Familial Cold Autoinflammatory Syndrome Type 1

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To the Editor: Familial cold autoinflammatory syndrome (FCAS) is a rare inherited inflammatory disorder, caused by mutation in *NLRP3* gene which encodes a protein NLRP3 [1]. In this report, we describe the first Indian family with FCAS, type 1. A 4-y-old boy, born to a nonconsanguineously married Indian couple, presented with multiple episodes of macular rashes during winters, lasting for 12–24 h. He had a strong family history involving at least 10 members across four generations of family members on the paternal side (father, grandfather, grandfathers' brothers and sister, and great-grandfather) with similar complaints. His father and grandfather also reported episodic arthritis involving large joints of lower limbs on exposure to cold weather. On examination, he was found to have multiple blanching macular rashes on his lower limbs. Systemic examination was unremarkable. Complete blood counts, inflammatory markers, and immunoglobulin profile were normal. A pathogenic heterozygous mutation c.13222C>T (p.Ala441Val) was identified in exon 3 of the *NLRP3* gene by whole exome sequencing. A diagnosis of FCAS type 1 was established and colchicine was initiated.

FCAS is characterized by early onset fever, urticarial rashes, and joint pains after 1–3 h of generalized cold exposure [2]. Cold sensitivity is unique to FCAS among the autoinflammatory disorders and has been shown to increase the activity of the transcription factor AP-1, which increases synthesis of secretory proteins from inflammatory cells [3]. Mean age of presentation in a large series after cold exposure

was 47 d, with a range of 2 h to 10 y. Amyloidosis was reported only in 2% patients [4]. In the index family, none of the family members developed amyloidosis, suggesting a milder phenotype. To the best of our knowledge, this is the first family with FCAS to be reported from India and is only a milestone towards diagnosing many more cases.

Declarations

Conflict of Interest None.

References

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