Lasting remission of a Muckle-Wells syndrome with CIAS-1 mutation using half-dose anakinra

Muckle–Wells syndrome (MWS) is an auto-inflammatory syndrome of genetic origin [1], diagnosed on the combination of urticaria, nondestructive arthritis, biological signs of inflammation, hyperleukocytosis, and an inconstant sensorineural deafness. The discovery of mutations of the CIAS-1 gene (coding for cryopyrin) allowed a better understanding of MWS pathogenesis. Indeed, cryopyrin combine with other molecules in a cytoplasmic complex named inflammasome [2]. This inflammasome can get activated by several stimuli, like bacterial residues, or crystals, which leads to caspase-1 activation and shedding of IL-1β and IL-18 [2]. This rationale prompted highly effective trials of anakinra in several open studies, and a convincing double-blind study in CINCA syndrome (ascribed to other mutations of CIAS-1) [3,4]. Although the short-term toxicity of anakinra is rather low, its long-term benefit–risk ratio is still unclear. We report on a case of a 64-year-old male suffering from typical MWS since birth, which has been dramatically improved, by anakinra 100 mg/d, then once every other day. Daily urticaria completely disappeared, as well as arthalgia/arthritis of knees and ankles, hyperleukocytosis, and biological signs of inflammation. After one month of anakinra 100 mg/d, the analogic subjective score of MWS activity collapsed from 80/100 to 0, VAS for pain from 72 to 0, ESR from 88 to 15, CRP from 103 mg/l to 4 mg/l, and leukocytosis from 11.67 × 10^9/l (8.06 × 10^9 PMN/l) to 7.10 (2.3 × 10^9 PMN/l). Only severe sensorineural deafness remained unaffected. Owing to the neutropenia, anakinra 100 mg daily was reduced to 100 mg every other day. One month later, no clinical relapse had occurred despite a slight leukopenia was still present (6.16 × 10^9/l and 2.15 × 10^9 PMN/l).

This report illustrates the high effectiveness of anakinra to treat MWS, and suggests that 100 mg once every other day can be sufficient in some patients to get them rid of the troublesome clinical manifestation of MWS. Lower doses of anakinra might allow: (1) to treat more people with a fixed budget; (2) to lower the long-term toxicity of anakinra, as compared with rheumatoid arthritis. Indeed, a recent study concluded that the risk of infection in this setting was two or three times higher after three years of treatment by anakinra [5] than before it, mostly in patients still treated by corticosteroids.

References


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