

An Unusual Case Study of Idiopathic Bilateral Deep Vein Thrombosis and Osteonecrosis of the Left Distal Tibia in an 11-year-old Girl

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Learning Point of the Article:

Clinicians should consider the possibility of DVT and traumatic osteonecrosis in children with persistent leg pain and swelling.

Abstract

Introduction: Deep vein thrombosis (DVTs) in children is rare, normally linked to pathologies such as major traumatic injury, thrombophilia, and malignancy. Osteonecrosis is still poorly understood. There is growing support to include hypercoagulable states as a predisposing factor, however, no definitive correlation has been found. At present, there are no conclusive literature on the links between osteonecrosis and DVT.

Case Presentation: This report describes an unusual and rare case of osteonecrosis and idiopathic DVT in an 11-year-old girl who initially presented with a sprained left ankle. On follow-up, pain was persistent and subsequent radiological investigations revealed extensive DVT, and magnetic resonance imaging scan revealed osteonecrosis of the distal left tibia. Initial blood tests were normal, however with follow-up with hematology, a diagnosis of antithrombin deficiency was made, with the treatment of lifelong anticoagulation. Our patient had continued orthopedic input for clinical and radiographic surveillance to monitor leg length discrepancy.

Conclusion: This case highlights the need to engage in close follow-up and the cautionary care required when young children present with non-resolving severe pain, to consider osteonecrosis and DVT. Our case also highlights the need for further research into the relationship between minor injuries and DVTs and osteonecrosis in children, and the potential synergistic relationship between DVTs and osteonecrosis.

Keywords: Osteonecrosis, pediatric orthopedics, deep vein thrombosis, coagulopathy.

Introduction

Deep vein thrombosis (DVTs) in children is rare. Estimates of the annual incidence range from 0.14 to 0.21 per 10,000 children [1]. This rises to up to 58 per 10,000 in hospitalized admissions [2]. Rates are higher in children with pathologies such as thrombophilia, malignancy, and cardiac disease. Major traumatic injury is also indicated as a risk factor. Studies have shown that although the risk is greater following traumatic injury, it is still substantially lower than with adult trauma patients, with rates currently reported at 0.03–0.4% [1]. Although rare, the importance of correctly diagnosing and treating DVT is paramount to prevent mortality from complications, such as

pulmonary embolism, which has been reported [3].

Osteonecrosis normally arises from direct damage to the bone's blood supply, bone, or marrow. However, in many patients, the mechanism of this pathology is not fully understood [4]. In children, osteonecrosis normally is caused by sickle cell disease, injury to bone through fracture or dislocation, and long-term corticosteroids for both non-cancer and cancer diseases such as ALL or lymphoma.

At present, there is no conclusive literature on the links between osteonecrosis and DVT.

To the best of our knowledge, no case reports have been published of DVT and osteonecrosis occurring in children at the

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Author's Photo Gallery



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Figure 1: Initial normal anteroposterior and lateral radiographs.



Figure 2: Radiographs on the 2-week follow-up post-initial injury.



Figure 3: Radiographs showing periosteal reactions.

same time. We present a rare and unusual case of a child who developed both osteonecrosis and bilateral DVTs following a minor ankle injury.

Case Report

An 11-year-old girl was seen in A&E after spraining her left ankle while ice skating. Examination and plain radiographs showed no obvious injury (Fig. 1) and she was discharged home. She represented 3 days later, unable to weight bear on the left leg and was reviewed in fracture clinic. She was diagnosed with a soft-tissue injury, provided with a functional walking boot, for follow-up 2 weeks later.

On follow-up of her left ankle, she had both lateral and medial malleolar tenderness, ankle swelling, and decreased range of movement. She was neurovascularly intact. Repeat plain films demonstrated periosteal reaction at the left distal tibia (Fig. 2). She continued with the walking boot and referred for physiotherapy.

A month following, she developed swelling and blue discoloration in the right leg; lower limb duplex confirmed a right-sided DVT. Hematological review and subsequent thrombophilia screen were deemed normal and she was started on dalteparin for 6 months. A repeat duplex scan a month later showed acute iliofemoral DVT bilaterally extending to the distal inferior vena cava.

The patient was reviewed in fracture clinic, 6 weeks from the initial injury. Plain films confirmed established periosteal reactions in the left distal tibia (Fig. 3). Magnetic resonance

imaging (MRI) confirmed associated osteonecrosis of the left distal tibia (Fig. 4).

A repeat MRI 6 weeks later (Fig. 4) showed progression of bony changes with patchy osteoporosis throughout all the joints in the left hind foot and mid foot. There was marked edema in the head of the talus and navicular. It was noted that there was a possible new area of osteonecrosis in the head of the talus. Radiographic follow-up, 3 months post the initial injury (Fig. 5) demonstrated evidence of patchy necrosis and early closure of the medial growth plate. By her 6-month follow-up, the patient was essentially symptom free.

Hematologists on follow-up reviewed all previous hematological tests. A diagnosis of antithrombin deficiency was made, with the treatment of lifelong anticoagulation. There is continued vascular surgery input for the lower limb edema and long and short saphenous varices which are currently treated with compression stockings. Our patient has continued orthopedic input for clinical and radiographic surveillance to monitor for an angular deformity and leg length discrepancy. On the patient's 2nd year of follow-up, the patient had noted no difference in her leg length and had an anatomical leg length discrepancy of 15 mm (Fig. 6). In summary, our patient has a 15 mm anatomical discrepancy and left leg and abdominal varicosities with a diagnosis of anti-thrombin deficiency.

Discussion

This is a rare and unusual case of a child who developed bilateral DVTs and osteonecrosis following a minor injury. DVTs in



Figure 4: Sagittal and coronal view of magnetic resonance imaging at 6 weeks follow-up.



Figure 5: Plain films at 3-month follow-up of initial injury.





Figure 6: Plain films taken of patient at 14 years of age.

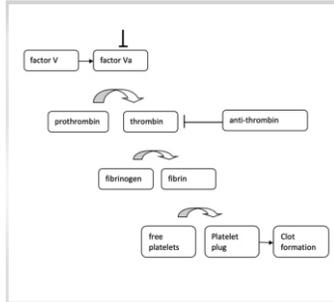


Image 1: Summary of the key components of the coagulation cascade.

children are rare, with an increased risk in children with other conditions. An analysis of the Canadian registry of DVT and PE in children, highlighted conditions associated with DVT. These included: Inherited pre-thrombotic disorder, systemic infection, cancer, congenital heart disease, central venous catheters, trauma, total parenteral nutrition due to short gut syndrome, nephrotic syndrome, surgery, oral contraceptives, obesity, SLE, sickle cell anemia, and liver failure [5]. 137 children were included in study and 132 had identifiable associated conditions. The study found that 8.8% of the children were found to have inherited prothrombotic disorders. The authors added that only 45 children out of the 137 were evaluated for prothrombotic disorders, and therefore, thrombophilia could be more prevalent than their findings. The same study showed that DVT without any associated condition is extremely rare.

During a 7-year study, Raffini et al. found that the annual rate of VTE had increased by 70% from 34 to 58 cases per 10,000 hospital admissions at Children's Hospital of Philadelphia [2]. The authors state that it is difficult to argue whether there is a true increase in pediatric VTEs or whether there is an increase in detection of previously undiagnosed VTE due to heightened awareness of VTE. Other authors have hypothesized that progress in radiological imaging and increased survival of children with previously incurable diseases due to medical and surgical advances, could add to the rise of pediatric VTE cases [6].

Although DVTs are rare in children, diagnosis and subsequent treatment should be carried out promptly. This is to prevent the complication of PE [7] and potential fatalities which have been reported in children. Sridhar et al. described a case of 6 years old with a fatal PE following DVT of the lower extremity where the initial diagnosis was irritable hip and pneumonia [3].

Our patient had no family history of coagulopathy or any medical history. Preliminary hematological investigations were considered normal and the initial diagnosis was of an idiopathic DVT. However, further review by hematologists suggested that our patient most likely had a new mutation of antithrombin deficiency. Antithrombin deficiency disorder is characterized by a tendency to form clots in the veins. Antithrombin is an

important glycoprotein in the coagulation cascade (Image 1). It inhibits thrombin and factor Xa and IXa which are required to form thrombin. With reduced levels of antithrombin, more thrombin is activated, leading to increased likelihood of clot formation.

Antithrombin deficiency is diagnosed by detecting low antithrombin levels in the blood. The initial antithrombin level for our patient was below the normal range (51.9 iu/d). This was not initially considered to be abnormal, as acute clots can consume antithrombin, reducing its levels. The diagnosis of antithrombin deficiency was later made as antithrombin levels persistently stayed low (49 iu/d) despite treatment. It is, therefore, imperative that antithrombin levels are checked post-treatment, to make the definitive diagnosis of antithrombin deficiency disease.

de la Morena-Barrio et al. looked at 968 patients known to have antithrombin deficiency. They found 7.5% of their subjects formed a thrombus before the age of 19. They also noted that the peak incidence to form a thrombus was during neonatal and adolescent periods [8].

Other authors have stressed the need to carefully investigate children with thrombosis to find an underlying cause due to the high recurrence rate [9].

Osteonecrosis arises due to direct damage to the bone's blood supply, however, in many patients, the mechanism of osteonecrosis is not fully understood. Prevalence for osteonecrosis varies widely in literature, this may reflect the differences in the definition and cause of osteonecrosis. It is thought that several factors could cause osteonecrosis, such as glucocorticoids, alcohol, SLE, antiphospholipid antibodies, trauma, sickle cell disease, Gaucher disease, ALL, decompression disease, transplantation, inherited thrombophilia, radiation therapy, and HIV infection [13]. It is pertinent to mention that in children, in addition to the factors mentioned, many conditions within the osteochondrosis family (such as Legg-Calve-Perthes and Kohler disease) can present with osteonecrosis but with elements of reossification [4].

The classic MRI appearance of osteonecrosis is that of a segmental area of low signal intensity in the subchondral bone, surrounded by a low signal intensity border. A double line sign can be present. When osteonecrosis presents as an area of diffuse low signal intensity, it can be difficult to differentiate it from tumors. With calcifications, osteonecrosis can also simulate those of chondroid lesions [10]. We would like to note that differentiating a bone infarct from an enchondroma or low-grade chondrosarcoma on plain films is difficult. Cartilaginous tumors such as chondrosarcoma may show endosteal scalloping which would not be present in osteonecrosis. A case reported by

Shimizu et al. discusses the difficulty of differentiating osteonecrosis from chondrosarcoma from T1-weighted MRI and that contrast-enhanced T1 MRI played an important role in diagnosis [11]. It is important for clinicians to be aware of other pathologies that can give a similar MRI image to osteonecrosis. Our patient's MRI images and clinical picture gave us a confident diagnosis of osteonecrosis.

It has been hypothesized for over 50 years that increased intravascular coagulation could be a pathogenetic mechanism that contributes to osteonecrosis [11, 12, 13, 14, 15]. However to date, there is no definitive correlation. Lykissas et al. discussed the theories behind the hypothesis, exploring both primary factors of hypercoagulability, such as protein C and protein S deficiency, and secondary factors such as pregnancy, systemic lupus erythematosus, and sickle cell disease. The authors stressed that with the growing support for the hypothesis, there is a need for research to demonstrate definitive correlation [15].

At present, there is no evidence to suggest any correlation between minor injuries (no fractures) and osteonecrosis. A case report in the journal of pediatric orthopedics, discussed a 5-year-old boy developing osteonecrosis 2 years after sustaining an ankle sprain [16]. The osteonecrosis in the distal fibular epiphysis required surgical treatment. This patient was healthy with no previous medical history. Further research in this area would be beneficial, to see whether minor injuries could be a trigger for osteonecrosis.

Our patient's osteonecrosis in the left distal tibia extended to her physis. Leg length discrepancy and growth were, therefore, monitored. When children have not reached skeletal maturity, it is being advised that observation is undertaken until growth is complete. When leg length discrepancy is >2 cm, simple non-surgical interventions such as shoe lifts could be offered or surgical options can be explored. Our patient required no treatment for her osteonecrosis as there was so evidence of bone collapse or instability. Our patient is left with an anatomical leg length discrepancy of 15 mm, but functionally asymptomatic pursuing activities, she was able to enjoy, before her injury.

Declaration of patient consent : The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

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At present, there is no conclusive literature on the links between DVT and osteonecrosis. We have two hypotheses to explain how our patient developed both DVT and osteonecrosis at the same period of time. Our first hypothesis is that the initial ankle injury triggered osteonecrosis. With the pain, reduced mobility, and underlying antithrombin deficiency, this promoted the development of the DVT. Our second hypothesis is that the pain from the initial ankle injury and resultant reduced mobility, with the underlying antithrombin deficiency triggered the DVT. The formation of the DVT subsequently compromised the blood supply to the left distal tibia causing osteonecrosis.

Conclusion

We have presented a rare and unusual case of a child who developed both osteonecrosis and bilateral DVTs. The main cause for the formation of the DVT was our patient's antithrombin deficiency, however, we are unable to definitively confirm the cause of her osteonecrosis. Our case highlights that further research is required to look at whether there is a pathological link between DVTs and osteonecrosis, and whether there is a definitive correlation between hypercoagulable states and osteonecrosis. The case also highlights the need for further research on the relationship between minor injuries, DVT, and osteonecrosis. In those diagnosed with DVT, it is imperative that risk factors such as thrombophilia are considered and antithrombin levels are checked post-treatment to make a definitive diagnosis.

Clinical Message

Both DVT and traumatic osteonecrosis are rare in children. Clinicians should consider the possibility of these diagnoses in children with persistent leg pain and swelling. Further research is required to look at the relationship between DVTs and osteonecrosis, and other factors such as minor injuries. Injuries near the physis require follow-up to monitor growth and leg length discrepancy. Complex cases require a multispecialty approach.



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