

Title:

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Azathioprine-induced alopecia: rare adverse event early marker of myelotoxicity

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To the Editor:

Though not exempt from adverse events, Azathioprine (AZA) is an inexpensive and effective drug in the induction and maintenance treatment of patients with inflammatory bowel disease.

We present a 20-year-old patient with left ulcerative colitis in whom AZA was started at a dose of 1.5 mg/kg/day due to dependence on corticoids (thiopurine methyltransferase activity: 14.9 U / ml). Two weeks after commencing treatment, she began to report excessive hair loss, resulting in an almost complete loss of the scalp. Laboratory tests showed pancytopenia with severe neutropenia (<500 / mcL), for which AZA was suspended in the third week of treatment.

A dermatological examination showed a clearly positive pull test.

Given the suspicion of AZA-induced alopecia, a genetic study of the polymorphisms of the nudix hydrolase 15 gene (NUDT15) was requested, verifying that the patient was a carrier

of the p.R139C variant in homozygosis. Both alopecia and pancytopenia improved with drug withdrawal, with full recovery of the scalp at six months.

Myelotoxicity is one of the most severe adverse events that AZA produces. Leukopenia is the most common finding, with thrombocytopenia and pancytopenia being rarer (1). Variants of NUDT15 have been associated with alterations in thiopurine metabolism due to a deficit in enzyme activity, causing AZA-induced leukopenia and alopecia (2,3). The most frequent is the p.R139C variant, which is found mainly in the Asian population (3,4). Anagen effluvium occurs in these patients, a consequence of the abrupt cessation of mitotic activity in the hair matrix cells (4,5). Rapid and massive hair loss has been found to be an early clinical marker of myelotoxicity (3,5).

This is one of the few cases reported in Europe to date of AZA-induced alopecia and myelotoxicity due to the NUDT15 p.R139C mutation.

STATEMENT OF INFORMED CONSENT:

Informed consent was obtained from the patient to publish the attached image.

BIBLIOGRAPHY:

1. Luber RP, Honap S, Cunningham G, et al. Can We Predict the Toxicity and Response to Thiopurines in Inflammatory Bowel Diseases? *Front Med (Lausanne)*. 2019;6:279.
2. Yang S-K, Hong M, Baek J, et al. A common missense variant in NUDT15 confers susceptibility to thiopurine-induced leukopenia. *Nat Genet*. 2014 Sep;46(9):1017–20.
3. Kishibe M, Nozaki H, Fujii M, et al. Severe thiopurine-induced leukocytopenia and hair loss in Japanese patients with defective NUDT15 variant: Retrospective case-control study. *J Dermatol*. 2018 Oct;45(10):1160–5.

4. Nomura H, Kurihara Y, Saito M, et al. Azathioprine-induced alopecia and leukopenia associated with NUDT15 polymorphisms. *J Eur Acad Dermatol Venereol*. 2018 Oct;32(10):e386–9.
5. Bhokare AB. Azathioprine-induced alopecia as an early clinical marker of its myelotoxicity. *Indian J Drugs Dermatol* 2017;3:40-1.



Figure 1. Photograph of the patient's scalp three weeks after commencing azathioprine treatment. Generalized and significant scalp loss may be observed.