Scientific Research Publishing

Journal of Biosciences and Medicines, 2022, 10, 289-293
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Association between Immunological Thrombocytopenia and Thrombosis, Is It an Exotic Phenomenon?—A Case Report

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How to cite this paper: Salah, M., Hamaz, S., Bachir, H., Alaoui, H. and Serraj, K. (2022) Association between Immunological Thrombocytopenia and Thrombosis, Is It an Exotic Phenomenon?—A Case Report. *Journal of Biosciences and Medicines*, **10**, 289-293.
https://doi.org/10.4236/jbm.2022.109020

Received: July 10, 2022
Accepted: September 27, 2022
Published: September 30, 2022

Abstract

Immunologic thrombocytopenia (ITP) is an autoimmune disease associated with the production of autoantibodies against specific platelet membrane glycoproteins. A thrombotic event as an unusual occurrence during ITP is becoming more and more frequent. In fact, several recent studies have shown an increased thrombotic risk in this situation. The case presented here is that of a fifty-one-year-old woman with extensive cerebral venous thrombosis 2 years after her ITP diagnosis. During IT, thrombosis may be triggered by the release of pro-thrombotic platelet micro-particles and by platelet activation due to the interaction between autoantibodies and platelet glycoproteins. Immunosuppressive therapy has also been linked in several studies to the thrombotic phenomenon. Increased thromboembolic risk should be taken into account in all ITP patients.

Keywords

Immune Thrombocytopenia, Thrombosis, Immunosuppressive Therapy, Corticosteroid Therapy, Corticosteroid Dependence

1. Introduction

Thrombocytopenia is a hematological condition defined by a platelet count of fewer than 100,000 platelets per microliter; ITP is diagnosed after all other possible etiologies of thrombocytopenia have been ruled out [1].

It exposes the patient to a hemorrhagic risk but paradoxically associations with thrombotic events have been reported.

Several mechanisms, including circulating platelet-leucocyte-monocyte aggregates, endothelium activating antibodies, a larger proportion of young activated

platelets and increased platelet microparticle release have been proposed to explain this thrombotic tendency [2] [3].

Additional co-morbidities or therapeutic interventions, such as the presence of antiphospholipid antibodies, splenectomy or intravenous immunoglobulin use, may be additional risk factors for TEs in ITP patients [4] [5].

The interest of this article is to show that in addition to the mechanisms mentioned above, other factors such as immunosuppressive treatment can promote the occurrence of thrombosis.

We report the case of a 51-year-old woman, treated for ITP, who presented a cerebral thrombophlebitis, revealed by a status epilepticus, 2 years after her disease was diagnosed.

2. Case Presentation

A 51-year-old woman came to the emergency room with generalized tonic-clonic seizures with ocular revulsion and post-critical deficit associated with apyrexia. She had a history of cortico-dependent immunological thrombocytopenia, and vincristine and dexamethasone therapy was indicated during the acute phase, of which she received 4 courses with positive evolution. The patient was a good candidate for splenectomy due to her corticode dependence.

The haemogram showed a platelet count of 247,000/microlitre, haemoglobin = 12.9 g/dl, leukocytes = 6800/microlitre, lymphocytes = 3640/microlitre, C-reactive protein = 15.06 mg/l.

Cerebral magnetic resonance imaging (MRI) revealed upper longitudinal sinus thrombophlebitis extending to the right lateral (**Figure 1**).

The patient was given effective doses of low molecular weight heparin for anticoagulation, followed by anti-vitamin K.

An etiological work-up of the thrombophlebitis was requested and came back negative, *i.e.* 24 h proteinuria, thrombophilia work-up, anti-nuclear antibody and anti-phospholipid antibody, serum protein electrophoresis and search for Jack 2 mutation, as well as a paraneoplastic workup: mammography, cervical thoracic abdominal pelvic CT scan, cervical vaginal smear showed no unusual findings.

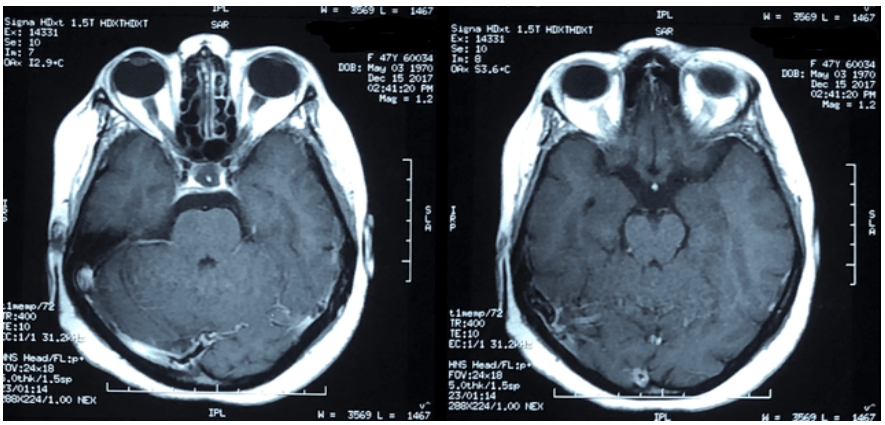

Figure 1. Upper longitudinal sinus thrombophlebitis extending to the right lateral sinus.

3. Discussion

Patients treated for ITP have reported several venous thrombosis events, some of which involved thrombosis as the index event [6].

Recent observational studies of adult populations showed causality between ITP and thrombosis.

A retrospective study in the United States reported a 3% prevalence of thromboembolic events in patients treated for ITP [7], studies in Denmark showed a doubling of the relative risk of venous or arterial thrombotic events in patients known to be treated for ITP compared to the control population [8].

The occurrence of venous or arterial thrombotic events during immune thrombocytopenia raises the question of causality between these two events. Several hypotheses have been developed to explain this association.

Active disease is characterized by a higher platelet replacement rate in the bone marrow and higher levels of circulating platelet microparticles (PMP) may increase the risk of thrombin formation and thus promote venous thrombosis [9].

Patients treated with immunoglobulins (IVIG) (Immunoglobulins) and thrombopoetin receptor analogue (TPO-RA) have a higher risk compared to other types of treatment [9].

IVIGs are used for acute conditions because they prevent platelet destruction while simultaneously promoting thrombosis by increasing blood viscosity and thrombin production [9].

TPO-RAs are agents that mimic the action of thrombopoietin on megakaryocytes. They promote their growth and differentiation and therefore increase platelet production. An increase in platelet count (above the normal target) may contribute to thrombosis, as activated megakaryocytes lead to a higher risk of thrombosis, despite a low platelet count [9].

A multi-center retrospective study carried out in France on thrombosis under thrombopoietin receptor agonists during ITP showed that thrombosis can occur regardless of the duration of exposure to TPO-RA. The development of thrombosis seems to be independent of the management of TPO-RA during the episode [10].

Corticosteroid therapy has also been incriminated by some studies like the one carried out by the International Society of Thrombosis and Hemostasis in 2014 which showed that the use of steroids (mainly prednisone) over a long period of time, splenectomy and immunosuppressive drugs (azathioprine, cyclophosphamide, cyclosporine and vincristine) are significantly associated with an increased thrombosis [11].

Our patient's thrombotic episode occurred with a normal platelet count and without any indication of IVIG or TPO-RA initiation, which suggests that the thrombosis was caused by corticosteroid therapy, given the cortico-dependent and corticosteroid-sensitive nature of this patient's IT. This does not entirely rule out the use of vincristine, since it was only administered once and far from the thrombotic phenomenon.

4. Conclusion

Patients with immunologic thrombocytopenia have a higher risk of venous thromboembolic events compared to unaffected patients. Disease activity, IVIG, TPO-RA are known factors promoting the occurrence of thrombosis during ITP. Immunosuppressive treatment, especially long-term corticosteroids, should not be ruled out as a causative factor.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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