A Novel Mutation of IRF2BP2 Gene Associated with Common Variable Immunodeficiency and Pyoderma
Nancy I. Joseph, DO
d Robert W. Hostetter Jr., DOHaig Tcheurekdjian, MD

1) University Hospitals Cleveland Medical Center, Cleveland, Ohio
2) Allergy and Immunology Associates Inc., Mayfield Heights, Ohio
3) Case Western Reserve University School of Medicine, Cleveland, Ohio

INTRODUCTION
Common Variable Immunodeficiency (CVID) is a primary immune deficiency characterized by decreased levels of IgG, IgA and/or IgM in the setting of recurrent sino-pulmonary infections and frequently in association with inflammatory or autoimmune disorders. The cause of CVID is known in less than 10% of cases. We describe a novel mutation of the Interferon Regulatory Factor 2 Binding Protein 2 (IRF2BP2) associated with CVID and pyoderma gangrenosum.

CASE
The patient is a 63 year old male who had presented with a history of few but severe infections including pneumonia. He then developed facial pyoderma gangrenosum. The patient was found to have with decreased levels of IgG, IgM, and IgA and no response to pneumococcal immunization. The patient was diagnosed with CVID. He was tried on a myriad of therapies, including rituximab and high-dose intravenous immunoglobulin, with no significant sustained improvement in his facial lesions. He was then placed on anakinra, and though his lesions did not resolve, they improved in both number and severity. Whole exome sequencing identified a heterozygous mutation in IRF2BP2 (c.1180 A>C; p.T394P).

DIAGNOSTICS

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>100</td>
<td>1600</td>
</tr>
<tr>
<td>IgA</td>
<td>10</td>
<td>220</td>
</tr>
<tr>
<td>IgM</td>
<td>40</td>
<td>400</td>
</tr>
</tbody>
</table>

Figure 1: Immunoglobulin levels and Immunodeficiency profile before starting Intravenous Immunoglobulin (IVIG) therapy

<table>
<thead>
<tr>
<th>Protein</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>40-200 mg/dL</td>
</tr>
<tr>
<td>IgA</td>
<td>7-40 mg/dL</td>
</tr>
<tr>
<td>IgM</td>
<td>70-300 mg/dL</td>
</tr>
</tbody>
</table>

Figure 2: Immunoglobulin levels and Immunodeficiency profile after starting IVIG therapy

FIGURES

Figure 3: Pyoderma lesions

GENETICS

Figure 4: IRF2BP2 gene location denoted by red line and arrow

DISCUSSION
CVID is one of the most common symptomatic primary immunodeficiency syndromes, however, the exact cause of this disease entity is not known in most cases. Several genes have been postulated to be involved in the pathogenesis of CVID including IRF2BP2. A heterozygous IRF2BP2 mutation (c.1652G>A; p.551N) was recently reported to be associated with CVID and autoinimmune disease. We describe a novel mutation of IRF2BP2 associated with CVID and pyoderma gangrenosum.

ACKNOWLEDGEMENTS

Dr. Steven Holland at the National Institutes of Health (NIH) for invaluable assistance in this patient’s care.

REFERENCES