Short report

Cerebral venous thrombosis as presenting sign of myeloproliferative disorders

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SUMMARY Two patients with cerebral venous thrombosis are described. In both patients laboratory findings suggested an underlying haematological disorder and bone marrow biopsy showed a myeloproliferative disorder. Both chronic cerebral venous thrombosis and early myeloproliferative disorders are difficult to diagnose. Their combined occurrence may be less rare than is frequently supposed.

Myeloproliferative disorders, including polycythaemia vera, essential thrombocytthaemia, chronic myelogenous leukaemia, myeloid metaplasia, and myelofibrosis, frequently cause arterial and venous thrombosis.1 The neurological manifestations of myeloproliferative disorders are well established, but attention has largely been focused on arterial ischaemic disease.2 3 Cerebral venous thrombosis has been described in patients with previously diagnosed myeloproliferative disorders,4 5 and as a presenting sign of that disease.6 7 We describe two patients with angiographically proven cerebral venous thrombosis, as the first sign of myeloproliferative disorders.

Patient 1
Seven months prior to admission to our department, this 30 year old woman developed frontal headache, and noted blurred vision of both eyes. She had never been seriously ill before, did not take any drugs or oral contraceptives, and she did not smoke. One month after the onset of her symptoms an ophthalmologist found a slightly enlarged blind spot and bilateral papilloedema. General and neurological examination revealed no further abnormalities. CT scan of the brain was normal. On lumbar puncture an opening pressure of 28 cm H2O was found; the composition of CSF was normal. The ophthalmological examination was repeated frequently, and remained unchanged.

Because of increasing headache she was admitted to our hospital. Examination still only revealed bilateral papilloedema. Lumbar puncture revealed colourless CSF, with a pressure up to 30 cm H2O. CT scan of the brain showed haemorrhagic infarction in the left temporoparietal region, and on angiography thrombosis of the superior sagittal sinus from the vertex to the torcular was seen.

The following laboratory investigations were normal: ESR, haematoctrit, red cell indices, bleeding time, thrombin time, prothrombin time, factors VIIIC, IXc, XI, fibrinogen, antithrombin III, and Protein C and S. Lupus anticoagulant was not present. Platelet count was repeatedly elevated, the highest value being 795 × 109/l. Spontaneous platelet aggregatability was found. WBC count was slightly elevated, the differentiation being normal. Blood volume was 4.2 l (normal 4.0) and erythrocyte concentration 28.4 ml/kg (26.0). Peripheral blood-smeat showed anisocytosis, poikilocytosis, neutrocytosis and leucocytosis, hypersegmentation of the granulocytes, and thrombocytosis with multiple pathological forms. Bone marrow smear revealed increased megakaryopoiesis, and a bone marrow biopsy specimen showed pathological clusters of large atypical megakaryocytes with increased granulopoiesis. Furthermore, reticulin fibrosis with formation of fibres around megakaryocytes was seen. A diagnosis of myeloproliferative disorder was made. The patient was treated with coumarin. Her symptoms steadily decreased, but did not disappear completely. Frequent ophthalmological examination showed persistence of the papilloedema but unchanged visual acuity.

Patient 2
A 40 year old woman was well until a few months before admission, when she developed progressive headache, blurred vision, and a burning feeling in the right foot, provoked by increasing temperature. A few weeks later she complained of nausea and vertigo. Ophthalmological examination disclosed bilateral papilloedema, enlarged central scotoma and slightly decreased visual acuity. Physical
examination showed a blue-red erythema of the right toes suggestive of erythromelalgia. Neurological examination revealed no abnormalities, nor did CT scan of the brain. Angiography revealed a filling defect in the posterior suprarenal region. On lumbar puncture the opening pressure was 26 cm H₂O, the composition of CSF being normal. Routine laboratory findings and coagulation studies were normal. The cause of the sinus thrombosis was not found and she was given oral anticoagulant therapy.

There was a temporary improvement of the symptoms, but 2 months later she developed a left sided hemiparesis affecting the face and arm more than the leg. A repeat CT scan showed a low-density area in the right temporoparietal region. Ophthalmological examination now disclosed right visual loss, left visual acuity of 5/60, increased papilloedema and right-sided venous engorgement of retina, eyelid and face, due to cavernous sinus thrombosis. Repeat analysis revealed erythrocytosis (6.5 × 10¹²/l), leucocytosis (11.9 × 10⁹/l), and slight thrombocytosis (490 × 10⁹/l, later on rising to 950 × 10⁹/l). Coagulation studies were normal except for the coumarin effect. Peripheral blood-smear showed anisocytosis and giant platelets. Bone marrow smear revealed increased megakaryopoiesis and granulopoiesis. Bone marrow biopsy disclosed hypercellularity and trilamellar hyperplasia with pronounced clusters of enlarged megakaryocytes. There was an increase of reticulum fibres and no stainable iron. Chromosomal investigation revealed a trisomy 8. A diagnosis of polycythaemia vera was made. Anticoagulant therapy was stopped and the patient was treated with radioactive phosphorus and aspirin, resulting in a normalisation of the laboratory parameters and a stable clinical condition.

Discussion

Cerebral venous thrombosis is a disorder which is often not recognised during the patient's lifetime, because the signs and symptoms are nonspecific. Frequently symptoms of increased intracranial pressure develop, occasionally followed by focal neurological signs. Cerebral venous thrombosis can be demonstrated by angiography, and in a minority of cases by CT or magnetic resonance imaging.

Attempts to establish the causes of cerebral venous thrombosis in series of patients have rarely included detailed coagulation studies. Bousser et al only found hyperaggregability of thrombocytes with the lowest dose of epinephrine. Coagulation parameters have been investigated in females, however only during pregnancy, in the puerperium, or on oral contraceptives. Because these conditions are often associated with coagulation abnormalities, it is difficult to extrapolate the results to the general female population.

In patients with myeloproliferative disorders, thrombosis is common but unpredictable, as there is no correlation between the extent of qualitative or quantitative platelet dysfunction and clinical haeostatic complications. Neurological complications often occur in myeloproliferative disorders. Standard textbooks almost always mention the occurrence of cerebral venous thrombosis in myeloproliferative disorders, however, without reference to the frequency. In contrast, the literature on cerebral venous thrombosis is limited to four cases of associated myeloproliferative disorders.

We presume that the number of cerebral venous thrombosis patients with an underlying myeloproliferative disorder, and the frequency with which myeloproliferative disorders patients develop cerebral venous thrombosis, may be higher than currently recognised. Because of the therapeutic consequences, we believe that a search for myeloproliferative disorders should be performed in otherwise unexplained cases of cerebral venous thrombosis.

References

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