CASE REPORT

Spinal subdural haematoma: a rare complication of low-molecular-weight heparin therapy

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A 52-year-old man presented with chest pain, diarrhoea, rash, and arthritis. The use of low-molecular-weight heparin for suspected pulmonary embolism or angina led to a spinal subdural haematoma 3 days later. He was retrospectively confirmed to have *Salmonella paratyphi* infection. The clinical presentation and management of spinal subdural haematomas, and the incidence and manifestations of reactive arthritis related to *Salmonella* infections are briefly discussed.

Case report

A 52-year-old man presented to us with a 1-day history of chest pain, abdominal pain, watery diarrhoea, vomiting, and rash in February 2007. He had no fever and no respiratory symptoms. There was no history of a back injury but 4 days before the onset of his symptoms, he had eaten dinner in Macau with friends. A physical examination revealed mild central abdominal tenderness without rebound and a petechial rash over his thighs, groin and the application site of an analgesic plaster on his left knee. Apart from a marginally elevated white cell count (10.9 x 10^9/L), investigations, including a complete blood count, liver and renal function tests, amylase and troponin I, were all normal. He was incidentally found to have diabetes mellitus, with a fasting blood glucose of 14.4 mmol/L and a glycosylated haemoglobin A_{1c} of 9.1%. Electrocardiograms, chest and abdominal radiographs were also normal. Intravenous fluids and insulin were prescribed.

The diarrhoea persisted despite the initial treatment and, 2 days later, his general condition deteriorated. His chest pain worsened and he developed shortness of breath and generalised joint pain. An examination revealed tenderness and mild swelling over his elbows, wrists, knees, ankles, and sternoclavicular joints. His left conjunctiva was congested and a new petechial rash appeared on his upper and lower limbs (Fig 1). An abdominal and chest examination was unremarkable. His oxygen saturation fell to 95%. Arterial blood gases confirmed hypoxaemia with PaO_2 of 8.7 kPa. A repeated chest radiograph demonstrated a newly elevated right hemidiaphragm. Electrocardiograms showed T-wave inversion in leads V_{1-3}, S wave in lead I, and Q and T wave inversion in lead III. Troponin I was again normal. Aspirin (at a dose of 160 mg daily), isosorbide dinitrate, low-molecular-weight heparin (LMWH; enoxaparin 0.4 mg subcutaneous twice daily) and amoxicillin plus clavulanic acid (Augmentin; GlaxoSmithKline, Shandong, China) were prescribed to manage a suspected pulmonary embolism, angina and chest infection. Spiral computed tomography (CT) of the thorax revealed atelectases at both lung bases. There was no definite evidence of a pulmonary embolism. An echocardiogram also failed to reveal vegetations or any evidence of myocardial ischaemia or dysfunction. Augmentin was replaced by ceftriaxone, azithromycin, and doxycycline. Enoxaparin was given for a total of five doses before it was stopped in view of the negative CT and echocardiographic findings.

On the day after stopping enoxaparin, the patient complained of lower limb weakness that appeared to be out of proportion to his arthralgia. His lower limb power was grade 3/5 bilaterally, with normal tone, and upgoing plantar reflexes on both sides. Pinprick and light touch sensation was reduced below T10. Anal tone was lax. His upper limbs and cranial nerves were normal. The neurological deficits progressed rapidly; he lost both bowel and bladder function. He developed acute urinary retention requiring catheterization a few hours later, and his lower limb power dropped to grade 0/5 on the next day. Tendon reflexes were also lost. Urgent magnetic resonance imaging (MRI) showed a spinal haematoma extending from C7 to L1, with maximal cord compression at T11 (Fig 2). It was impossible to distinguish between a subdural and extradural haematoma on the MRI. No bleeding tendency was evident apart from his petechial rash. The platelet count (235 x 10^9/L), coagulation profile (international normalised ratio, 1.04; activated partial thromboplastin time, 27.5 seconds) and bleeding time (10 minutes) were all normal. An emergency laminectomy with clot evacuation and duroplasty at levels T11 and T12 was performed

Key words
Hematoma, subdural; Heparin, low-molecular-weight; *Salmonella paratyphi*

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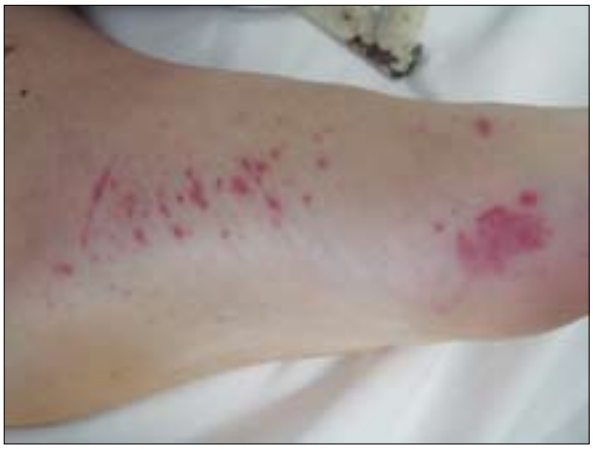

FIG 1. A petechial rash appeared over the patient's left foot

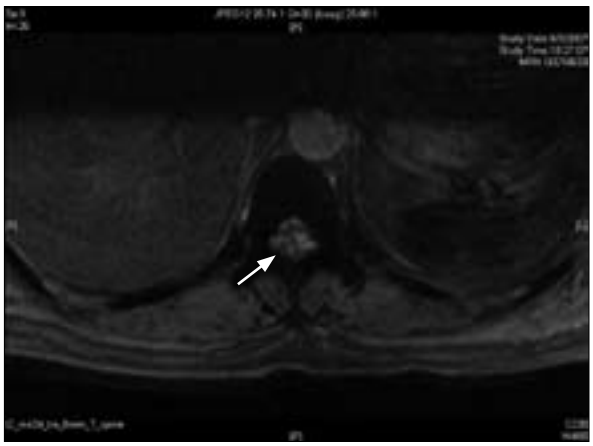

FIG 2. Subdural haematoma on the right side of the spinal canal, compressing the spinal cord at T11 level (white arrow)

by the neurosurgeons the same day and he was put on mega-dose methylprednisolone (2 g followed by infusion of 5.4 mg/kg/h). Intra-operatively the haematoma was found to be subdural. No meningeal, vascular, or bony abnormalities were detected, nor was there any local mass. Histological examination revealed an organised blood clot.

The patient had a smooth convalescence, apart from an episode of bleeding from a chronic duodenal ulcer. His chest pain, arthralgia, diarrhoea, and rash subsided a few days after surgery. His limb strength and sensation also improved gradually. His lower limb power was grade 4/5 after 4 weeks. His bowel function recovered but he still required intermittent urinary catheterization for persistent bladder dysfunction.

A convalescent serum sample showed a markedly elevated titre for *Salmonella paratyphi (S paratyphi* convalescent sample A-H 1:≥1280, B-H 1:640, C-H 1:320 vs first sample A-H 1:<20, B-H 1:20, C-H 1:20), signifying recent *S paratyphi* infection. The stool culture was negative.

硬脊膜下血腫：低分子肝素治療的罕見併發症

一位52歲男性出現胸痛、腹瀉、紅疹和關節炎的症狀，他因為懷疑患上肺栓塞或心絞痛而接受了低分子肝素治療，治療3天後發生硬脊膜下血腫，追查發現患者曾受副傷寒沙門菌感染。本病例報告亦簡略討論硬脊膜下血腫的臨床症狀和療法，以及與沙門菌有關的反應性關節炎的發生率和徵狀。

Discussion

We present a case of a non-traumatic spinal subdural haematoma (SDH) in a patient who had no risk factors for bleeding apart from the recent administration of LMWH. The patient also had polyarthritis, rash, and gastroenteritis associated with *S paratyphi* infection, and was incidentally found to have diabetes mellitus.

Spinal SDHs, most commonly located in thoracic or thoracolumbar regions, are rare. Most cases are associated with trauma, including minor injuries, lumbar punctures, epidural anaesthesia, and other medical procedures. Non-traumatic cases have also been reported, either in association with a bleeding diathesis due to coagulopathy, anticoagulant therapy or thrombocytopaenia, or secondary to arteriovenous malformations.[1] More than 20 cases of non-traumatic acute spinal SDH have been reported in association with the administration of coumarin derivatives,[1-4] usually due to over-anticoagulation. Only one case of spinal SDH has been reported to occur in association with LMWH therapy.[5] Low-molecular-weight heparins are inhibitors of Factor Xa in the coagulation pathway. The anticoagulation activity peaks between 3 and 5 hours after subcutaneous injection and persists for about 12 hours. Monitoring of blood coagulation profiles is not considered necessary except in patients with gross obesity or impaired renal function, neither of which was present in our patient.

The prevalence of intracerebral haemorrhage secondary to anticoagulant therapy is approximately 1.6% per year in patients older than 40 years.[6] The prevalence of anticoagulant-associated spinal haematomas, however, remains unknown. Common presenting symptoms are back pain or radicular pain followed by paraplegia, bowel and bladder paralysis.[7] Meningism and headache may occur in cases in which subarachnoid haemorrhage predominates. The motor-sensory deficits are typically symmetrical, although some cases present with Brown-Séquard or anterior spinal syndromes. The period from onset of back pain to paraplegia ranges from 10 to 26 hours. Early surgical removal of the blood clot is

recommended. The functional outcome is largely dependent on the timing of cord decompression and is significantly better when decompression is performed within 36 hours in patients with complete sensorimotor loss and within 48 hours in patients with incomplete sensorimotor deficits.[8] Our patient had surgical decompression within 48 hours of the onset of lower limb weakness and within 24 hours of complete paralysis, possibly explaining his relatively good recovery.

In our patient, the diagnosis of *S paratyphi* gastroenteritis was established by the rise in antibody titres in his convalescent serum. A petechial rash that was clinically compatible with leukocytoclastic vasculitis, conjunctivitis and polyarthritis complicated it. Since a cardiac or pulmonary cause for his chest pain was not evident after extensive investigations, we believe it was likely to be musculoskeletal in origin. Reactive arthritis is a well-documented complication of *Salmonella* infection, with the incidence ranging from 1.2 to 11.5%. The arthritis may be oligoarticular or polyarticular. The onset of joint symptoms ranges from 1 to 9 days, with a median of 2 days.[9] Most reported cases have been associated with *Salmonella typhimurium* or *Salmonella enteritidis*. In most cases, the arthritis is short-lived, though it has lasted for more than 6 months in some patients. Antimicrobial treatment does not alter the incidence or duration of reactive arthritis.[9] Inflammatory low back pain, enthesopathy, iritis and conjunctivitis have also been reported. Rashes are uncommon in *Salmonella* infection,[10] though the occurrence of leukocytoclastic vasculitis in *S typhi*,[11] *S typhimurium*[12] and *S paratyphi*[13] infections has been described in anecdotal reports. Purpura or skin petechiae may be associated with endocarditis, and have been reported to complicate 11 out of 41 cases of *Salmonella* endocarditis.[14]

Conclusions

Spinal SDH is a rare complication of anticoagulation therapy. Although most cases have been reported in association with coumarin derivatives, LMWHs are not exempt from causing this complication. Clinicians should entertain this possibility when patients who are on anticoagulants complain of back or radicular pain and develop paraparesis, since early decompression is important for good functional recovery.

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