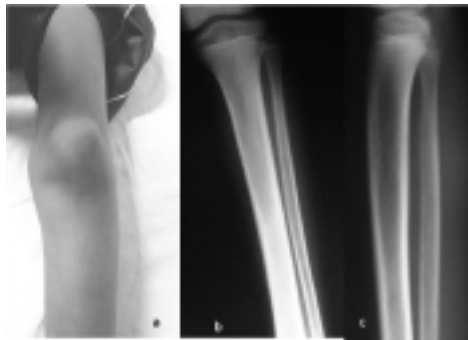


Fig 1: Clinical Photograph of the patients with Radiographs at the time of presentation. 1a) ?, b) ?, c)?

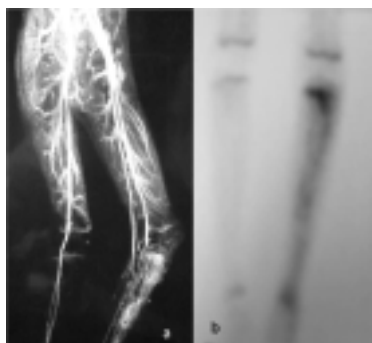


Fig 2a -MR venography showing DVT of left popliteal and distal femoral vessels. 2b-Bone scan showing increased radioactive tracer uptake in affected tibia

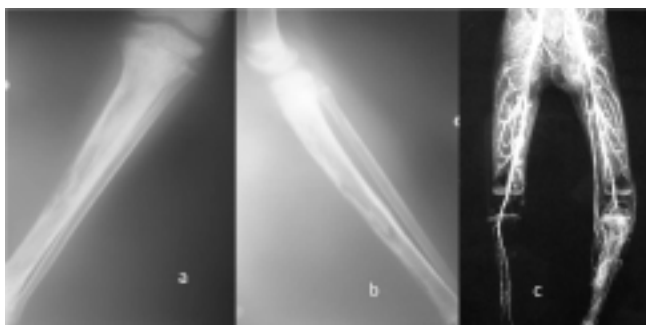


Figure 3 – Antero-posterior radiographs at 10 days post surgery showing osteomyelitis (a,b), six weeks post operative MR venography showing recanalization of occluded vessels (c).

DISCUSSION:

Deep venous thrombosis is uncommon in pediatric age group due to relative immaturity of thrombotic cascade.¹ In adults, post operative incidence has been described as high as 30-40% in contrast to children in whom the reported rate is as low as 1% after surgery. The commonly associated conditions

are intravenous catheters, post operative complications, extremity trauma and inheritable causes like factor five Leiden mutation, Anti thrombin 3 deficiency, Protein C and Protein S deficiency.^{1,6} Presentation of deep venous thrombosis is characterized by swelling of calf, tenderness over calf (Mose's sign) and tenderness on forced dorsiflexion of affected foot (Homan's sign).

Osteomyelitis usually present with sudden onset swelling, with high grade fever usually associated with chills. On clinical examination there is usually local warmth, tenderness, and tachycardia.

The problem in diagnosing a case of deep venous thrombosis in children is that you really need to have suspicion of having DVT in patient of osteomyelitis because DVT is not a common condition seen in pediatric age group. On the other hand, osteomyelitis is one of the common conditions presenting to the physician. Second thing is that it takes at least 10 days for earliest X-ray changes in osteomyelitis to appear. Radionuclide studies can be done using isotopes technetium-99m phosphate, gallium-67 citrate and indium-111-labeled leukocytes in suspected cases of osteomyelitis.⁷ Bone scan diagnoses osteomyelitis before the changes appear on X- Ray.^{8,9,10,11} Out of the three most commonly used radioisotopes 67Ga-Citrate scan augments diagnostic value of ⁹⁹Tc-MDP scan.¹¹ In-labeled WBC scan is useful in diagnosis of abscess⁸ On standard ^{99m}Tc-MDP scan, it sometimes may be difficult to differentiate between soft tissue uptake and bony uptake in cases with known cellulitis and possible underlying osteomyelitis. To address this problem, 3 phase ⁹⁹Tc-MDP scan was developed consisting of dynamic flow or angiogram images, blood pool images and 2-5 hr delayed images. It can detect osteomyelitis within 48 hours after clinical onset of infection but sometimes it may be negative in early phase of disease so bone scan might need to be repeated later.¹⁰ MRI can diagnose osteomyelitis as early as 48 hrs showing hypointense changes in marrow in T1 wt images and hyperintense changes in T2W. Post traumatic or surgical scarring is seen as hypointense on T1 and no changes on T2 images.¹¹

Review of literature shows definite association between osteomyelitis and development of deep venous thrombosis in pediatric patients.^{1,2,6,12,13} DVT is common in adults with sepsis in contrast to popular belief. A high index of suspicion should be maintained whenever infection is caused by S aureus involving spine, pelvis or lower extremities, especially in older children and having high C-reactive protein level >6mg/dl.^{2,13,14} A predisposing factor like Protein C deficiency might increase the risk of developing deep venous thrombosis but thrombosis is also found in patients with normal hematological profiles in association with osteomyelitis.² Also recent literature shows that the osteomyelitis is usually caused by S.aureus producing a toxin known as Panton Valentine leucocidin toxin has been proposed as predisposing factor.^{2,13,14} Higher rates of deep venous thrombosis has been

observed associated with methicillin resistant *S.aureus* as compared to methicillin sensitive *S.aureus*.^{2,13,15} Management of venous thrombosis in this setting may be complicated by rapid evolution of septic emboli.^{12,13,15} Location of osteomyelitis i.e. usually involving proximal tibia, femur, pelvis has been shown to have higher incidence of associated DVT.^{2,12} Diagnostic venous imaging should be done in these high risk patients such as Doppler venous ultra sound or magnetic resonance venography for early detection of DVT, hence preventing of catastrophic complications.

Key message is that factors such as generalized limb swelling, Staphylococcal sepsis, pulmonary septic emboli, older children, methicillin resistant *S.aureus* and proximal location of osteomyelitis should alert clinician to rule out the possibility of DVT associated with osteomyelitis so that treatment of DVT can be done at the earliest to prevent the complications or other investigations can be done to find out the etiology such as inheritable causes of DVT especially in children.

References:

1. Walsh S, Philips F. Deep venous thrombosis associated with paediatrics musculoskeletal sepsis. *J Paedtr Ortho*. 2002; 22: 329-32.
2. Hollmig ST, Copley LA, Browne RH, Grande LM, Wilson PL. Deep venous thrombosis associated with osteomyelitis in children. *J Bone Joint Surg Am*. 2007 Jul; 89(7): 1517-23.
3. Clark DJ. Venous thromboembolism in pediatric practice. *Pediatr Anaesth* 1999; 9: 475-84.
4. Gite A, Trivedi R, Ali US. Deep vein thrombosis associated with osteomyelitis. *Indian Pediatr*. 2008 May; 45(5): 418-9.
5. Jupiter JB, Ehrlich MG, Novelline RA, Leeds HC, Keim D. The association of septic thrombophlebitis with subperiosteal abscesses in children. *J Pediatr*. 1982 Nov; 101(5): 690-5.
6. Horvath FL, Brodeur AE, Cherry JD. Deep thrombophlebitis associated with acute
7. osteomyelitis. *J Pediatr*. 1971 Nov; 79(5): 815-8. Gupta NC, Prezio JA. Radionuclide imaging in osteomyelitis. *Semin Nucl Med*. 1988 Oct; 18(4): 287-99. Gold RH, Hawkins RA, Katz RD. Bacterial osteomyelitis: findings on plain radiography, CT, MR, and scintigraphy. *AJR Am J Roentgenol*. 1991 Aug; 157(2): 365-70.
9. Berlin S, Heidelberg. Bone scan in acute osteomyelitis: *European journal of nuclear medicine and molecular genetics* Jun 1980; 5: 267-69.
10. Howie DW, Savage JP, Wilson TG, Paterson D. Technetium phosphate bone scan in diagnosis of acute osteomyelitis in children. *J Bone joint Surg Am*. 1983; 65: 481-86.
11. Lazzarini L, Mader JT, Calhoun JH. Osteomyelitis in long bones. *J Bone Joint Surg Am*. 2004 Oct; 86-A(10): 2305-18. Crary SE, Buchanan GR, Drake CE, Journeycake JM. Venous thrombosis and thromboembolism in children with osteomyelitis. *J Pediatr*. 2006 Oct; 149(4): 537-41.
13. Bouchoucha S, Benghachame F, Trifa M, Saied W, Douira W, Nessib MN, Ghachem MB. Deep venous thrombosis associated with acute hematogenous osteomyelitis in children. *Orthop Traumatol Surg Res*. 2010 Sep 9. [Epub ahead of print]
14. Smith L, Hamill J, Metcalf R, Walsh S. Caval thrombectomy for severe staphylococcal osteomyelitis. *J Pediatr Surg*. 1997 Jan; 32(1): 112-4.
15. Gonzalez BE, Teruya J, Mahoney DH Jr, Hulten KG, Edwards R, Lamberth LB, Hammerman WA, Mason EO Jr, Kaplan SL. Venous thrombosis associated with staphylococcal osteomyelitis in children. *Pediatrics*. 2006 May; 117(5): 1673-9.

Source of Support: Nil, Conflict of Interest: none