Janus kinase 2 V617F mutation and thrombotic events in Behcet’s disease: The Alexandria experience

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To the Editor,

Behcet’s Disease (BD) is a rare, multisystem inflammatory disorder, which is relatively more common in the Mediterranean and East Asia, and is associated with considerable heterogeneity in its clinical course. Phenotypic difference among patients makes BD a difficult condition to diagnose and manage. However, vascular involvement is one of its common complications, with venous thrombosis being the most frequent presentation.

Mutations of the Janus kinase-2 (JAK-2) gene result in production and constitutive over activation of JAK-signal transducer and activator of transcription pathway, which is associated with many hematological, rheumatologic, and autoimmune conditions (1). While the JAK-2 V617F mutation allows a reliable and early detection of polycythemia vera and has been shown to predict an increase in the risk of thrombosis in myeloproliferative disorders allowing the early identification of patients at high risk of developing this complication, the association between this mutation and risk of thrombosis among patients with other conditions associated with thrombosis is still being explored (2-3).

To date, there has been only one controlled study suggesting a non-association between the JAK-2 V617F mutation with 62 BD patients with thrombosis and 90 BD patients without thrombosis among the inhabitants of Turkey (4).

We explored the potential association between the JAK-2 V617F mutation and BD with thrombotic events in this case series between May 2013 and February 2014. Six patients (5 males and 1 female), who were inhabitants of Alexandria, Egypt and fulfilled the International Study Group Criteria for BD with at least one thrombotic event, were included in this study (Table 1). The presence of thrombosis was confirmed by imaging modalities including Doppler ultrasonography or computerized tomography.

Patient ages ranged between 26 and 36 years (median age: 28 years). Exclusion criteria included onc hematological conditions, other autoimmune conditions, or risk factors for thrombosis such as hyperhomocysteinemia; protein C, protein S, or antithrombin III deficiency; anti-phospholipid syndrome; factor V Leiden; or high platelet aggregation. Autoantibodies including rheumatoid factor, anti-nuclear antibody, and anti-neutrophil cytoplasmic antibody were negative in all patients.

Peripheral blood samples were collected from patients using ethylenediaminetetraacetic acid (EDTA) vacuum tubes. DNA was extracted using QiAamp DNA Mini kit (Qiagen; Hilden, Germany). The JAK-2 V617F gene was amplified with two forward and two reverse primers, which were used in different combinations, to generate three potential PCR products using amplification refractory mutation screening. Detection was performed by agarose gel electrophoresis (5).

Eight thrombotic events were observed, all of which had venous origin. Deep venous thrombosis was the most frequently observed thrombotic complication (5/8=63%), while other complications included Budd–Chiari syndrome, superficial thrombophlebitis, and retinal vein occlusion. None of our patients tested positive for the JAK-2 V617F mutation.

Our study represents the first descriptions of Egyptian patients with BD and its association with this mutation. While limited in scope and sample size, as it involved 6 patients and was without controls, we did not...
observe an association between thrombotic tendencies and the JAK-2 V617F mutation. As it is apparent that significant discrepancies exist between ethnic and genetic groups in relation to the phenotype of BD, it would appear important to explore the potential relevance of the JAK-2 V617F mutation in association with thrombosis in different ethnic BD populations.

Ethics Committee Approval: Ethics committee approval was received by the Alexandria University Local Ethics Committee.

### Table 1. BD patients with thrombotic events

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Sex (age)</th>
<th>Thrombotic Event(s)</th>
<th>JAK-2 V617F analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M (29)</td>
<td>DVT×3 episodes</td>
<td>Negative</td>
</tr>
<tr>
<td>2</td>
<td>M (36)</td>
<td>DVT</td>
<td>Negative</td>
</tr>
<tr>
<td>3</td>
<td>M (26)</td>
<td>Budd–Chiari syndrome</td>
<td>Negative</td>
</tr>
<tr>
<td>4</td>
<td>M (26)</td>
<td>Superficial thrombophlebitis</td>
<td>Negative</td>
</tr>
<tr>
<td>5</td>
<td>F (27)</td>
<td>DVT</td>
<td>Negative</td>
</tr>
<tr>
<td>6</td>
<td>M (34)</td>
<td>Retinal vein occlusion</td>
<td>Negative</td>
</tr>
</tbody>
</table>

M: male; F: female; DVT: deep venous thrombosis; JAK-2: Janus kinase-2; BD: Behcet’s disease

Informed Consent: Written informed consent was obtained from patients who participated in the study.

Peer-review: Externally peer-reviewed.


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### References


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