Scholar: Pilot and Validation Studies ISSN: 2689-7644
Volume 4 Issue 2 Pages: 1 – 2 DOI:10.32778/SPVS.71366.2023.38

Acute pulmonary embolism in a patient with STAT3 mutation after recent SARS-CoV2 infection

Authors: Henry Blunk, DO[1], Meghan Callahan, OMS-III[2], Katheryn Birch, DO[1], Robert W. Hostoffer, DO[1]

Affiliations:
1) Allergy/Immunology Associates Inc, Mayfield Heights, OH, 2) Lake Erie College of Osteopathic Medicine, Elmira, NY

Keywords: Job's syndrome, STAT3 mutation, COVID-19, pulmonary embolism, Hyper-IgE Syndrome, HIES

Article History: Date received: 06/19/2023 Date accepted: 10/15/2023
Corresponding Author: Henry Blunk **E-mail:** henry.blunk3@uhhospitals.org

Introduction:

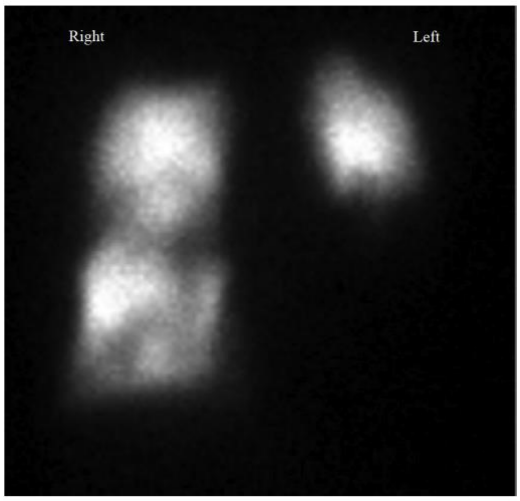
Signal transducer and activator of transcription 3 (STAT3) is a gene within the STAT family, which regulated cell proliferation, growth, and differentiation of the immune system.[1] A mutation in this gene is uncommon, but affects STAT dimerization causing disruption in the JAK/STAT molecular pathway leading to multiorgan dysfunction.[2] This mutation manifests as Hyper-IgE Syndrome (HIES), which is characterizes by recurrent lung and Staphylococcal infections, eczema, eosinophilia, and elevated serum IgE levels.[3] Other complications of this disorder have been identified, and include vascular abnormalities such as increased tortuosity, aneurysms, thrombus formation, and dilatations.[2,4] Here, we describe a patient with a STAT3 mutation who presented with a pulmonary embolism following SARS-CoV2 infection.

Case description:

A 53-year-old male with a STAT3 mutation presented with an acute pulmonary embolism (PE) after SARS-CoV2 infection. His case has been defined in a prior report documenting eosinophilia, elevated IgE, clinical picture consistent with HIES, and genetic sequencing confirming STAT3 mutation.[5] Other significant medical history includes hypertension, stage III chronic kidney disease secondary to amyloidosis, right hip avascular necrosis requiring Girdlestone procedure, pneumatocele and bronchiectasis requiring left lower lobectomy in childhood. His father and three children also have similar clinical findings suggestive of a STAT3 mutation. Kim et. al reported a case of cerebrovascular aneurysm in one of the patient's children.[6] The proband was being managed with intravenous immunoglobulin therapy (IVIG) every month. He was diagnosed with SARS-CoV2 infection, not requiring hospitalization, with management of supportive care at home. The patient then developed worsening dyspnea ten days later, prompting him to return to the hospital for further evaluation.

The patient was found to be hypoxemic and required supplemental oxygen. Due to the patient's diminished renal function, a Ventilation/Perfusion (V/Q) scan was obtained and demonstrated a high probability of acute PE with multiple segments of absent perfusion in the left lung (Figure 1).

Figure 1: Ventilation/Perfusion (V/Q) scan



Filling defect within the left lung indicating (dark field on lower left side) a high probability of an acute PE.

A duplex ultrasound of the lower extremities did not demonstrate deep vein thrombosis (DVT).

ISSN: 2689-7644
Volume 4 Issue 2 Pages: 1 – 2
DOI:10.32778/SPVS.71366.2023.38

He was initiated on intravenous (IV) heparin for acute PE. The patient's hospitalization was also complicated by multifocal pneumonia as noted on the chest computed tomography (CT) requiring IV antibiotics. Also noted on the chest CT was a pericardial effusion prompting consultation from cardiology and an echocardiogram. The echocardiogram demonstrated minimal mitral valve prolapse with a ruptured papillary muscle attached to the anterior mitral valve leaflet. The patient was eventually discharged from the hospital with oral apixaban and antibiotics for treatment of PE and pneumonia, respectively.

The STAT family has seven proteins. STAT3 specifically modulates immune responses and plays a vital role in both the innate and adaptive immune systems. Within the innate immune system STAT3 facilitates dendritic cell development and induces granulopoiesis in response to bacterial or fungal infections.[1] In the adaptive immune system, STAT3 is critical in the formation of B-cell precursors and differentiation of plasma cells secreting IgG.[1] A mutation in STAT3 causes a primary immunodeficiency due to a decreased amount of class-switched memory B-cells and IgG levels.[1]

STAT3 mutation is a rare primary immunodeficiency that clinically manifests as multiorgan disorders.[2] Connective tissue and skeletal dysfunctions including scoliosis, craniosynostosis, retained primary dentition, and recurrent fractures are other manifestations that have been described.[2] Vascular abnormalities causing formation of thrombi and aneurysms have been reported with this disorder.[2] Hakim et. al reported a patient with HIES that presented with recurrent hemoptysis secondary to pulmonary artery pseudoaneurysm.[7] There has also been a reported case of chronic right upper extremity DVT in a patient with autism and HIES.[8] the Increased incidence of PE and other thrombotic events is a well-known complication in patients infected with SARS-CoV2.[9]

Conclusion:

This case report has at least two important risk factors (HIES/STAT3 mutation and SARS-CoV2 infection) that would increase his likelihood of developing a PE. We describe the first case of a patient with STAT3 mutation that developed an acute PE less than two weeks after becoming infected with SARS-CoV2.

Author Contributions:
All authors contributed equally to the conception and design, acquisition of data, or analysis, interpretation of data, manuscript preparation and review.

Funding Sources: None.

Potential Conflicts of Interest Disclosures:
The authors disclose that there were no conflicts of interest or financial support in the development of this project. All data is authentic and accurate.

References:

1) Hillmer EJ, Zhang H, Li HS, Watowich SS. STAT3 signaling in immunity. Cytokine Growth Factor Rev. 2016 Oct;31:1-15. doi: 10.1016/j.cytogfr.2016.05.001. Epub 2016 May 9.
2) Yavuz H, Chee R. A review on the vascular features of the hyperimmunoglobulin E syndrome. Clin Exp Immunol. 2010 Mar;159(3):238-44. doi: 10.1111/j.1365-2249.2009.04044.x. Epub 2009 Nov 12.
3) Minegishi Y. Hyper-IgE syndrome, 2021 update. Allergol Int. 2021 Oct;70(4):407-414. doi: 10.1016/j.alit.2021.07.007. Epub 2021 Aug 18.
4) Gharib AM, Pettigrew RI, Elagha A, Hsu A, Welch P, Holland SM, Freeman AF. Coronary abnormalities in hyper-IgE recurrent infection syndrome: depiction at coronary MDCT angiography. AJR Am J Roentgenol. 2009 Dec;193(6):W478-81. doi: 10.2214/AJR.09.2623.
5) Meyer-Bahlburg A, Renner ED, Rylaarsdam S, et al. Heterozygous signal transducer and activator of transcription 3 mutations in hyper-IgE syndrome result in altered B-cell maturation. J Allergy Clin Immunol. 2012 Feb;129(2):559-62, 562.e1-2. doi: 10.1016/j.jaci.2011.09.017. Epub 2011 Oct 26.
6) Kim Y, Nard JA, Saad A, et al. Cerebral aneurysm in a 12-year-old boy with a STAT3 mutation (hyper-IgE syndrome). Ann Allergy Asthma Immunol. 2015 May;114(5):430-1. doi: 10.1016/j.anai.2015.02.016. Epub 2015 Mar 24.
7) Hakim A, Bazan IS, Sanogo ML, et al. Pulmonary artery pseudoaneurysm causing massive hemoptysis in hyperimmunoglobulin E syndrome: a case report. BMC Pulm Med. 2019 Feb 8;19(1):34. doi: 10.1186/s12890-019-0797-7.
8) Chowdhury T, Shankar M, Gousy N, Siddique B. A Rare Case of Job Syndrome With Autism: Complicated With Hidradenitis Suppurativa and Chronic Deep Vein Thrombosis. Cureus. 2021 Dec 30;13(12):e20832. doi: 10.7759/cureus.20832.
9) Klok FA, Kruip MJHA, van der Meer NJM. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020 Jul;191:145-147. doi: 10.1016/j.thromres.2020.04.013. Epub 2020 Apr 10.