Retroperitoneal haemorrhage and neuropathy complicating anticoagulant therapy

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Summary

Nine cases of retroperitoneal haemorrhage complicating anticoagulant therapy are reported. Six cases were receiving heparin for myocardial infarction: an incidence of 4.3% of patients on such treatment. All the cases presented with pain, six had neurological involvement and one patient died.

The incidence of this complication is higher than previously noted. Retroperitoneal haemorrhage requires a high index of clinical suspicion for early diagnosis and treatment if serious sequelae are to be prevented.

Introduction

Haemorrhage is a recognized complication of anticoagulant therapy. It is usually seen in patients on long term oral therapy, when the incidence has been estimated to vary between 10 and 40%. (Pastor, Resnick and Rodman, 1962). The reported incidence during heparin therapy has varied from 4% (O'Sullivan *et al.*, 1968) to 22% (Jick *et al.*, 1968). This may be related to poor anticoagulant control though Pitney, Pettit and Armstrong (1970) have shown an incidence of 7.6% of bleeding episodes in patients on carefully controlled heparin therapy. The onset of haemorrhage is commonly dramatic with external or obvious internal haemorrhage into gastro-intestinal or urino-genital tracts, skin or central nervous system. A more unusual presentation is occult retroperitoneal haemorrhage with no external signs of blood loss, presenting as a neurological lesion or with deep pain only. We present nine cases of retroperitoneal haemorrhage collected over 7 years from patients on anticoagulant therapy. Six of these, one of which proved fatal, were collected from a series of 139 patients on one medical unit who had received heparin for myocardial infarction.

Case reports

Case 1. A 64-year-old man admitted with acute coronary insufficiency and treated with a heparin drip. At 8 days, pain developed in the left groin. Shortly after this a complete left femoral nerve

lesion became apparent with weakness of the left ileo-psoas and hip adductors, together with sensory loss and absent left knee jerk. X-rays of the lumbar spin and hips were normal. Heparin was discontinued and 1 month later quadriceps power was improving and sensation was full although the knee jerk was still diminished. No swelling or bruising was detected at any stage.

Case 2. A 64-year-old man admitted with myocardial infarction and treated by heparin drip. Eight days after admission he complained of left leg pain in the sciatic nerve distribution. On examination all active movements of the leg produced sciatic pain and straight leg raising was completely restricted on the left. There was no definite sensory impairment or loss of reflexes. Heparin was discontinued but complete recovery took 8 weeks.

Case 3. A 56-year-old man admitted with acute coronary insufficiency which was treated by a heparin infusion. On the tenth day he complained of backache with pain in the right groin and thigh partly relieved by hip flexion. Examination showed groin tenderness with no swelling or bruising. There was quadriceps weakness with a diminished right knee jerk but no sensory loss. The pain cleared rapidly after discontinuing the heparin and recovery was complete in 1 week with no residual neurological deficit.

Case 4. A 54-year-old man admitted with myocardial infarction complained of increasingly severe pain in the left hip, groin and thigh on the tenth day of heparin therapy. Forty-eight hours later the pain was localized to the groin but there was numbness in the thigh. Examination showed local tenderness without swelling. Active hip flexion was painful, but passive movements were nearly painless. Quadriceps power and the left knee jerk were diminished and there was an area of anaesthesia in the femoral nerve distribution. Heparin was discontinued and both the sensory loss and the knee jerk returned to normal in a further 48 hr, by which time bruising was visible in the groin. The patient was ambulant by the fourth day and 1 month later no residual lesion was detected.

Case 5. A 62-year-old woman on long term Warfarin for a mitral valve prosthesis was admitted with acute left sided abdominal pain radiating to back and umbilicus, producing nausea and vomiting. Examination showed a distended abdomen with diminished bowel sounds and deep abdominal tenderness on the left. The prothrombin time was prolonged at 62 sec. Plain X-ray of the abdomen was normal and stools persistently negative for occult blood. Vitamin K was given and the condition settled on conservative therapy over 48 hr although deep tenderness persisted. Several days later bruising became apparent in the left flank suggesting that retroperitoneal rather than intramural intestinal haemorrhage had occurred.

Case 6. A 48-year-old man admitted from casualty with acute pain in the left buttock and thigh which developed while returning from holiday in Spain. He had been on Warfarin for 14 months since myocardial infarction, with good previous anticoagulant control. On examination, he was in severe pain with the left hip held flexed. Active hip movement was limited by pain but passive movements were full and relatively pain free. A complete lower motor neurone femoral nerve lesion was present. Hip and spine X-rays were normal but the prothrombin time was prolonged at 68 sec. No local swelling or bruising appeared. The pain rapidly settled on bed rest after discontinuing the Warfarin but the femoral nerve lesion persisted with quadriceps weakness and absent knee jerk at 2 months, in spite of intensive physiotherapy. A change in diet and alcohol consumption on holiday was thought to account for the loss of anticoagulant control.

Case 7. A 65-year-old diabetic man complained of backache 36 hr after the start of a heparin infusion for crescendo angina. No fresh abnormality was found on examination and the pain settled on simple analgesics. Twenty-four hours later severe pain returned, radiating forward to both hips and groins. Active hip flexion was now painful but no neurological lesion was found. His condition deteriorated over the next few hours and he became shocked. A mass was now palpable in the left flank. After blood transfusion a laparotomy was performed for a suspected leaking aortic aneurysm. A massive retroperitoneal haemorrhage was found but no aneurysm and the patient died after a cardiac arrest. Post mortem examination confirmed the extensive haemorrhage, involving all the retroperitoneal tissues and extending forward in the muscle planes, but failed to reveal any site for the bleeding. The aorta and main vessels were atheromatous but intact.

Case 8. A 20-year-old man was admitted with a 6-day history of continuous, increasingly severe right loin pain associated with vomiting. There were no other urinary or alimentary tract symptoms.

He was receiving oral anticoagulants for a deep venous thrombosis incurred 1 month earlier. His prothrombin time had been well controlled as an out patient, but it was slightly elevated, at 34 sec, on the day of admission. On examination he was not shocked but was markedly tender in the right flank where a diffuse, ill-defined swelling was palpable. There was no bruising. Bowel sounds were normal. There were no abnormal neurological signs. MSSU was sterile but contained an excess of red cells with no casts or protein. The haemoglobin was 2 g lower than the level recorded 1 month earlier. His anticoagulants were stopped in view of the diagnosis of retroperitoneal haematoma secondary to therapy. Pain subsided rapidly and mobility was restored within 48 hr. The patient was well, without pain or swelling when reviewed 2 weeks later.

Case 9. A 56-year-old man admitted with myocardial infarction, was treated with intravenous heparin. A large right iliac haematoma appeared on the fourth day at an injection site. Although this swelling had not changed in size, he had a syncopal attack the following day. Thirty-six hours later, a painful swelling was noted in the right groin and he complained of paraesthesia in the distribution of the right femoral nerve. Active right hip movement was painful, and the right quadriceps power and right knee jerk were diminished with impaired sensation over the right knee area medially (his haemoglobin had dropped to 8.0 g). The heparin was stopped and he was transfused with 3 pints of blood. Over the next 48 hr, the knee jerk became stronger and the sensory deficit improved. Bruising of the right flank was obvious on the tenth day. It was felt that he had had a large retroperitoneal haematoma in addition to the subcutaneous thigh haematoma. The haematoma slowly resolved and he was discharged 2 weeks later fully mobile and without neurological abnormality.

Discussion

We have described nine cases of retroperitoneal haemorrhage, presenting with pain together with a nerve lesion in the majority, which developed in patients on anticoagulants. Six of the cases occurred in patients receiving short term intravenous heparin. Five of these developed a transient femoral or sciatic neuropathy which later recovered but the sixth patient died after extensive haemorrhage. This is the largest series of cases of nerve palsies related to heparin therapy which has been described.

Retroperitoneal haemorrhage has been less extensively documented than other anticoagulant complications. It was first noted in 1953 by Russek, who found it twice among 122 fatal cases of myocardial infarction receiving anticoagulants. Reiter (1966) described three cases presenting as an acute

abdomen and similar cases were seen by Larsen *et al.* (1962), Hafner *et al.* (1962) and Hodin (1962). Isolated cases presenting as an acute neurological lesion have been described by several authors, Pieri and Pinas (1964); Spurny *et al.* (1964); Strain (1964); Prill (1965) and Gallois, Dhers and Badarov (1967), and more recently Lange (1966) collected four cases and Parkes and Kidner (1970) three cases presenting as femoral or sciatic nerve palsies. The majority of these cases occurred in patients on oral anticoagulants in contrast to the present series where the majority of the patients were on heparin.

The incidence of retroperitoneal haemorrhage in patients on heparin therapy has not been previously calculated. Pitney and Pettit (1970) found only one case in a series of seven bleeding episodes, the latter representing 7.6% of the patients on heparin. The present series was collected from 139 consecutive patients with myocardial infarction who received a 10-day course of intravenous heparin on the same wards over a period of 7 years, giving the much higher incidence of 4.3% of those at risk. The three subjects on oral anticoagulants were first seen by us because of their lesions and thus cannot be used to calculate an incidence in such patients.

The relationship between anticoagulant control and the occurrence of retroperitoneal haemorrhage is uncertain. Two of the patients on oral anticoagulants had poor control with a greatly raised prothrombin time at the time of presentation but it was only slightly elevated in the third case. The position is more obscure when the heparin series is considered. All these patients were receiving our current standard regimen for heparin which is 40,000 units in 24 hr given by continuous intravenous drip. No laboratory control was attempted although it is notable that this dose is in the middle of the weight-related dose range given by Pitney and Pettit (1970). The latter authors assessed three separate methods of laboratory control and failed to find a satisfactory correlation between individual tests, none of which seemed to relate to the incidence of bleeding episodes. The time of bleeding, which in five of our six cases occurred between the seventh and tenth day of heparin therapy suggests that the dose was not grossly excessive. The sixth case developed haemorrhage after only 36 hr of treatment and this was the only fatal case.

The predilection for retroperitoneal haemorrhage in the heparinized patients is not easy to explain although intra-psoas haemorrhage is well recognized in haemophilia (Bullock and Fildes, 1911; Seddon, 1930; Tallroth, 1939; Aggeler and Lucia, 1944; Davidson *et al.*, 1949). The striking fact that none of our patients had any spontaneous muco-cutaneous bleeding suggests an unusual weakness of the vascular tissues in the retroperitoneal site. There

was no history of local trauma or strain to explain the onset of bleeding. In the one fatal case very extensive haematomata were seen which appeared to have originated within the psoas sheath and then spread forward. No single site of bleeding was found and all the major vessels were intact. It is possible that the small intramuscular vessels in this area are relatively unsupported by connective tissue or unduly liable to rupture on minor stress. This would only become evident during anticoagulant therapy and would account for the wide variety of clinical manifestations of retroperitoneal haemorrhage which may present as deep seated pain, often simulating skeletal complaints; as an acute abdomen; or as a local neuropathy. We suggest that the latter is due to pressure from an intramuscular haematoma rather than to intra-neural bleeding. This is supported by the presence of local tenderness and the later development of superficial bruising in some cases, as well as the good eventual recovery in most.

The incidence of retroperitoneal haemorrhage in patients receiving anticoagulants appears to be commoner than generally appreciated. The sole complaint may be the pain and such incidents may easily escape diagnosis although they can rapidly progress to a neuropathy or even to a fatal conclusion. A high index of suspicion is necessary and anticoagulants should probably be discontinued when any undue pain is noted, even in the absence of definite physical signs and when control is apparently adequate.

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