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.\[2\] 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.

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**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/m^2/days 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
Laboratory tests were normal except for anemia. Based on the clinical and histopathological findings, a diagnosis of azacitidine-induced leukocytoclastic vasculitis was made. Azacitidine injections were stopped, and the patient treated with oral prednisolone 40 mg per day for 7 days which was tapered by 10mg/week for 4 weeks and discontinued. The patient improved remarkably with resolution of rashes as postinflammatory hyperpigmentation [Figure 3]. At that time, it was decided to treat the patient with decitabine intravenous before proceeding with an allogeneic transplant procedure. She tolerated decitabine without complications, and no recurrence of skin lesions was noted, thus confirming causal association of azacitidine with cutaneous vasculitis.

Azacitidine is a new drug to prolong survival and improve quality of life in patients with MDS while maintaining a controllable adverse effect profile.\(^3\) Skin reaction at the injection site is a common adverse effect. However, other adverse effects in the skin are uncommon.\(^4\) The adverse reactions to azacitidine include cytopenia, injection-site reactions, and gastrointestinal symptoms. Usually, adverse events occur transiently at the beginning of the treatment cycle and are resolved during ongoing therapy.\(^4\) With regard to skin reactions, injection-site reaction occurs in 46%–72% of patients as toxic reaction and usually resolves during the treatment. Other skin reactions are uncommon.\(^3,4\) Almeida reported generalized urticarial skin reaction in patients treated with azacitidine and recommended the use of concomitant low-dose steroids.\(^5\) Azacitidine-associated Sweet’s syndrome was also reported with prompt symptom resolution after discontinuation of azacitidine use and administration of appropriate corticosteroid therapy.\(^6\) Azacitidine caused allergic reactions as well as toxic reaction in our case. While toxic reaction at the injection site is common, allergic reaction is not widely known. We should require attention to systemic skin reactions because the incidences are likely to increase with the increasing use of azacitidine.

To the best of our knowledge, this is the first case report of a leukocytoclastic vasculitis associated with azacitidine, and hence it should be considered as a possible cause while evaluating a case of drug-induced leukocytoclastic vasculitis in MDS patients.

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Letters to Editor

Snehal Lunge1,2, Rohan Bhise2
1Department of Dermatology, JNMC, KLE University, 2Department of Oncology, KLES Dr. Prabhakar Kore Hospital and MRC, Belagavi, Karnataka, India

Address for correspondence:
Dr. Snehal Lunge,
Department of Dermatology, JNMC, KLE University,
Belagavi, Karnataka, India.
E-Mail: drsnehalun@gmail.com

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