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Clinical Images: Urticaria, fever, and hypofibrinogenemia

The patient, a 12-year-old girl, presented with a history of recalcitrant urticarial rash, arthralgias, and febrile episodes for >2 years. She repeatedly developed high-spiking fever and systemic inflammation unresponsive to antibiotics and antipyretic medication. Positron emission tomography revealed symmetric cervical and mediastinal lymphadenopathy. The chronic urticaria in combination with the recurrent fever and elevated serum amyloid A levels prompted us to search for a mutation in the *NLRP3* gene. Heterozygosity for the V198M substitution encoded by exon 3 confirmed the suspected diagnosis of a cryopyrin-associated periodic syndrome (CAPS) inherited from her asymptomatic father. This mutation was recently described as having reduced penetrance, causing variable CAPS phenotypes (1,2). No mutations in 2 other genes known to cause autoinflammation (*TNFRSF1A* and *MEFV*) were found. In the context of chronic inflammation, the patient developed a macrophage activation syndrome (MAS) with serositis, hyperferritinemia, hypofibrinogenemia, and bicytopenia as well as hemophagocytosis, which was controlled with anakinra and dexamethasone treatment. The urticarial rash (A) vanished within 1 week. The patient's disease remained stable for >1 year while she received canakinumab, but she experienced a relapse when the treatment intervals were prolonged. Surprisingly, she expectorated bronchial casts (B) for >6 months. Bronchoscopy revealed thick mucus in the left main bronchus (left) and left upper bronchus (right), partially with obstructing mucus impaction (C). The bronchial cast specimens consisting of fibrin vividly document the degree of hyperinflammation caused by CAPS and likely precipitated by MAS.

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