Patients with monogenic immune dysregulation show improvement in childhood interstitial lung disease following targeted therapy – a case series and single center approach

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December 12, 2021

Abstract

In recent years, a number of monogenic disorders have been described that are characterized by immune dysregulation. A subset of these 'primary immune regulatory disorders' can cause severe interstitial lung disease, often recognized in late childhood or adolescence. Patients presenting to pulmonary clinic may have long and complex medical histories but lack a unifying genetic diagnosis. It is crucial for pulmonologists to recognize features suggestive of multisystem immune dysregulation and to initiate genetic workup, since targeted therapies based on underlying genetics may halt or even reverese pulmonary disease progression. Through such an approach, our center has been able to diagnose and treat a cohort of patients with interstitial lung disease from gene defects that affect immune regulation. Here we present representative cases related to pathogenic mutations in three distinct pathways and summarize disease manifestations and treatment approaches. We conclude with a discussion of our perspective on the outstanding challenges for diagnosing and managing these complex life-threatening and chronic disorders.

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