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Clinical Study

Muscle haematoma due to antithrombotic treatment for ischaemic stroke

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ABSTRACT

The purpose of this study was to evaluate the incidence and clinical features of muscle haematoma in ischaemic stroke patients. Muscle haematomas are rare complications that occur during antithrombotic treatment for acute ischaemic stroke. Clinical and laboratory records of ischaemic stroke patients with muscle haematomas in the last 3.5 years were retrospectively reviewed. Muscular haematoma developed in three of 694 (0.4%) consecutive patients with acute ischaemic stroke who were admitted to our institution. In addition, one outpatient presenting with muscle haematoma was found during the same period. The types of haematomas were rectus sheath haematoma in two patients and iliopsoas haematoma in the remaining two. All three acute patients received both antiplatelet and anticoagulant therapies. The outpatient was treated with warfarin. Initial symptoms of haematoma included pain (n = 3) and syncope (n = 1). No patient was correctly diagnosed at the onset of muscle haematoma. At initial examination of muscle haematoma, no patients showed skin lesions. An ecchymosis developed in the abdominal area at an average of 3 days after the initial symptoms. Mean decrease in haemoglobin was 6.8 g/dL from baseline. None required surgery whereas two patients required blood transfusion. Muscle haematomas in stroke patients receiving antithrombotic therapy are rare complications that are difficult to diagnose at onset. The possibility of muscle haematoma should be considered in patients with ischaemic stroke undergoing antithrombotic therapy and presenting with acute pain and syncope, even if skin manifestations or a palpable mass are lacking.

1. Introduction

Antithrombotic treatment has been widely used for the treatment of thromboembolic disease, including ischaemic stroke (IS). Haemorrhage is a common complication of antithrombotic therapy which often occurs in various organs. Other known major complications of antithrombotic therapy include intracranial and retroperitoneal haemorrhage [1]. Haematoma of the muscle is a rare complication in acute IS patients receiving antithrombotic treatment and is considered to be of clinical importance because it often mimics several other conditions, resulting in misdiagnosis [2–8]. However, the clinical features and exact prevalence of muscle haematoma due to antithrombotic treatment of IS remain unclear. The purpose of this study was to evaluate the incidence and clinical features of muscle haematoma in IS patients.

2. Methods

2.1. Patients

The medical records of muscle haematoma in acute IS patients who were admitted to the Neurological Department of Chiba Rosai Hospital between April 2010 and September 2013 were retrospectively reviewed. In addition, outpatients who received oral anticoagulant or antiplatelet medications and presented with muscle haematoma were reviewed during the same period. The criteria for inclusion into this study were development of muscle haematoma after the onset of IS and diagnosis of muscle haematoma on the basis of clinical and CT scan findings. Muscle haematomas that resulted from invasive procedures or traumatic events were excluded from this study. Disease disability upon admission and at discharge were evaluated according to the modified Rankin Scale (mRS).

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2.2. Anticoagulant and antiplatelet therapy in the acute stage

Although European guidelines clearly state that early administration of unfractionated heparin is not recommended for the treatment of acute IS patients, Japanese guidelines published in 2009 state that the use of heparin can be considered for the treatment of IS within 48 hours of onset, however, adequate scientific evidence for this approach is lacking (grade C1) [9]. Japanese guidelines recommend that oral aspirin should be given to patients within 48 hours of acute IS (grade A) and also recommend intravenous infusion of ozagrel sodium, an antiplatelet agent, within 5 days of infarct onset (grade B) at 160 mg/day for patients with acute cerebral thrombosis (IS excluding cardioembolic stroke). At our institution, neurologists make the final decision regarding the use of anticoagulant and antiplatelet agents in the treatment of acute IS patients. However, most acute IS patients, excluding cardioembolic stroke, were treated with unfractionated heparin (only in the first several days following IS), intravenous ozagrel sodium and oral aspirin. In cardioembolic stroke, the timing of the initiation of heparin or warfarin treatment is decided on a case-by-case basis. In our patients, the major exclusion criteria for antithrombotic therapy during the acute stage were severe brain oedema, acute bleeding state, increased bleeding tendency or haemorrhagic stroke.

3. Results

3.1. Patients and the administered antithrombotic treatments

During the observation period, 694 acute IS patients were identified (436 men, 258 women, mean age 72 years). Muscular haematoma was observed in three out of 694 (0.4%) patients. One outpatient with muscle haematoma was admitted to our institution's department of surgery. The four patients included three men and one woman with a mean age of 72 years (range: 68–78 years). None had haematological disorders such as haemophilia, recent surgery or prior injections, including insulin. Two patients had a history of cigarette smoking (>10 cigarettes/day), two had hypertension, one was diabetic (elevated glycohaemoglobin), one had hyperlipidaemia and the outpatient had atrial fibrillation. In the three acute IS patients, stroke was confirmed both clinically and radiologically by cranial diffusion-weighted MRI. Two of the three patients had a lacunar stroke in the internal capsule or corona radiata and one patient had developed branch atheromatous disease in the territories of the lenticulostriate arteries. All three acute IS patients were referred to our hospital on the day of stroke onset and were immediately admitted to the hospital. None showed consciousness disturbance or aphasia. The outpatient had a history of two cardioembolic strokes, was treated with oral warfarin for 5 years and could independently perform daily activities. Intravenous treatment of the three acute IS patients consisted of ozagrel sodium, unfractionated heparin and edaravone (radical scavenger). Oral antithrombotic treatments were aspirin alone for two patients, and a dual antiplatelet regimen consisting of aspirin and ticlopidine for one patient based on a history of percutaneous coronary intervention for previous ischaemic heart disease. No patient received intravenous recombinant tissue plasminogen activator therapy.

3.2. Clinical features of muscular haematoma

The types of haematoma observed were unilateral rectus sheath haematoma (RSH) in two patients and unilateral iliopsoas haematoma in two patients. The clinical features and CT scan findings in all patients are presented in Table 1 and Figure 1, respectively. Initial symptoms of muscular haematoma included pain (n = 3) and syncope (n = 1). No patient was correctly diagnosed with muscle haematoma at onset. At the onset of haematoma, one of two iliopsoas haematoma patients showed a psoas position upon flexion of the hip. Of the three acute IS patients, the mean duration between the initial symptoms of muscle haematoma and the initiation of antithrombotic treatments was 3 days (range: 3–4). The mean latency between initial symptoms of muscle haematoma and diagnosis of muscle haematoma in four patients, as confirmed by CT scan, was 2 days (range: 1–3). During the initial symptoms, no patients showed skin lesions or swelling. Ecchymosis developed in the abdominal area at an average of 3 days (range: 2–4) after the initial symptoms of muscle haematoma.

3.3. Laboratory findings

The mean initial haemoglobin level (upon admission of three inpatients and prior to admission of the outpatient) was 14.0 g/dL (range: 13.5–15.2). The mean decrease in haemoglobin was 6.8 g/dL (range: 5.1–8.2) from baseline. Platelet count was normal in all patients. In one outpatient who received warfarin, the international normalised ratio (INR) at diagnosis of haematoma was elevated at 3.73 although his INR was consistently within the therapeutic range (2.0–3.0) prior to this episode. Activated partial thromboplastin time was evaluated in only one out of three acute IS patients receiving heparin and it was markedly elevated at >200 seconds in one iliopsoas haematoma patient.

3.4. Treatments and prognoses

Antiplatelet and anticoagulation treatments were discontinued in all patients. None required surgical treatment of the muscle haematoma. Blood transfusion was required in two of four patients (both developed iliopsoas haematoma). The outpatient did not show residual signs at discharge. mRS of the three acute IS patients at discharge was 1, 2 and 5, respectively.

4. Discussion

This study confirms that muscular haematoma is rare and difficult to diagnose using initial symptoms in IS patients who are treated with antithrombotic agents. Evidence facilitating our diagnosis included acute onset of pain in the abdominal wall or hip joint and syncope, and abdominal CT scans were useful in the assessment of suspected patients. Strong risk factors for muscle haematoma in IS were unclear in our small patient series. All three acute IS patients presenting with muscle haematoma received both antiplatelet and anticoagulant therapies whereas one outpatient showed a prolonged INR. In fact, our systematic review showed that the combination of heparin and aspirin therapy for IS increases extracranial haemorrhage [10]. Previous reports have indicated that RSH due to warfarin can result from overanticoagulation [11–13]. These findings indicate that careful monitoring, including coagulation testing, should be conducted in IS patients to prevent the occurrence of muscle haematoma.

Despite its clinical importance, published reports on muscle haematoma in IS patients receiving antithrombotic medications are limited. In fact, previous studies on muscle haematoma due to antithrombotic treatments have exclusively focused on patients with atrial fibrillation, deep vein thrombosis and/or pulmonary embolism, cardiac valve disease or ischaemic heart disease. Most series on RSH have reported a non-stroke indication for antithrombotic treatment [3–7,14–18] with only a few series and reports on RSH due to antithrombotic treatments for IS [2,8,12,19]. In a previous literature review of approximately 51 iliopsoas haematoma