CASE REPORT

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ORTHOSTATIC SYNCOPE IN A YOUNG WOMAN WITH ESSENTIAL THROMBOCYTHEMIA FOUND TO BE AN INITIAL SIGN OF ISCHEMIC STROKE – THERAPEUTIC CONCERNS. UNUSUAL CASE

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Abstract

Purpose: Essential thrombocythemia (ET) is characterised by an overproduction of platelets in the absence of the states that induce secondary thrombopoiesis. The most common and significant complication of ET is arterial and venous thrombosis. The most serious complication of ET is stroke.

Case description: We present a patient with a stroke that started with an unusual symptom – syncope, successfully treated with recombinant tissue plasminogen activator alteplase. Three years after the stroke, the patient lives an independent life but with cerebellar-stem symptoms. Further long-term treatment is supervised by a haematologist.

Comment: Syncope in ET may be the first sign of stroke. To assess brainstem and cerebellar stroke, magnetic resonance imaging should be performed. In ET, thrombolytic treatment of ischemic stroke may be a life-saving treatment. Long-term treatment involving a platelet-lowering medication, along with anti-aggregation drugs, is necessary to treat stroke patients with ET. Females with ET who have suffered from a stroke should not use oral contraception.

Key words: ischemic stroke, essential thrombocythemia, JAK2 V617F mutation, platelets, risk factors.

PURPOSE

Essential thrombocythemia (ET) is characterised by an overproduction of platelets where no causes that could provoke secondary thrombopoiesis were identified. Symptoms related to circulatory disorders in small vessels – headache, dizziness, blurred vision, erythromelalgia, paraesthesia, skin ulceration, mental disorders and convulsions – occur in approximately 50% of the patients with ET. Thrombotic events in arteries are observed in 10-25% of the patients. However, ET is a rare risk factor for ischemic stroke [1-5]. Presented below is an unusual case of a female patient with ET suffering from headaches, who suddenly fainted after getting up in the morning, which was found to be an initial sign of a severe brainstem stroke. Both the diagnostic and therapeutic difficulties encountered in the process, as well as the way to address them, are discussed.

CASE DESCRIPTION

A 29-year-old woman was admitted to the Neurological Department of the Hospital in Piła, Poland due to persistent headaches. According to her medical history, she suffered from paroxysmal occipital headaches with nausea, as well as constant headaches of the entire head. Moreover, she was diagnosed with thrombocythemia, but did not consult a haematologist. During headache episodes, she was taking non-steroidal analgesics for short-term pain relief. She was not taking any medication on a long-term basis. She did not consult a neurologist regarding her headaches. Also, on admission

to the hospital, she did not disclose that she was using oral contraceptives. A normal neurological condition was stated on admission. The patient was tall (175 cm) and slim (65 kg). On admission, the level of platelets was 910 K/µl; other blood parameters were normal. Intravenous fluids of 1000 ml per day were introduced and the level of platelets dropped to 762 K/µl the next day. Magnetic resonance (MR) examination of the head, as well as a consultation with a haematologist, were scheduled. On the third day of hospitalization, she fell down in the morning after getting out of bed. She was pale and sweating; her heart rate increased to 112/min. The initial diagnosis identified orthostatic syncope. The patient was put back to bed and a multi-electrolyte fluid was administrated intravenously. She regained consciousness immediately after, but she was still feeling weak. Computed tomography (CT) of the head showed no changes (Figure I). The patient weakened. After an hour, the following symptoms appeared: nausea, dizziness, horizontal-torsional nystagmus when looking to the sides, weakness of the limbs. After a neurological examination, an MRI was immediately performed; it revealed ischemic focus in the cerebellum (mainly in the right hemisphere), medulla, pons and both occipital lobes (Figure II). A stroke in the cerebellum and both occipital lobes was diagnosed and the recombinant tissue plasminogen activator alteplase (t-PA) was administered intravenously at a dose of 0.9 mg per kg of body weight. During the infusion, angio-CT was performed; it showed no obstruction of the large intracerebral and extracranial arteries (Figure III). Despite thrombolytic therapy, a significant degree of quadriparesis with dysphagia occurred. The patient required intubation and enteral tube feeding. ASA 75 mg/24 h and Nadroparin 5700 AXa IU/0.6 ml were implemented 24 hours after thrombolysis. Hydroxycarbamide was added after a consultation with a haematologist who diagnosed ET. Additionally, JAK2 gene mutation was identified. Hydroxycarbamide was co-administered with ASA and Nadroparin. Unfortunately, the level of platelets rose to the value of 1253 K/µl. For this reason alone, the haematologist replaced Hydroxycarbamide with Anagrelide (1-2 capsules of 0.5 mg

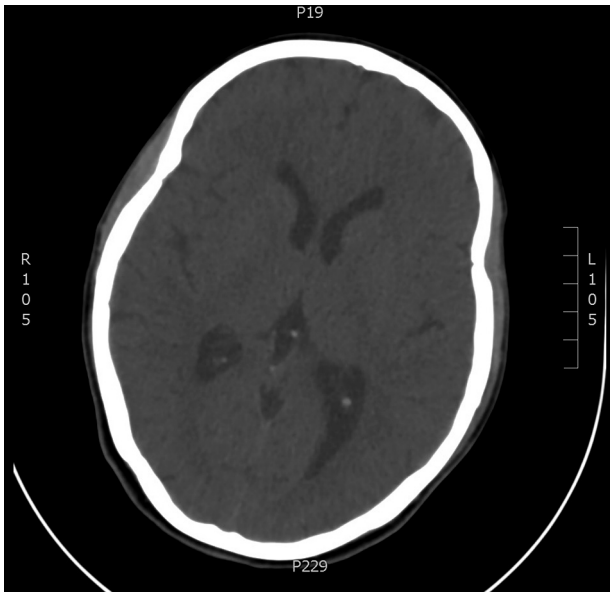

Figure I. Normal computed tomography image after syncope (examination with no contrast)

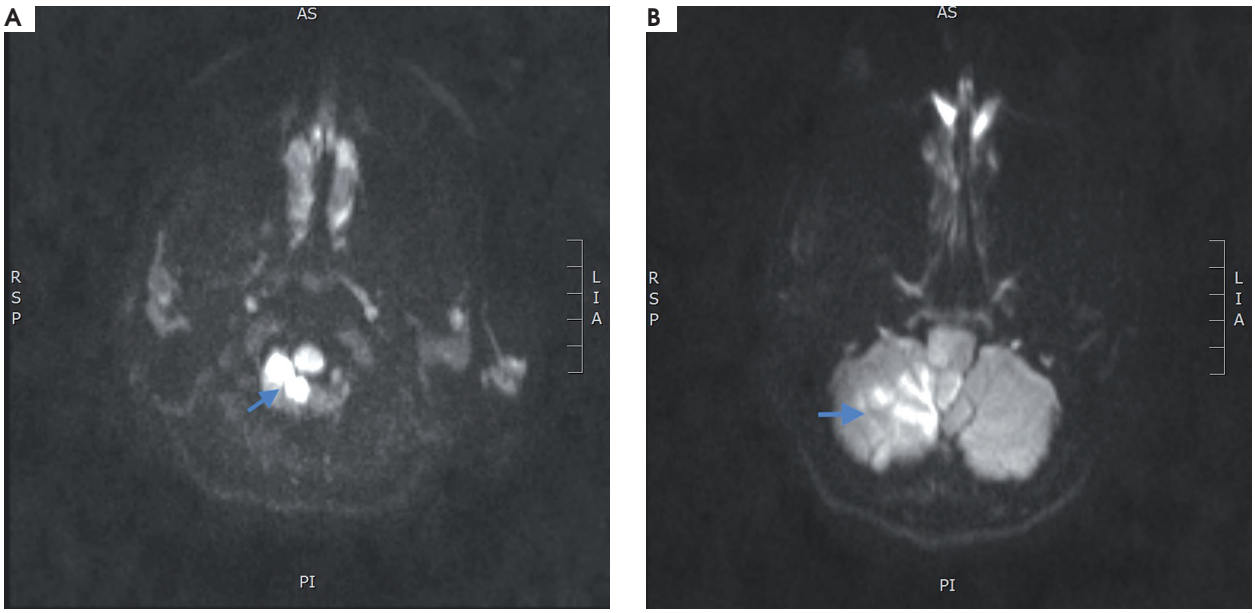

Figure II. Magnetic resonance imaging of the head in the T2-dependent sequence: ischemic focus in the cerebellum in the right hemisphere, medulla (arrow)

per day), which was administered to the patient along with ASA and Nadroparin. Following this combined treatment, the platelet count dropped to 170-440 K/µl. The patient underwent a tracheostomy and a PEG was inserted, through which she was fed. The patient stayed in the Intensive Care Unit for a month, then returned to the Neurological Department, where she was treated for another 40 days. It was only during her second stay at the Neurological Department that the patient admitted to using oral contraceptives. The patient's condition improved: the paresis of the limbs decreased to 4/5 according to the Lovett scale: she started to walk with a support and to talk and dysarthria, dysphagia and the cerebellar syndrome remained, at 3 points on the mRs scale. At discharge, the level of platelets was normal. She was discharged with Anagrelide and ASA to the rehabilitation ward, where she stayed for 8 months intermittently. A year after the onset of the disease, she is able to walk independently, the muscle strength of the limbs is close to normal, she is able to swallow independently, and her tracheostomy has been removed. Brainstem stroke syndrome, dysarthria and cerebellar symptoms persist, at 2 points on the mRs scale.

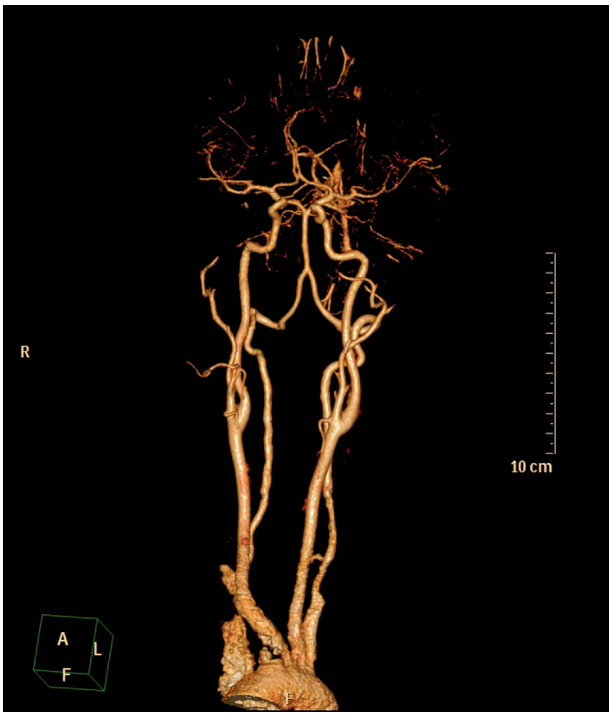

Figure III. Patent extracranial and large intracerebral arteries

CONCLUSIONS

Syncope in thrombocythemia may be the first sign of stroke. To assess brainstem and cerebellar stroke, MRI should be performed. In ET, thrombolytic treatment of ischemic stroke is possible and may be a life-saving treatment. Subsequent long-term treatment involving a platelet-lowering medication along with an anti-aggregation medication under the control of a haematologist is necessary to treat stroke patients who suffer from ET. Patients with ET who have suffered from a stroke should not use oral contraception.

COMMENT

Headaches are one of the possible symptoms of ET [1-4]. The patient discussed above suffered from headaches, but these were tension headaches, and no other characteristic symptoms were found. The patient had never had a thrombotic event before. Prior to her admission to the hospital, she did not use any anti-platelet medication. According to the International Prognostic Score for Thrombosis in Essential Thrombocythemia (IPSET), prior to the occurrence of a thrombotic event, the patient was in a group with a low risk of thrombosis (age < 60 years, no history of thrombosis, JAK2 mutation), for which cytoreductive therapy is not recommended. On the other hand, acetylsalicylic acid (ASA) is used in all patients with ET in the dose of 75-100 mg, except for the group at very low risk (age < 60 years, no history of thrombosis, no JAK2 gene mutation) [6]. The patient discussed here did not use ASA before she was admitted to the hospital and, additionally, was using oral contraceptives, which is also included among the risk factors for stroke [7]. However, there are cases of stroke patients suffering from ET who develop recurrent stroke despite receiving cytoreductive therapy combined with ASA. Nevertheless, patients with ET should use antiplatelet therapy if they are in the low, intermediate or high-risk groups of thrombosis, according to the above-mentioned IPSET scale. Having analysed 10 cases of patients with migraine and ET with JAK2 gene mutation, Michiels *et al.* concluded that not using ASA in this group of patients increases the risk of arterial thrombosis, including stroke [4]. Moreover, attention should be drawn to the syncope, which in case of this patient was the first sign of a brainstem stroke. It should be emphasised that in this group of patients, fainting may not be a simple orthostatic syncope, but the beginning of a stroke. In those cases, MRI should be the examination of choice. Usually, a stroke is caused by a thrombus in the small vessels. Immediate implementation of thrombolytic treatment may improve the patient's condition. Moreover, in women with ET, oral contraception shall not be prescribed or should be discontinued following an ischemic stroke. Although stroke is not common in patients with ET, it should be considered, as it may constitute a serious complication. In these patients, intravenous thrombolytic therapy with t-PA is the treatment of choice in accordance with the current guidelines, unless there are other contraindications [3, 8].

Conflict of interest

Absent.

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