

# Azathioprine induced anagen effluvium and its association with myelosuppression

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**Dear Editor,**

Azathioprine, a steroid sparing immunosuppressant, is used in organ transplantation and various immunological diseases like pemphigus vulgaris, pemphigus foliaceus, vitiligo, lichen planus, and alopecia areata. Anagen effluvium (AE) is the abrupt loss of hairs in their growing

phase most commonly due to chemotherapy and radiation<sup>1</sup>. Azathioprine can cause AE in association with myelosuppression<sup>2</sup>.

A 20 year old married female presented to our department with extensive cutaneous and oral lesions and was diagnosed as pemphigus vulgaris based on clinical examination (Figure 1A) and histopathology.



**Figure 1.** (A) Multiple flaccid vesicles with moist erosions and hyperpigmented patches over trunk (B) Normal hair before starting azathioprine (C) Positive hair pull test (D) Diffuse nonscarring alopecia after starting azathioprine.

Baseline hematological investigations including complete blood count (CBC), liver and kidney function tests were within normal limit. Thiopurine S-methyltransferase level (TPMT) was within normal limit. Dexamethasone pulse (DP) therapy along with azathioprine (50mg BD), were started for her with regular monitoring of blood parameters. After 1<sup>st</sup> cycle of DP therapy, new lesions ceased to appear. However, during 2<sup>nd</sup> cycle, she developed sudden hair loss from vertex which gradually progressed to involve the entire scalp over a period of 15 days. Hair pull test was positive (Figure 1C). Examination revealed diffuse non-scarring alopecia with no signs of inflammation, scaling or atrophy (Figure 1D). CBC showed myelosuppression. Hemoglobin was 7.4gm/dl, WBC was 1200/ $\mu$ l and platelet count was 129000/ $\mu$ l. Azathioprine was discontinued and the patient continued with modified DP therapy and oral prednisolone. Two months after stopping azathioprine, CBC was completely within normal limit with 40% hair regrowth (Figure 2).

Azathioprine acts by inhibition of TPMT which prevents 6-methylmercaptopurine from



**Figure 2.** Regrowth of hair two months after discontinuation of azathioprine.

conversion into the active cytotoxic thioguanine nucleotide metabolites which lead to bone marrow (BM) suppression<sup>2</sup>. TPMT inhibition affects proliferating cells such as T-cells and B-cells. Hence, TPMT deficient patients are at greater risk of BM suppression and regular monitoring of CBC is recommended during treatment<sup>1</sup>. TPMT levels should be checked in all patients receiving azathioprine<sup>1</sup>. However, in resource poor setting, serial measurement of CBC remains the most practical method for early detection of azathioprine induced myelosuppression. Azathioprine inhibits mitosis of hair matrix resulting in abrupt loss of anagen hair usually within 2-4 weeks of starting of therapy<sup>2</sup>. The anagen phase of the hair is characterized by proliferation of the bulb matrix cells which make the hair shaft. Any insult that causes abrupt cessation of mitotic activity of these matrix cells leads to weakening of the proximal portion of the hair shaft, resulting in narrowing and subsequent breakage of hair shaft which results in AE<sup>3</sup>. Hair shedding usually begins 1 to 3 weeks after the insult. Causes of AE include chemotherapy (tyrosine kinase inhibitors and epidermal growth factor receptor inhibitors), radiation to the head and neck, severe protein energy malnutrition, pemphigus vulgaris, alopecia areata, toxic agents like mercury and lithium; drugs like bismuth, levodopa, colchicine, cyclosporine and systemic diseases like systemic lupus erythematosus and secondary syphilis<sup>1,2,4</sup>. AE is more common and severe with combination chemotherapy than with the use of a single drug<sup>1</sup>. In AE, only the proliferating cells in the hair bulb are affected and the quiescent stem cells of the bulge are spared, so hair loss is usually completely reversible<sup>5</sup>. The normal hair follicle cycling begins within a few weeks of cessation of insult and regrowth is apparent within 1-3 months<sup>4</sup>. The duration of development of azathioprine induced AE however depends on the dose and duration of the treatment<sup>5</sup>. In our patient, low CBC count correlated with azathioprine induced AE. Rapid regrowth of hair after drug discontinuation within 2 months correlated with recovery of BM suppression. Azathioprine is not commonly known to cause AE and to the best of our knowledge, we found only two reports of azathioprine-induced AE coinciding with myelosuppression<sup>2,4</sup>. In both cases, the hair loss reversed within two months of

azathioprine cessation as in our case. The sudden pancytopenia experienced by the patient results in hair shaft damage leading to hair loss and hair shaft cuticular damage resulting in development of AE and plica neuropathica<sup>6</sup>.

We report this case to highlight this rare but significant side effect of azathioprine which is an early indicator of myelosuppression. Also, in a case of pemphigus vulgaris with AE, we need to look beyond the disease to evaluate the exact cause of AE.

Vaishali Wankhade, MD

Vrutika Shah, MD

Rajesh P. Singh, MD

Gitesh Sawatkar, MD

*Department of Dermato-venereo-leprology, Government Medical College and Hospital, Nagpur, India.*

*Corresponding author:*

*Vrutika Shah, MD*

*A-1101, Savoy building, Raheja Gardens, Opp. Tip Top Plaza, L.B.S. Marg, Thane West – 400604.*

*Phone No: 9870894102*

*Email: vrutikashah25@gmail.com*

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## REFERENCES

1. Kanwar AJ, Narang T. Anagen effluvium. *Indian J Dermatol Venereol Leprol.* 2013; 79 (5):604-12.
2. Bhokare AB. Azathioprine-induced alopecia as an early clinical marker of its myelosuppression. *Indian J Drugs Dermatol* 2017;3: 40-1.
3. Balasubramanian P, Jagadeesan S, Anjaneyan G, et al. An interesting case report of azathioprine induced anagen effluvium. *Indian J Dermatol.* 2015;60 (3):324.
4. Sharma S, Budhiraja RK, Bassi R. Azathioprine induced anagen effluvium: a rare case report. *Int J Res Dermatol* 2017;3 :300-2.
5. Sonthalia S, Daulatabad D. Azathioprine associated anagen effluvium. *Indian J Dermatol Venereol Leprol* 2016;82:322-4.
6. Joshi R, Singh S. Plica neuropathica (plica polonica) following azathioprine induced pancytopenia. *Int J Trichology* 2010;2:110-2.