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Biotherapy Skin Reaction

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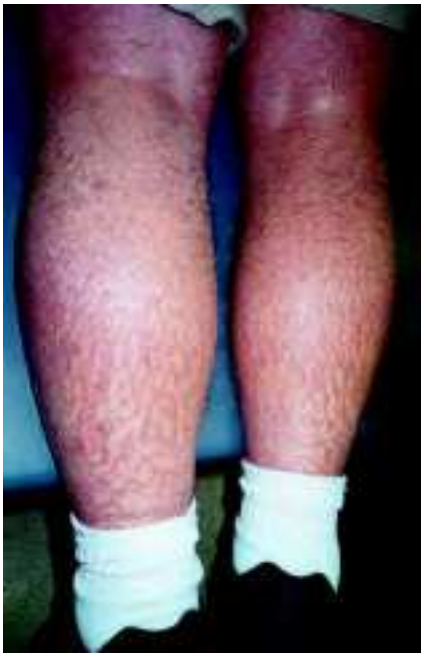
Case Study

M.B. is a 71-year-old male who presented in January 2001 with renal cell carcinoma metastatic to paraesophageal, peri-aortic, hilar, and mediastinal lymph nodes. He was started on interleukin-2 (IL-2, aldesleukin) 18 million units, interferon alpha 10 million units, and 5-fluorouracil 1 g, all administered by IV continuous infusion for 96 hours every three weeks. No significant complications occurred after his first cycle of combined chemotherapy/biotherapy, except for a rise in his serum creatinine level from 1.3–1.5 mg/dL. However, during the second treatment, his creatinine level rose from 1.8–3.1 mg/dL (normal range is 0.6–1.5 mg/dL), and he was placed on a renal dose (5 mcg/kg/hr) of dopamine. He developed grade II diarrhea and grade II stomatitis and subsequently was started on octreotide acetate and an oral rinse of equal parts of diphenhydramine, nystatin, and viscous lidocaine. The IL-2 infusion was stopped after day three. The interferon and 5-fluorouracil were continued for the full 96 hours.

Twelve days after receiving the second course of chemotherapy/biotherapy, M.B. called the office and complained that his legs were swelling; it was so severe that he was having trouble standing. He also described the presence of a red, flat rash and red streaks that he said looked like a "roadmap going up my legs." The rash had been present for three or four days.

A bilateral doppler ultrasound was ordered to rule out deep vein thrombosis, and the test result was negative. The advanced practice nurse in the physician's office then examined M.B. The examination revealed 3+ edema in both legs. His skin was dry and flaky, and a bright red, lacy-looking rash covered his upper and lower legs. Examination supported the patient's description of this phenomenon. M.B. reported that the rash was accompanied by the sensation of a severe sunburn.

M.B. was placed on furosemide 20 mg by mouth twice a day for two weeks and given Eucerin® cream (Beiersdorf, Inc., Wilton, CT), which he was instructed to apply to the dry areas of his extremities twice a day. He was instructed to stay out of the sun, avoid hot baths or showers that may increase moisture loss, and gently towel dry after bathing.



Ten days later, M.B.'s physician examined him. Assessment revealed that his rash had resolved. His lungs were clear, his heart rate was regular, and no organomegaly was present. However, he still had 2+ edema in his lower extremities.

Discussion Questions

Given M.B.'s clinical picture, which of the drugs he received has the highest incidence of causing this type of skin rash? Are the clinical signs and symptoms consistent with the clinical course usually observed with biologic therapy for renal cell carcinoma?

Discussion

Biologic therapy often is used to treat renal cell carcinoma because it stimulates the host's immune system to attack and kill foreign cells. The process of stimulating the immune system involves the use of cytokines, which function as messengers in the immune system response by communicating between macrophages and lymphocytes. IL-2 and interferon alpha belong to the class of cytokines termed lymphokines and monokines. The lymphokines and monokines are produced by the lymphocytes, monocytes, and macrophages and control the immune system function and inflammatory response (Corwin, 2000).

IL-2 is a cytokine that causes T cell proliferation in response to an antigen. The body stimulates further production of T cells through a positive feedback mechanism. In addition, IL-2 mediates the secretion of other cytokines through immunomodulation. IL-2 activates natural killer (NK) cells, monocytes, and cytotoxic T cells to produce a host defense mechanism against infection and in response to injury (Corwin, 2000).

IL-2 activation of T cells, B cells, and NK cells stimulates the pro-inflammatory cytokine production of interferon gamma, granulocyte macrophage colony-stimulating factor, tumor necrosis factor, and C-reactive protein. The activation of these pro-inflammatory cytokines initiates the events that cause IL-2 dose-dependent side effects. Adverse reactions from IL-2 are dose dependent, self-limiting, and usually reversible within two to three days of therapy completion (Sundin & Wolin, 1998).

Interferon alpha is a cytokine that targets uninfected host cells and is capable of inhibiting viral replication (Corwin, 2000). Interferon alpha comes from T- and B-lymphocytes and macrophages and belongs in the lymphokine/monokine classification of

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Digital Object Identifier: 10.1188/02.CJON.181-182