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SCIENTIFIC LETTER

Cleavage Resistant RIP Kinase1 Induced Autoinflammatory Syndrome (CRIA) - A Novel Autoinflammatory Syndrome

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To the Editor: A 16-mo-old boy presented to us at 10 mo of age with recurrent febrile episodes lasting for 2–3 d and recuring every 10–14 d since 3 mo of age. His mother had a similar undiagnosed periodic fever from the age of 6 y. Physical examination revealed weight 8.5 kg (10^{th}-25^{th} centile), length 73 cm (25^{th}-50^{th} centile), cervical lymphadenopathy and mild hepatosplenomegaly. Investigations revealed neutrophilic leucocytosis, thrombocytosis, transaminitis, raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Next generation sequencing revealed a pathogenic heterozygous missense variant c.970G>A p.Asp324Asn in exon 8 of *RIPK1* in the proband (previously reported by Lalaoui et al.) [1]. Sanger sequencing confirmed the variant in the proband and his mother, but was absent in his father. Hence a diagnosis of Cleavage resistant Receptor interacting protein kinase1 (RIPK1) induced autoinflammatory syndrome (CRIA) was made. The child was initiated on monthly intravenous tocilizumab (8 mg/kg) to which he responded. He developed an anaphylactic reaction to the third dose of tocilizumab and is currently on 0.2 mg/kg/d oral prednisolone with colchicine 0.5 mg/d showing good clinical response. His mother was found to have elevated ESR, CRP and cervical lymphadenitis during one of her febrile episodes. Currently she has only one episode of fever per month and hence is not on specific therapy.

CRIA syndrome is a novel autoinflammatory syndrome due to heterozygous missense variations in *RIPK1* gene and symptoms include periodic fever, lymphadenopathy, oral ulcers, abdominal pain, splenomegaly and arthralgia [2]. The differential diagnosis includes hyper IgD with periodic fever syndrome (HIDS- early onset recurrent fever, lymphadenopathy, oral ulcers, pharyngitis), PFAPA (early onset periodic fever, aphthous stomatitis, pharyngitis, adenitis) and caspase 8 deficiency (lymphadenopathy, splenomegaly). CRIA syndrome shows good response to tocilizumab [3]. This is the youngest patient diagnosed with CRIA syndrome and also the first report from India.

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Declarations

Conflict of Interest None.

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