Levamisole-induced Drug Fever

Sir,

A 42-year-old female patient with stable vitiligo lesions on feet and flanks for the past 5 years was prescribed 150 mg tablet of levamisole to be taken on 2 consecutive days in a week. The patient developed moderate-grade, continuous fever associated with mild headache and chills, 8 h following intake of levamisole tablet. The fever was unassociated with skin rash, rhinorrhea, lacrimation, arthralgia, myalgia, sore throat, or burning micturition. She took symptomatic treatment with paracetamol and the fever subsided in 3 days. Four days later, the fever recurred in an identical pattern, 6 h after taking levamisole tablet. The patient got admitted in the medical ward and was thoroughly evaluated for the cause of fever. She was otherwise in apparently good health and not on any other medication. Patient denied of history of reaction to any drug including levamisole in the past. Physical examination revealed temperature of 102.4°F. There was no icterus, hepatosplenomegaly, or lymphadenopathy. Systemic examination was normal. All investigations including complete blood counts, routine urine and culture, liver function and renal function tests were normal. Peripheral blood smear did not reveal the presence of malarial parasite. There was no peripheral eosinophilia. Typhidot® for IgG and IgM was negative. Serology for dengue and chikungunya was negative. Skiagram of the chest was normal. She was symptomatically treated with paracetamol. The fever subsided in 4 days. The patient denied for provocation. She was advised not to take levamisole in the future.

Drug fever is defined as fever coinciding with the administration of a drug and disappearing after discontinuation of the drug when no other cause for the fever can be ascertained after a careful physical examination and appropriate laboratory study. Drug fever is frequently a diagnosis of exclusion made in febrile patients whose fever abates within 48–72 h of discontinuing a suspected pyrogenic agent.[1] Fever as the only manifestation of a drug reaction, though infrequent, has been reported.[2–4]

There have been reports of levamisole-induced fever alone[4] as well as fever with skin rash.[5,6] Repeated
episodes of fever in association with erythema and itching of palms and soles, 4-12 hours after levamisole intake and confirmed by rechallenge has been reported in a patient of vitiligo by Gupta et al. [6] Secher et al reported similar nature of drug reaction to levamisole when used in patient of rheumatoid arthritis. [5] The occurrence of fever on two occasions 8 and 6 h after taking levamisole strongly suggests levamisole as a cause of fever in our patient. Fever was not associated with any skin rash or hematological alteration. Fever occurred in association with headache and chills on both the occasions. Chills and headache with drug fever have been reported in 53% and 16% of cases, respectively. [1] The other causes of fever were excluded during admission in the medical ward.

The mechanism of drug-induced fever is unclear. Drug fever is believed to be hypersensitive or idiosyncratic in origin and therefore is unavoidable and unpredictable. [2] Accompanying eosinophilia seen in some patients suggests an allergic basis for such reactions. [1] Our patient, however, did not have peripheral eosinophilia. Besides being used as an anti-helminthic agent, levamisole has also been used in the treatment of several dermatological conditions like skin infections, leprosy, warts, lichen planus and aphthous ulcers. [7] It has also been used as an immunomodulatory agent in rheumatoid arthritis. Clinicians should therefore be aware of this rare side effect of levamisole. The familiarity with the condition may help to avoid unwarranted and expensive diagnostic and therapeutic interventions.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Azacitidine-induced Leukocytoclastic Vasculitis

Sir,
Azacitidine is a hypomethylating agent for the treatment of patients with myelodysplastic syndrome (MDS), an indication approved by the Food and Drug Administration in May 2004 through its accelerated approval process. [1, 2] We describe a female patient who was treated with azacitidine and developed a leukocytoclastic vasculitis. Leukocytoclastic vasculitis is a very rare side effect of azacitidine.

A 59-year-old married Indian female had a 1-year history of breathlessness and tiredness. As her symptoms progressed, she visited a hemato-oncologist in our hospital and was diagnosed as a case of refractory anemia with thrombocytopenia transformed from MDS. She was prescribed with 75 mg/m²/day of subcutaneous azacitidine injection for 7 consecutive days every 4 weeks. After 2 days, she developed erythematous plaques of varying sizes over the trunk [Figure 1] and extremities...