*Case report*

# Deep vein thrombosis associated with *Staphylococcus aureus* septicemia

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A 12-year-old boy was admitted to a provincial hospital with a history of high fever, right knee pain and swelling. He had fallen and injured both his knees one month previously, but did not seek treatment. He received intravenous antibiotics for seven days before being transferred to Chiang Mai University Hospital, with persistent knee pain and constant high fever. His blood cultures were positive for *Staphylococcus aureus*. Doppler ultrasound of the right leg showed venous thrombosis in the thigh, and a subsequent bone scan was positive for osteomyelitis adjacent to the thrombus. He was treated with anticoagulants. Three days after the transfer, he had severe right lower lobe pneumonia, and cloxacillin, clindamycin, and amikacin were prescribed. He showed clinical improvement markedly and was transferred back to the provincial hospital for planned long-term anticoagulation and antimicrobial treatment. **Chiang Mai Medical Journal 2012;51(3):87-91.**

**Keywords**: *Staphylococcus aureus*, septicaemia, deep vein thrombosis

Pediatric deep vein thrombosis (DVT) is uncommon and occurs in only 0.7-4.9 cases per 10,000 children [1-2]. Two thirds of DVT cases are associated with indwelling central lines and oncological diseases, and few are associated with sepsis [1-2]. DVT is often overlooked in pediatric patients presenting with limb pain. *Staphylococcus aureus* especially antibiotic resistant strains, is reported to be the main cause of DVT [3-4]. Panton-Valentine leukocidin-positive (PVL+) *S. aureus* is associated with enhanced inflammatory response and local disease in children with severe acute hematogenous osteomyelitis [5-7]. The PVL+ genes are found most likely in methicillin-resistant *S. aureus* (MRSA) strains; however, they can be detected also in methicillin-sensitive strains. Physicians should include the possibility of *S. aureus* septicemia as an underlying cause of DVT when making a differential diagnosis, and they should be aware of such conditions when facing children who present with swelling of the extremities with pain.

## Case report

A 12-year-old boy, who had been healthy previously, presented at a provincial hospital with seven days of fever and tenderness around the right thigh and knee. He reported falling and injuring both knees one month earlier, but did not seek any treatment because of having no pain and being able to walk normally. An arthrocentesis was performed, and organisms were exhibited in the culture of fluid from the affected part. Two separate blood cultures were taken prior to starting the boy on cloxacillin and gentamicin. After 24

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hours, when the blood cultures returned a positive result for methicillin sensitive staphylococcus aureues (MSSA), antibiotics was switched to cloxacillin and cefotaxime. His fever was resolved with antibiotics, but he exhibited persistent right knee and right thigh pain accompanied by swelling and restricted range of motion. He was then transferred to our medical center for further management.

On arrival, he was febrile (38.9 °C), and had a respiratory rate of 24 breaths per minute. On physical examination, his right knee was notably in a flexed position, grossly swollen and erythematous in comparison to the left knee (Figure 1A). Deeper palpation revealed an indurated, tender, cord-like mass in the distal right thigh near the medial aspect of the knee (Figure 1B). His physical examination was otherwise unremarkablel

Laboratory investigation noted a hemoglobin level of 11.6 g/dL, white blood cell count of 1.16 cells/L, platelet count of 574 cells/L, erythrocyte sedimentation rate (ESR) of 104 mm/hour, and C-reactive protein level of 10.3 mg/L. A coagulation panel revealed a prothrombin time of 11.3 seconds, and partial thromboplastin time of 25.5 seconds. Electrolytes, liver function tests, and urinalysis were normal. Blood cultures showed nogrowth. The levels of anticardiolipin IsM, IgG, protein C and protein S were normal. Laboratory testing of PVL genes was not available. The electrocardiogram, echocardiogram and arterial blood gas were within normal limits. Bilateral knee films on admission were normal. An initial chest x-ray revealed an infiltrate in the area of the right lower lung (Figure 2A). Doppler ultrasound of the right leg showed evidence of venous thrombosis in the superficial femoral and great saphenous vein without evidence of abscess formation (Figure 3A and 3B). The bone scan exhibited osteomyelitis of the right proximal tibia (Figure 4).

Severe *S. aureus* septicemia with osteomyelitis, pneumonia and DVT were diagnosed. Antibiotic treatment with intravenous cloxacillin, clindamycin, and amikacin was initiated. Anticoagulation therapy with heparin was started, and transitioned to low molecular weight heparin after 36 hours. Despite reports of defervescence at the provincial hospital, the patient's fever on admission continued for the first three days and he developed tachypnea. A chest x-ray on day three of hospitalization showed that the right lower lobe lung infiltrate had progressed (Figure 2B), accompanied by decreased breath sounds of the right lung. The antibiotics were switched to cloxacillin, clindamycin and amikacin. On the 7$^{th}$ day of admission, the patient had no fever or tachypnea, and his lung signs were normal. He had no clinical symptoms of pulmonary embolism such as hemoptysis, dyspnea, tachypnea or pleuritic chest pain during admission. He could walk without pain or support. Heparin was transitioned to oral warfarin with planned long-term anticoagulation, as well as a six weeks course of IV cloxacillin and clindamycin at the provincial hospital. Amikacin was discontinued at this time. Six weeks after treatment, had the patient's ESR was 34 mm/hour and his level C-reactive protein less than 2.9 mg/L.

## Discussion

*S. aureus* septicemia presents a rare but potentially serious cause of DVT. Septicemia triggers thromboses through the processes described in Virchow's triad: stasis, hypercoagulability and endothelial damage. More specifically, exotoxins released by *S. aureus* cause the aggregation of platelets and spasm of smooth muscles

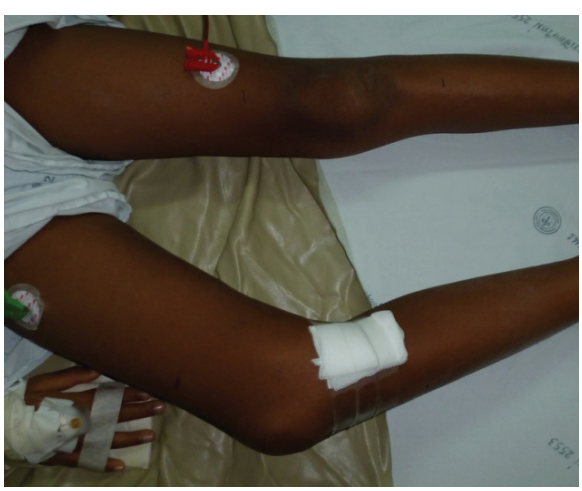

**Figure 1. A**: Right knee and thigh swelling with restricted range of motion

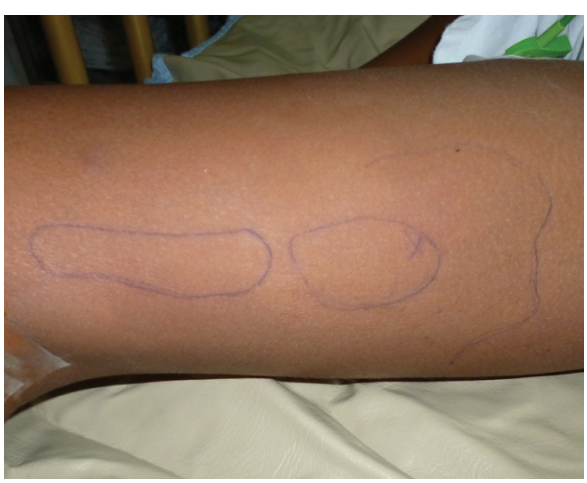

**Figure 1. B**: Cord-like mass present in the distal right thigh near the medial aspect of the knee

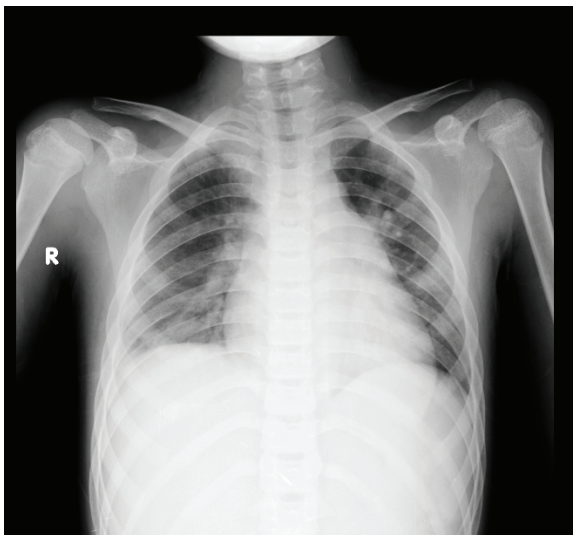


**Figure 2. A**: Chest x-ray at transfer to our medical centre showing right lower lung infiltration

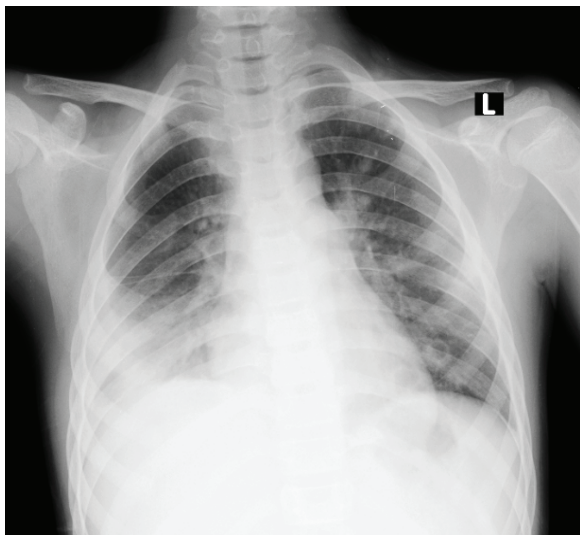


**Figure 2. B**: Chest x-ray three days after admission showing progressive right lower lobe infiltrate

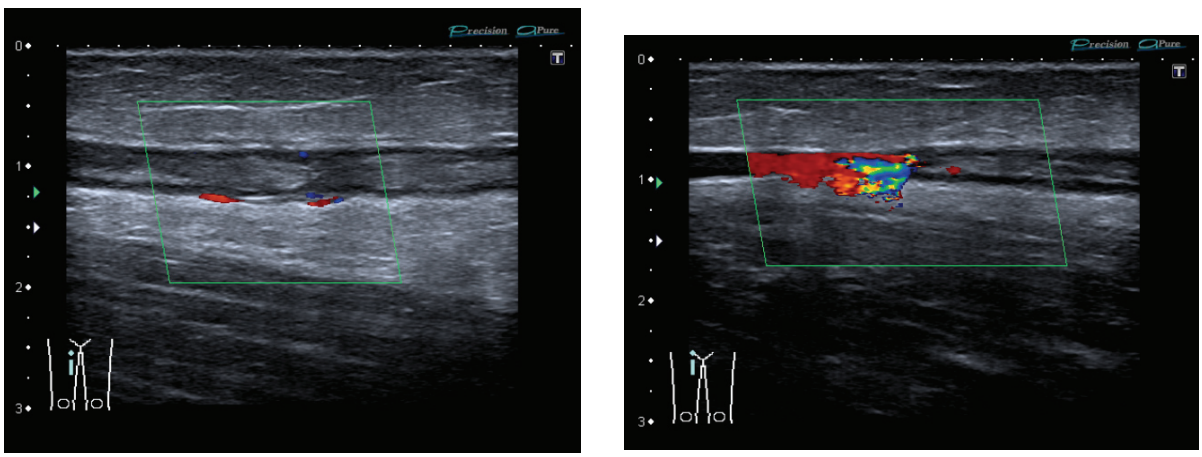

**Figure 3.** Doppler ultrasound of the right leg showing venous thrombosis in the superficial femoral vein (A, left) and great saphenous (B, right) vein of the right thigh

through their association with cell membranes. Coagulation is supported further by the release of local staphylococcal enzymes (like coagulase), which cause clot formation by interacting with fibrinogen. Through these processes, a localized infection, like osteomyelitis, creates an environment that is favourable to the formation of an adjoining DVT [8-12] As noted, DVT associated with *S. aureus* septicemia is rare, and the outcomes in this context are often serious. Existent case reports are uncommon, but demonstrate serious complication rates of up to 33% [13-14]. Serious complications of severe septicaemia that are common include pulmonary embolism, unwanted side effects from anticoagulation, and death. Findings from previous studies show that DVT associates with musculoskeletal infection, and is more common in children who

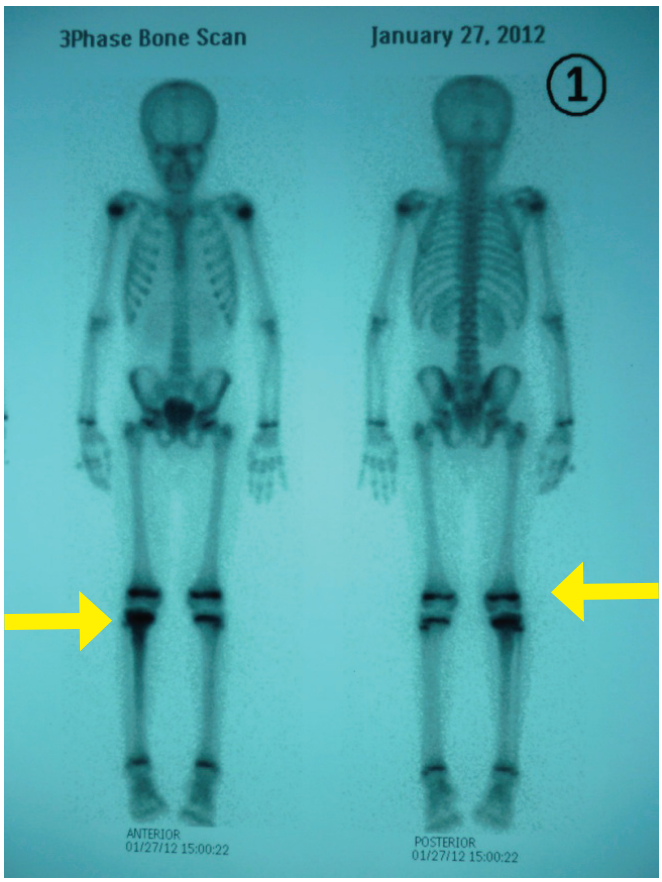


**Figure 4.** Bone scan showing right proximal tibial osteomyelitis (arrow)

present with a C-reactive protein level of more than 60 mg/L [9-10]. In this case, however the C-reactive protein level was relatively low (10.3 mg/L). Anticoagulants and antibiotics, including beta-lactams such as cloxacillin for MSSA infection, remain the mainstay of treatment. In severe cases, aminoglycoside such as gentamicin or amikacin, and clindamycin may be added [1, 3-5, 8]. Surgical involvement is reserved for failure or contraindication of anticoagulation therapy, and is followed usually by long-term anticoagulation. Physicians should assess the risk factors for any children with *S. aureus* septicemia and provide early treatment in order to prevent DVT. While DVT in this context is rarely described in the literature, outcomes without serious morbidity are even less common. In this case, the treatment outcome was satisfactory, unlike those reported in previous case reports, where a delay in treatment caused harmful complications [13, 14]

## Conclusion

DVT due to *S. aureus* septicemia is associated with significant morbidity and mortality. Physicians should consider this condition when facing patients with *S. aureus* septicemia and pain of the extremities. Successful outcome relies on early diagnosis, and treatment with antibiotics and anticoagulants.

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ภาวะลิ่มเลือดอุดตันในหลอดเลือดดำจากการติดเชื้อสแตปฟิโรคอคคัสออเรียสในกระแสเลือด

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**บทคัดย่อ**

ผู้ป่วยเด็กชายอายุ 12 ปี เข้ารับการรักษาในโรงพยาบาลจังหวัด ด้วยอาการไข้สูง ปวดบวมบริเวณหัวเข่าขวา ผู้ป่วยมีประวัติตกจากที่สูง 1 เดือนก่อนมาโรงพยาบาล ขณะรักษาที่โรงพยาบาลจังหวัดได้รับยาปฏิชีวนะเข้าทางหลอดเลือดดำเป็นเวลา 7 วัน ก่อนถูกส่งตัวมายังโรงพยาบาลมหาราชนครเชียงใหม่ ผลเพาะเชื้อในกระแสเลือด พบว่า มีเชื้อสแตปฟิโรคอคคัสออเรียส ผลการตรวจอัลตร้าซาวน์คลื่นเสียงบริเวณขาขวา พบว่ามีลิ่มเลือดอุดตันในหลอดเลือดดำบริเวณขาขวา และมีภาวะของกระดูกอักเสบในบริเวณใกล้เคียง ผู้ป่วยได้รับการรักษาด้วยยาต้านลิ่มเลือด และยาปฏิชีวนะกลุ่มคลอคซาซิลิน คลินดามัยซิน และอมิกาซิน ขณะนอนโรงพยาบาลผู้ป่วยมีอาการปอดบวมบริเวณซีกขวาล่างร่วมด้วย และผู้ป่วยมีอาการดีขึ้นหลังจากได้รับการรักษา ก่อนถูกส่งตัวกลับเพื่อรักษาต่อที่โรงพยาบาลจังหวัด **เชียงใหม่เวชสาร 2555;51(3):87-91.**

**คำสำคัญ:** สแตปฟิโรคอคคัสออเรียส การติดเชื้อในกระแสเลือด ลิ่มเลือดอุดตันในหลอดเลือดดำ