Azathioprine-induced Alopecia as an Early Clinical Marker of its Myelotoxicity

Sir,

Azathioprine is an immunosuppressive drug used in organ transplantation and autoimmune diseases and belongs to the chemical class of purine analogs. Azathioprine is commonly used in dermatology for various immunological diseases such as immunobullous disease, vitiligo, lichen planus, and alopecia areata. Synthesized originally as a cancer drug and a prodrug for mercaptopurine in 1957, it has been widely used as an immunosuppressant for more than 50 years. Azathioprine acts as a prodrug for mercaptopurine, inhibiting an enzyme required for the synthesis of DNA. Thus, it most strongly affects proliferating cells such as the T-cells and B-cells of the immune system. The main side effects of azathioprine are bone marrow suppression, which can be life threatening, especially in people with a genetic deficiency of the enzyme thiopurine S-methyl transferase.

A 20-year-old girl, a known case of widespread vitiligo, was under treatment for the same for almost 2 years. She was not responding to standard regimen used in vitiligo so was shifted on azathioprine 1.5 mg/kg body weight. Within 15 days, the patient revisited for weakness and hair loss [Figure 1]. Investigations revealed low blood counts. Her total leukocyte count was 1300/cumm while differential leukocyte was as follows: neutrophils - 25%, lymphocytes - 70%, eosinophils - 3%, and monocytes - 2%. Platelet count was also reduced, i.e., 16,900/cumm. Azathioprine was stopped. Within the next 6 weeks, she lost all hairs from the scalp (total alopecia) [Figure 2]. She was started on folic acid 5 mg/day and multivitamins along with topical minoxidil. Alopecia in our patient was correlating with low blood counts. After 2 months, her hair started to grow which was associated with increased blood counts [Figure 3]. Her leukocyte count was, i.e., 5100/cumm along with increase in polymorphs (56%) and platelets (206,000/cumm). Naranjo’s causality assessment scores were 6 indicating that azathioprine was a “probable” cause of total alopecia.

Side effects of azathioprine such as nausea and vomiting are common and hypersensitivity is also known. Hair loss is often seen in transplant patients receiving the drug. As azathioprine suppresses bone marrow mostly in thiopurine S-methyltransferase (TPMT)-deficient patients, regular monitoring of blood count is recommended during treatment.[1,2] The TPMT enzyme is responsible, in part, for the methylation of 6-methylmercaptopurine (MP) into the inactive metabolite 6-MP. This methylation prevents 6-MP from further conversion into the active, cytotoxic thioguanine nucleotide metabolites.[3-5] TPMT should be done in all patients receiving azathioprine therapy. However, the test is expensive, and facility for TPMT determination is not available in many parts of India. In such a resource-poor setting, serial measurement of total leukocyte count remains the most practical method for early detection of azathiorine-induced myelosuppression. In our patient, blood counts correlated well with azathioprine-induced hair loss. Azathioprine can cause both telogen effluvium and anagen effluvium. Azathioprine inhibits mitosis of hair matrix resulting in abrupt onset of loss of anagen hair resulting rapid onset and progression of alopecia.[6] There was a rapid loss of hair after 15 days of azathioprine therapy for vitiligo. Azathioprine-induced alopecia usually starts within 1 month of the therapy as reported by previous authors in two cases.[7,8] However, Sonthalia and Daulatabad noted anagen effluvium within 48 h of 50 mg of azathioprine therapy.[9] Rapid regrowth of hair after drug discontinuation within 2 months correlated with recovery of bone marrow suppression.

Thus, from this case report, we suggest that patients on azathioprine therapy should be evaluated for hair loss which

Figure 1: Hair loss 15 days after starting on azathioprine.

Figure 2: Alopecia totalis after azathioprine therapy.
would indicate early or impending azathioprine-induced myelotoxicity. Such patients should be then subjected to blood examination to look for decreased blood counts.

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Conflicts of interest
There are no conflicts of interest.

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