A Novel Mutation of IRF2BP2 Gene Associated with Common Variable Immunodeficiency and Pyoderma

Nancy I. Joseph, DO[1]., Robert W. Hostoffer Jr[1,2]., DO, Haig Tcheurekdjian, MD[3]

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

IGG	421 (L)	700-1600	mg/dL
IGA	10 (L)	70-400	mg/dL
IGM	22 (L)	40-230	mg/dL

CD3 %		65	%	59-87
CD3 ABSOLUTE		0.787	X10E9/L	0.710-4.180
CD3+CD4+ %		29	%	29-57
CD3+CD4+ ABSOLUTE		0.351	X10E9/L	0.350-2.740
CD3+CD8+ %	H	36	%	7-31
CD3+CD8+ ABSOLUTE		0.436	X10E9/L	0.080-1.490
CD4/CD8 RATIO	L	0.81		1.00-3.50
CD3+CD4-CD8-%		3.00	%	0.00-5.90
CD45 %		100	%	
CD3-CD16+CD56+ %		10	%	0-18
CD3-CD16+CD56+ ABSOLUTE		0.121		0.000-0.860
CD19 %	H	25	%	6-19
CD19 ABSOLUTE		0.303	X10E9/L	0.070-0.910

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

IGA,SERUM		55		MG/DL (81-463)
IGG,SERUM		1205		MG/DL (694-1618)
IGM,SERUM		16		MG/DL (40-271)
CD3%	H	90	%	59 - 87
CD3 ABSOLUTE		2.349	X10E9/L	0.710 - 4.180
CD3+CD4+ %		29	%	29 - 57
CD3+CD4+ ABSOLUTE		0.757	X10E9/L	0.350 - 2.740
CD3+CD8+ %	H	61	%	7 - 31
CD3+CD8+ ABSOLUTE	H	1.592	X10E9/L	0.080 - 1.490
CD4/CD8 RATIO	L	0.48		1.00 - 3.50
CD3+CD4-CD8-%	H	6.00	%	0.00 - 5.90
CD45 %		100	%	
CD3-CD16+CD56+ %		10	%	0 - 18
CD3-CD16+CD56+ ABSOLUTE		0.261	x10E9L	0.000 - 0.860
CD19%	L	0	%	6 - 19
CD19 ABSOLUTE	L	0.000	X10E9/L	0.070 - 0.910

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

FIGURES

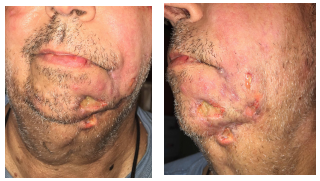

Figure 3: Pyoderma lesions

GENETICS

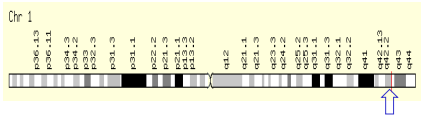

Figure 4: Chromosome 1 with IRF2BP2 gene location denoted by red line and arrow

Figure 4: IRF2BP2 gene
⇨= mutation found in this patient (p.T394P)
➡= previously described mutation (p.551N)

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 autoimmune disease. We describe a novel mutation of IRF2BP2 associated with CVID and pyoderma gangrenosum.

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