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LETTER TO THE EDITOR

Headache and vision loss in a middle-aged women

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A 49-year-old woman has experienced progressive headache with blurred vision for 3 years until the right eye turned blind 1 day ago. She denied hypertension, diabetes, abortion, consumption of alcohol, tobacco, illicit drugs, or nutritional supplements.

On neurologic examination, the patient's only deficit was blindness of the right eye and bilateral papilloedema. The fundus examination showed moderate edema and unclear border of bilateral optic discs. The degree of right eye optic disc edema is 4D; the left eye was 3D. Fundus fluorescein angiography revealed the right central retinal artery occlusion. The patient also has the enlargement of the spleen. Laboratory tests revealed abnormal routine blood counts: red blood cell (RBC) was 6.14×10^{12}/L, white blood cell (WBC) was 13.79×10^{9}/L, and the platelet (PLT) was 565×10^{9}/L. Other initial investigations including urea and electrolytes were within normal limits. The lumbar puncture showed the cerebrospinal fluid (CSF) pressure at 400 mmH_2O, whereas no abnormality was found in routine and biochemical tests. Further examinations consisting of cerebral magnetic resonance artery (MRA), enhanced magnetic resonance vein (MRV), cerebral magnetic resonance image (MRI), and cardiac ultrasound were conducted in this patient. The enhanced MRV showed thrombosis on the right side of the transverse sinus, sigmoid sinus, and internal jugular vein (Fig. 1). The other three tests were normal.

The coexistence of artery and venous thrombosis accompanying with the increasing blood cell counts lead us to further investigate the hematological system. Therefore, we conducted the bone marrow puncture. The morphological examination of bone marrow cells showed obvious proliferation of hematopoietic cells, and molecular genetic analysis indicated that $JAK2^{V617F}$ is mutated. Until now, we conclude the final diagnosis, which is the myeloproliferative neoplasms (MPN) with heterozygous mutations in $JAK2^{V617F}$. We performed oral anticoagulation warfarin 3 mg each day for 1 year and hydroxyurea 500 mg twice a day for 3 months. During the 1 month and the 2 years of follow-up, we were delighted to find the degree of bilateral optic discs dropped to 1D and headache was better than before. Furthermore, the CSF pressure and platelet count were both decreased. The enhanced MRV indicated less thrombus in the internal jugular vein, in spite of the unobvious changes of transverse sinus and sigmoid sinus.

Alternative diagnoses were considered. The venous sinus thrombosis could cause headache and increased intracranial pressure, but it would not explain the right central retinal artery occlusion. The headache, vision loss, and thrombosis were also seen in anticardiolipin antibody syndrome; however, no history of habitual abortion and the reserve change of platelet counts did not support it. Because of the occupying effect and blood hypercoagulability caused by cerebral tumor, this kind of patient could occur symptoms alike. The normal cerebral MRI and tumor markers helped exclude it. The patient had no history of alcohol, illicit drugs, and hormone usage as well as toxic exposure. Laboratory examination showed normal blood glucose, lipid, and vitamin levels. Therefore, potential metabolic, toxic, or hormonal causes of intracranial hypertension should not be considered.

MPN belongs to the hematologic diseases mainly affecting the hematopoietic stem cell level which leads to excessive differentiation into one or more lineage blood cells. Generally, MPN can be divided into typical MPN and atypical MPN [1]. Typical MPN mainly includes the following four types: polycythemia vera (PV), chronic granulocytic leukemia, primary myelofibrosis, and essential thrombocythemia (ET). Thrombosis is mostly found in PV and ET. The bone marrow biopsy is the gold standard in favor of ET diagnosis. In this case, the patient had the whole blood account raising,

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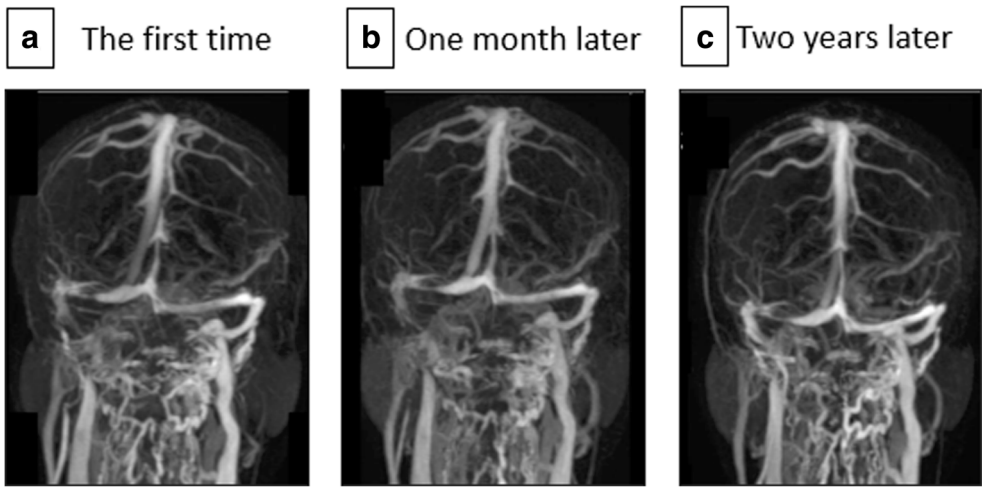

Fig. 1 **a** The initial magnetic resonance vein (MRV) showed obvious thrombosis on the right side of the transverse sinus, sigmoid sinus, and internal jugular vein. **b** After 1 month, the thrombosis severity was still similar to the A. **c** After 2 years, the MRV indicated less thrombus in internal the jugular vein, in spite of the unobvious changes of transverse sinus and sigmoid sinus

thrombosis, and enlargement of the spleen, which is accordance with MPN's manifestation. The patient's clinical symptoms and examination reach the ET diagnostic criteria which requires platelet count exceeding 450×10^9, remarkable megakaryocyte proliferation, and $JAK2^{V617F}$ mutation. Differing from PV, $JAK2^{V617F}$ mutation can be merely found in half of the ET patients. It is well known that splanchnic venous thrombosis is a typical manifestation of MPN. Previous literature reported the ET patients are susceptible to ischemic stroke especially on watershed infarcts [2]. Fortunately, our patient was free from strokes.

As far as the treatment is concerned, different kinds of ET patients have their own therapies. ET patients without symptoms require no treatments. The general treatments for ET patients are antiplatelet drugs and hydroxyurea. ET patients with $JAK2^{V617F}$-positive genotype seem to be more responsive to hydroxyurea, and the effective drug dose is relatively low [3]. This patient is unusual because of the coexistence of arterial and venous thrombosis. It is commonly accepted that arterial thrombosis requires antiplatelet, and venous or sinus thrombosis requires anticoagulation. Anticoagulation therapy combined with low-dose aspirin is recommended for MPN patients with vein thrombosis associated with the $JAK2^{V617F}$ mutation [4]. For patients with arterial and venous thrombosis, direct oral anticoagulants represent a major advance in oral anticoagulant therapy and have replaced vitamin K antagonists as the preferred treatment [5]. For our patient, the possible explanation for the minimal change in neuroimaging during the follow-up may be that once the sinus thrombosis is formed and exist for a long time, anticoagulant therapy may have little effect on the dissolution of the thrombosis. The improvement of symptoms is mainly attributed to the formation of cerebral venous collateral circulation. This is similar with a case report in neurology that after anticoagulant therapy, the level of consciousness is increased; however, repeat neuroimaging showed unchanged extensive venous sinus thrombosis [6].

The case highlights several challenges. Initially, the systemic etiology, particularly hematological system should be considered when encountering arteria and venous thrombosis simultaneously. Therefore, bone marrow puncture and related genetic analysis are in need. In addition, the successfully curing of this patient relied on the doctors from Ophthalmology and Hematology Department, which reflects the significance of multidisciplinary cooperation. This case reminds us to grasp the key clues and seek out the etiology behind carefully and patiently. Meanwhile, the concept of holistic diagnosis and treatment should be taken into account.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of relevant financial interests in this manuscript.

Ethical statements The manuscript has not been submitted to more than one journal for simultaneous consideration or published previously (partly or in full). The study is not split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time. No data have been fabricated or manipulated (including images) to support your conclusions. No data, text, or theories by others are presented as if they were the author's own. Proper acknowledgements to other works must be given, quotation marks are used for verbatim copying of material, and permissions are secured for material that is copyrighted.

Consent to submit has been received explicitly from all co-authors, as well as from the responsible authorities at the institute/organization where the work has been carried out, before the work is submitted. Authors whose names appear on the submission have contributed sufficiently to the scientific work and therefore share collective responsibility and accountability for the results.

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