Anagen Effluvium as an Early Sign of Azathioprine Toxicity

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Dear Sir,

Azathioprine is a purine analog which is Food and Drug Administration (FDA) approved for organ transplant and severe rheumatoid arthritis (RA). Off-label use in dermatological diseases like immunobullous diseases, atopic dermatitis, autoimmune connective tissue disorders like systemic lupus erythematosus (SLE) and dermatomyositis, and other medical conditions like Crohn's disease, Churg–Strauss syndrome, and myasthenia gravis has long been in the picture.[1–3] The active metabolite of this prodrug is 6-thioguanine (6-TG), which gets incorporated into DNA/RNA structure, causing decreased purine metabolism resulting in its immunosuppressive effect. Thiopurine methyltransferase (TPMT) converts 6-mercaptopurine (6-MP) to an inactive metabolite. TPMT deficiency will cause increased conversion of 6-MP to active metabolite 6-TG, which increases the risk of myelosuppression, one of the life-threatening side effects of the drug.[1,2]

A 29-year-old female, a known case of pemphigus vulgaris, was started on oral prednisolone and azathioprine 100 mg/day. Her blood counts were normal when starting azathioprine, but the counts were not repeated after 1 week of starting the drug. After 20 days, she presented to the hospital with upper respiratory tract infection (URTI), body ache, and a history of acute hair fall since 5 days, but was otherwise in good general health. The hair pull test was strongly positive (Fig. 1). Hair microscopy showed dystrophic anagen hair (Fig. 2). Her blood counts showed significant neutropenia. Total leukocyte count (TLC)—1100/µL, neutrophils—3.6%, lymphocytes—93.6%, monocytes—2.8%, and platelets—39000/µL. Azathioprine was stopped immediately, and she was given

Fig. 1: Positive hair pull test

Fig. 2: Anagen hair on microscopy

Fig. 3: Alopecia totalis

intravenous broad-spectrum antibiotics. She was also put on injection filgrastim [granulocyte colony-stimulating factor (GCSF)] 300 µg for 5 days, after transfusion of 4 units of platelets. Within the next 1 week, she presented with total loss of scalp hair (alopecia totalis—Fig. 3), though her blood counts had come back to normal. Azathioprine suppresses bone marrow, especially in TPMT-deficient patients or in patients who are on febuxostat or allopurinol.[3] Regular monitoring of blood counts is recommended. Ideally, TPMT levels should be done in all patients receiving azathioprine therapy, but since it is an expensive test, in resource-poor countries, regular measurements of blood counts remain the most practical way to detect myelosuppression.[2] Anagen effluvium refers to abrupt shedding of hair in the anagen phase due to impaired follicular mitotic activity.[1] Azathioprine is theoretically known to inhibit mitosis of hair matrix, resulting in anagen effluvium. Two authors have reported hair loss after 1 month of initiating azathioprine, while Sonthalia and Daulatabad noted its occurrence after 48 hours only.[3,4] In our case, the shedding of hair started after 10–15 days, and it correlates with the decreased blood counts, which suggests that this hair loss can be a marker of myelosuppression.

Hence, from this case report, we understand that anagen effluvium is an uncommon but early side effect of azathioprine that may indicate life-threatening myelosuppression.

References

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