



## Case Report

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# Essential Thrombocythemia Following Immune Thrombocytopenia With *JAK2* V617F Mutation: A Case Report

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**Citation** Payandeh M, Aeinfar M, Dadashizadeh K, Yari S. Essential Thrombocythemia Following Immune Thrombocytopenia With *JAK2* V617F Mutation: A Case Report. *Case Reports in Clinical Practice*. 2021; 6(4):141-144.

**Running Title:** Essential Thrombocythemia and *JAK2*V617F Mutation

**Article info:****Received:** 06 July 2021**Revised:** 17 July 2021**Accepted:** 08 August 2021**Keywords:**

*Jak2* mutation; Essential thrombocythemia; Immune thrombocytopenia

**ABSTRACT**

Immune Thrombocytopenia (ITP) is an autoimmune bleeding disorder. Tyrosine Kinase *JAK2* (*JAK2* V617F) mutation occurs in nearly 60% of Essential Thrombocythemia (ET) patients. Both diseases produce impaired platelet. We describe a case with ET following ITP. So far, only 3 reports described ET following ITP. We report the fourth patient with *JAK2* V617F mutation at the onset of ITP presented 20 years ago that needed splenectomy. The association of these two diseases may recommend similar pathogenic mechanisms between Myeloproliferative Neoplasms (MPNs) and ITP that should be further explored.

**Introduction**

The *JAK2* gene is a cytoplasmic tyrosine kinase that plays a role in cellular signaling of several hematopoietic growth factors, and differentiation, proliferation, and self-regeneration of stem cells [1]. The mutation

in this gene directly affects the coding sequence of *JAK2* and activates the JAK-STAT pathway; thus, disrupting the function of the hematopoietic stem cells is associated with hematopoiesis [2, 3]. The *JAK2* V617F is a base substitution mutation that has been identified in Philadelphia-negative Myeloproliferative Neoplasms (Ph-MPNs), such as Primary Myelofibrosis (PMF), Polycythemia Vera

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## Introduction

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ET is the expansion of clonal hematopoietic stem cells and is characterized by continuous clonal thrombosis, excessive megakaryocyte expansion in bone marrow, increased platelet count, usual erythrocytic mass, and the lack of prominent bone marrow fibrosis. Because the ET and other Ph-negative MPNs have common clinical and biological symptoms that make them difficult to diagnose, it is very important to use molecular techniques to classify the clinical and pathophysiological features of these diseases [2, 5].

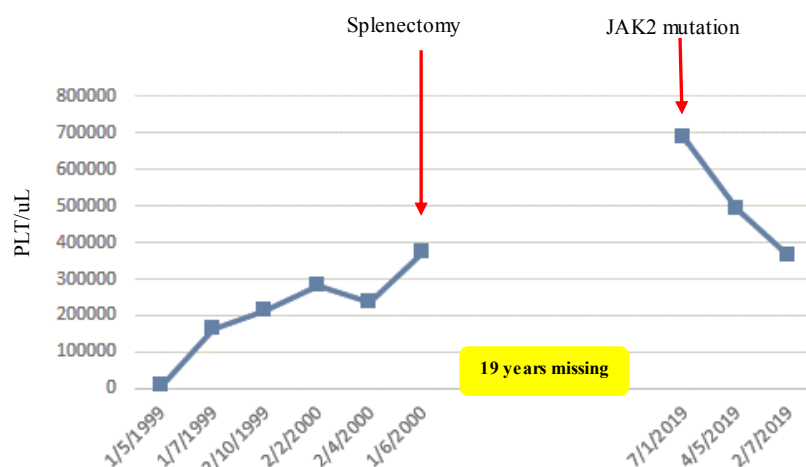
Immune thrombocytopenia (ITP) is an acquired autoimmune disease characterized by platelet destruction and suppression of the production of megakaryocyte platelet [7, 8]. In this hematologic disorder that is identified by mild or severe thrombocytopenia, the platelet count is less than 100 G/L, leading to the manifestation of a hemorrhagic disorder [9, 10]. The most important symptoms of this disease include petechia, mucosal bleeding, ecchymosis, and purpura [11]. The incidence of ITP is 1

to 13 per 100,000 people and may occur at any age [12]. ET and ITP are two different blood disorders that highly affect the number of platelets. So far, only three cases with ET following ITP have been reported. Limited data are available on two types of platelet disorders that occur in succession. In this study, we report the fourth case of the diagnosed ET, 19 years after the diagnosis of ITP.

## Case Presentation

In May 1999, an 18-year-old single female patient presented with a complaint of mucosal bleeding with petechiae, epistaxis, ecchymosis, and Platelet (PLT) count of 10,000/ $\mu$ L that had been diagnosed with ITP. Hemoglobin (Hb), White Blood Cell count (WBC), and coagulation tests were normal. All tests for Cytomegalovirus (CMV), hepatitis B and C, and HIV were negative. Bone marrow aspirate indicated increased myeloid/erythroid ratio and megakaryocytes. Treatment had been initiated with daily prednisone (1 mg/kg) with proper PLT response (161,000 / $\mu$ L), but after tapering, the platelet decreased significantly. Due to poor tolerance and efficacy, in June 2000, splenectomy was performed and her platelet count reached normal (372,000/ $\mu$ L). Over the following 19 years, no close follow-up has been considered for the patient and in January 2019, she (age 39) was again referred to our clinic by her general practitioner because of a PLT count of 689,000/ $\mu$ L (Figure 1). A bone marrow trephine indicated increased cellularity and clustering of large and giant mature megakaryocytes with folded nuclei. A real-time Polymerase Chain Reaction (real-time PCR) analysis revealed the presence of *JAK2* V617F mutation in her peripheral blood.

The patient was diagnosed with ET based on the World Health Organization (WHO) 2008 criteria [13],



**Figure 1.** Platelet count over the follow-up of the patient with Immune Thrombocytopenia (ITP) and Essential Thrombocythemia (ET)

**Table 1.** Information of the reported case with Immune Thrombocytopenia (ITP) and Essential Thrombocythemia (ET)

Variables	Sex Female
ITP Diagnosis	May 1999 (age: 18, y)
ITP Treatment	Prednisone, Splenectomy
ET Diagnosis	January 2019 (age: 18-39, y)
JAK2 Mutation	Positive
Splenomegaly	Yes
ET Treatment	Hydroxyurea



treating with Hydroxyurea (HU; 500 mg) daily in divided doses. PLT count reached the normal range in July 2019. Presently, the patient does not have the side effects on a similar dosage of HU. Patient characteristics are summarized in [Table 1](#).

## Discussion

The discovery of the mutation in the *JAK2* gene made significant advances in understanding the pathophysiology of Ph-negative myeloproliferative neoplasms. The *JAK2* V617F mutation, which is restricted to blood cells and causes specific phosphorylation along with triggering of the tyrosine kinase function, has been proposed as a beneficial molecular marker in the detection of MPNs [14]. Researchers have found that mutations in this gene can be detected in approximately 0.2% of adult patients with no hematological disorder [15]. In this study, we examined a case, for whom ITP and ET were detected in the gap of 19 years. These two diseases have different clinical symptoms and the intrinsic relationship between them is complex, but according to the results of a population-based study, a 20% increase in the risk of developing MPN is observed in cases with a history of autoimmune diseases, such as ITP [16]. Also, a study by Sobas et al. on a 45-year-old woman suggested the association between autoimmune disorders and the JAK/STAT signaling pathway, and it was introduced as a potential factor for neoplastic ET progression in women with a history of ITP [8]. Huang et al. reported a *JAK2*-positive patient with a small MPN clone caused by low *JAK2* allele burden, which was related to thrombocytosis and leukocytosis after splenectomy, and thrombocytosis was probably covered due to cellular destruction by immunity in the spleen pre-splenectomy [17]. Firstly, Caocci et al. investigated the *JAK2* allele burden at the onset of ITP, which resulted in a small 3% *JAK2*-positive clone at the beginning of ITP diagnosis, which

increased to 27% in the 13 next years. In this case, a splenectomy was performed on the patient, followed by progressive thrombocytosis [18]. Finally, in our case, who was a *JAK2*-positive patient, we faced thrombocytosis after splenectomy. It can be concluded that the interaction between autoimmune disorders and MPNs is a complex issue that needs further investigation.

## Conclusion

In conclusion, it can be speculated that splenectomy and autoimmunity may influence the development of the *JAK2* V617F mutation and MPNs; thus, analysis of this mutation could be suggested to ITP patients.

## Ethical Considerations

### Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information. They were free to leave the study whenever they wished, and if desired, the research results would be available to them. Written consent has been obtained from the subjects. Principles of the Helsinki Convention was also observed

### Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

### Conflict of interest

The authors declared no conflicts of interest.

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