Sweet's syndrome associated with norfloxacin in a prostate cancer patient

Sir,

Acute febrile neutrophilic dermatosis, also termed Sweet's syndrome (SS), is an uncommon disease first described by Robert Sweet in 1964. It is a hypersensitivity reaction in response to systemic factors, which may include malignant disease, infection, or drug exposure. Patients with malignancy often take several medications, and if SS develops, it can be difficult to tell whether it is drug-related or a paraneoplastic syndrome.

Norfloxacin is an antibiotic from the family of fluoroquinolones with both bactericidal and bacteriostatic actions. It is effective against both Gram-positive and Gram-negative organisms, including pseudomonads, gonococci, *H. influenzae*, staphylococci, streptococci, etc. It is usually prescribed for the treatment of gastrointestinal and genitourinary tract infections. We report a case of SS in a patient with disseminated prostate adenocarcinoma few days after the initiation of a treatment with norfloxacin.

A 66-year-old man with advanced prostate adenocarcinoma (diffuse bone metastasis diagnosed 2 years earlier), presented with fever, myalgias and a skin eruption consisting of painful red papules, with confluent plaques and some vesicles, affecting hand palms, feet and back skin over the lumbar zone. The mucous membranes were spared. He was under treatment with oral tramadol, naproxen and bicalutamide, with a monthly administration of intravenous zoledronic acid for his prostate cancer. Four days before the onset of the skin reaction, he was prescribed norfloxacin 400 mg b.i.d. because of a urinary infection. At admission, he was febrile (38.5°C), blood count showed leukocytosis with neutrophilia, and the erythrocyte sedimentation rate was high. A skin biopsy was taken, showing predominantly neutrophilic infiltration in the dermis without leukocytoclastic vasculitis, changes consistent with the diagnosis of SS. Discontinuation of norfloxacin and steroid therapy resulted in a rapid improvement of symptoms with clinical resolution of skin lesions after the first week of therapy.

The clinical picture of SS typically consists of a patient with fever preceding an abrupt skin eruption with painful reddish or violaceous papules, plaques or nodules that may be studded with pustules. The distribution is usually asymmetric, affecting face and extremities, and lesions can coalesce into circinate plaques. Oral and conjunctival mucosa can also be involved. Systemic symptoms such as myalgias, arthralgias and headache are common, and extracutaneous manifestations such as pulmonary infiltrates, proteinuria and renal failure can complicate the course of the disease.

The classic histopathological pattern on skin biopsy is of a dense diffuse neutrophilic infiltrate in the reticular dermis. True vasculitic changes are typically absent, although subtle vasculitic changes may occur. The epidermis is usually spared.

Potential causes for SS are numerous, but some associations are well documented. Classic SS occurring in young women after mild respiratory illness is the most common presentation, and accounts for more than 50% of cases. SS associated with a malignant neoplasm and SS associated with inflammatory (infectious) conditions are the next most frequently identified causes. Myelodysplasia and chronic myelogenous leukaemia are the most frequent malignancies associated with SS, and also can be seen in association with acute myeloid leukaemia, non-Hodgkin lymphoma and Hodgkin’s disease. Non-haematological malignancies rarely reported in association with SS include osteosarcoma, head and neck cancer, rectal cancer, and there appears to be a slight increase in genitourinary cancers (prostate, ovarian testicular). Streptococcal pneumonia, *Yersinia* colitis, and atypical mycobacteria infection are commonly described as causes of SS. An association with SS has also been established in a variety of systemic disorders, such as Crohn’s disease, ulcerative colitis, sarcoidosis, Sjögren’s syndrome, Behçet’s disease, and lupus erythematosus.

Drug-related SS is a recognized presentation. It is well established with granulocyte colony-stimulating factor, all-trans retinoic acid, and tetracycline.
but several other drugs including furosemide, hydralazine, trimethoprin-sulfamethoxazole, carbamazepine, and lithium have also been reported as causing SS.\textsuperscript{15–17} However, some of these observations have been described in patients with underlying malignancies, so the real association is unclear. To the best of our knowledge, this is the first report of SS related to the use of norfloxacin.

Our patient had a prostate adenocarcinoma with diffuse bone metastasis that could be an unusual association with SS, but there was a clear relation between the start of the treatment with norfloxacin, and the onset of the SS 4 days later, so we think it most likely that it was a reaction to the norfloxacin.

We conclude that SS must be taken into count into the differential diagnosis of acute dermatosis in cancer patients, specially in those with haematological malignancies. Physicians should be aware of norfloxacin as another potential cause of drug-related SS.

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