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CORRESPONDENCE

Mevalonate Kinase Deficiency: Diagnostic and Management Challenges

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To the Editor: We report a 4-y-old girl presenting with recurrent episodes of fever, arthritis, and gastroenteritis since 3 mo of age. On examination, she was febrile, had arthritis of the bilateral knee and left wrist joints, generalized lymphadenopathy, and hepatosplenomegaly. She was malnourished with dysmorphic features (depressed nasal bridge, hypertelorism, and widely spaced teeth) along with motor and language delay. Investigations revealed hemoglobin of 7.5 g/dL, total leucocyte count of 21×10^9 cells/L (neutrophils 64%), platelet count of 520×10^9 cells/L with raised CRP (164 mg/L). Normal serum procalcitonin levels (0.04 ng/mL) and sterile cultures (blood and urine) ruled out any overt evidence of infection. The chest radiograph was normal. Serum levels of IgG [19.3 g/L (4.2–10.5)], IgM 2.7 g/L (0.48–1.68) and IgE 125 IU/mL (0.31–29.5) were elevated, whereas level of serum IgA 1.13 g/L (0.14–1.23) was normal. Clinical exome sequence revealed homozygous mutation *c.976G > A(p.Gly326Arg)* in exon 10 of the *MVK* gene, and a definitive diagnosis of mevalonate kinase deficiency (MKD) was offered. She was prescribed naproxen and oral prednisolone at 1 mg/kg/d and isoniazid prophylaxis for latent tuberculosis. However, the symptoms flared on tapering steroids; following which, tocilizumab at 12 mg/kg four-weekly was started, which resulted in subsidence of symptoms.

MKD is a rare autosomal recessive autoinflammatory disorder presenting with recurrent episodes of fever, arthritis, gastrointestinal symptoms, lymphadenopathy, and organomegaly. Severe disease may have dysmorphism, growth retardation and neurocognitive impairement [1]. The definitive diagnosis is often delayed due to episodic clinical manifestations erroneously attributed to infections, especially in resource-poor settings. The diagnosis of MKD can be confirmed by disease-causing mutations in the *MVK* gene. Our patient had homozygous mutation *c.976G > A(p.Gly326Arg)* in exon 10 of the *MVK* gene, which has also been previously reported from our center [2].

Our patient was managed with NSAIDs, corticosteroids, and tocilizumab. In Eurofever registry of 114 patients, complete response with NSAID and corticosteroids was observed in 11% and 39% patients; canakinumab, anakinra, and etanercept showed response in 80%, 22%, and 8% patients, respectively [3]. There are anecdotal reports showing response of tocilizumab in MKD [4], and may be considered especially where IL-1 blockers are not available. High index of suspicion and a targeted therapeutic approach is the key for successful outcome.

Declarations

Conflict of Interest None.

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