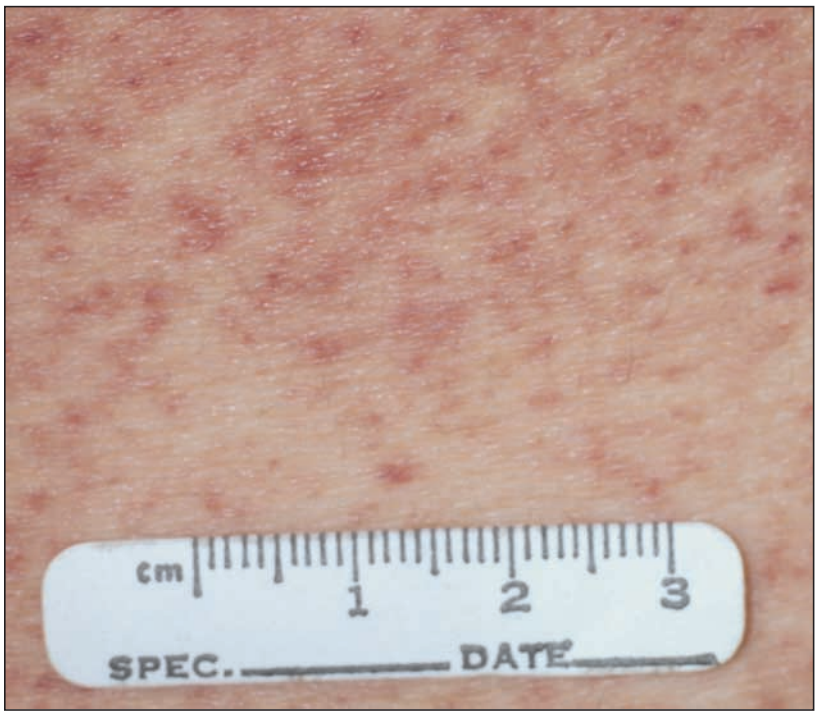
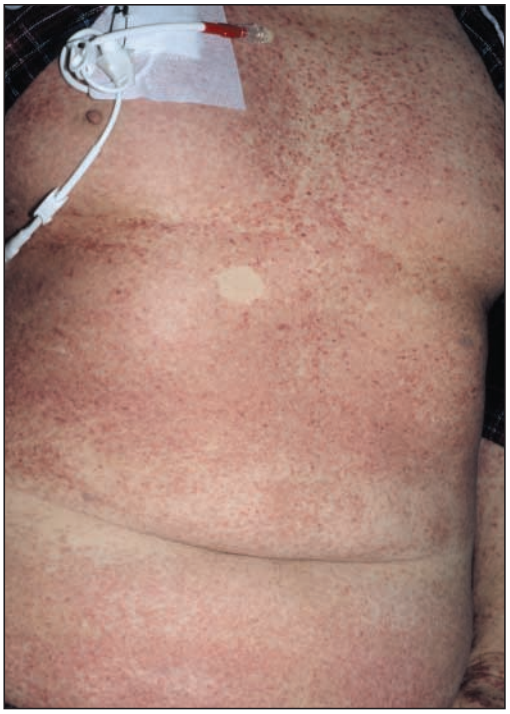
Erythematous eruption in a man with acute myeloid leukemia





Courtesy: Jason Tay

A 66-year-old man with type 2 diabetes mellitus initially presented to his family physician with fatigue and was noted to have pancytopenia. History taking and physical examination revealed no abnormal findings. The patient was referred to a hematology service and, after bone marrow aspiration, was found to have myelodysplasia. The man was followed up as an outpatient while he remained relatively asymptomatic, with monthly complete blood counts.

A year later the patient's condition progressed to acute myeloid leukemia. He was given conventional induction chemotherapy with idarubicin and cytarabine, a combination commonly known as "7 & 3" because the course lasts 7 days, with cytarabine being given each day and idarubicin given for the first 3. Although patients receiving this regimen often have fever, most also have profound neutropenia owing to bone marrow suppression; prophylactic fluconazole and acyclovir therapy is routinely given to prevent opportunistic infections, and allopurinol is routinely given to prevent secondary hyperuricemia due to tumour lysis.

On the fifth day of chemotherapy a florid, nonpruritic, nonblanching, maculopapular erythematous skin eruption developed on the patient's anterior chest wall (Fig. 1). Over the next 24 hours it spread to his trunk (Fig. 2) and upper and lower limbs, with relative sparing of his head and neck. He also complained of malaise, generalized myalgias, intermittent chest wall discomfort and a low-grade fever (37.5°C). A focused physical examination of his ears, nose and throat, lungs, heart and abdomen for possible sources of infection was unremarkable. Blood work revealed pancytopenia (hemoglobin concentration 78 g/L, platelet count 72 × 10^9/L and leukocyte count 1.0 × 10^9/L, with absolute neutrophil count of 0.5 × 10^9/L [normally 2.0 to 7.5 × 10^9/L]), but the rash was not felt to be petechial and related to his thrombocytopenia. A "septic" screen was performed, including a chest radiograph and cultures of blood samples from both lumens of his Hickman central catheter and both his arms. The results of this screen were ultimately negative, but before they were known, empirical treatment was started with intravenous ceftazidime therapy 3 times daily and the allopurinol therapy was stopped in case it was the cause of the reaction.

By the sixth day of chemotherapy the nondermatologic symptoms, including fever, began to abate and the ceftazidime therapy was stopped. The patient completed the cytarabine regimen, and his rash gradually resolved 5 days later, which supports the probability that the symptoms were likely an adverse effect of the cytarabine therapy.

Cytarabine is an antimetabolite of the nucleotide cytidine, which is important in DNA synthesis. When used with an anthracycline (which forms a complex with DNA and topoisomerase II that leads to DNA strand breaks) such as idarubicin, 60%–80% of patients with acute myeloid leukemia may experience remission.[1] Multiple cases of dermato-

logic reactions attributed to cytarabine have been reported;[2–7] however, a "cytarabine syndrome" was first identified in 1981 and is characterized by fever, myalgias, bone pain, and occasional chest pain, maculopapular rash and conjunctivitis.[8] Symptoms usually occur within 6–12 hours after the drug is first infused and abates with the cessation of therapy. Estimates of the incidence of this syndrome vary widely (3%–72%) depending on the methodology used,[9] and the syndrome appears to be more common in patients receiving high doses of cytarabine (> 2 g/m^2 daily) and continuous infusions.[2,5,8] Our patient received a standard dose of 200 mg/m^2 daily by continuous infusion.

Although the exact cause of the cytarabine syndrome is unknown, it may result from a hypersensitivity reaction, because corticosteroids can sometimes prevent or treat the symptoms[3,10] and a variety of pro-inflammatory cytokines are implicated in the development of the symptoms, including tumour necrosis factor α, interleukin-6 (IL-6), interferon-α and IL-1, which has been isolated in patients with the reaction.[11]

This case underscores the need to thoroughly and rapidly evaluate patients receiving chemotherapy who experience any unexpected symptoms, even those associated with relatively common and self-limited adverse effects of a drug, to distinguish them from life-threatening infections and sepsis in these relatively fragile patients.

Jason Tay
Resident in Internal Medicine
Memorial University of Newfoundland
St. John's, Nfld.

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