Acute Graft-Versus-Host Disease of the Esophagus

Acute graft-versus-host disease (GVHD) affects the terminal ileum and right colon, and manifests with symptoms of secretory diarrhea, abdominal pain, and hemorrhage (1). There is also gastroduodenal involvement, characterized by nausea, vomiting, and anorexia, but it is unusual to find severe necrosis in the upper intestinal tract (2). It has been difficult to demonstrate the presence of acute GVHD in the esophagus, due to the high incidence of esophageal

damage caused by chemotherapy, infections, and acid peptic reflux. Unequivocal esophageal involvement with acute GVHD is illustrated in Figures 1 and 2, showing that the diagnosis can be made by endoscopic and histological criteria.

It is not surprising that there is esophageal involvement in patients with acute GVHD, as the squamous epithelium of the skin and mouth are common targets of this lympho-

cyte-mediated form of tissue destruction (3). In the last few years, antiviral and antifungal prophylaxis has almost eliminated infections caused by herpes simplex virus, cytomegalovirus, and *Candida albicans*. In the case presented here, infection was ruled out by sensitive tests for viral, fungal, and bacterial organisms, allowing a confident diagnosis of acute GVHD.

The endoscopic appearance of desquamation of esophageal epithelium is analogous to what occurs in GVHD of the skin, where peeling, bullae, and ulceration can be severe (4). Mucosal sloughing may also be seen in the oropharynx. Histologically, the present case showed characteristic apoptotic damage to basally located epithelial cells and desquamation of epithelial sheets. The endoscopic appearance of the esophagus in this patient is similar to that in other immune-mediated esophageal injuries – for example, epidermolysis bullosa and chronic GVHD. In the latter illness, the upper esophagus is involved, with desquamation, web formation, and submucosal fibrosis (5). Treatment of the underlying immunological disorder – acute GVHD – is necessary in order to effect healing of the esophageal epithelium.

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Figure 1: Endoscopic view of the distal esophagus, showing two ulcerations surrounded by epithelium that is desquamating from the underlying submucosal tissue. This patient had received a transplant from a human leukocyte antigen-mismatched unrelated donor 45 days earlier, and had developed severe acute GVHD of the skin and intestinal tract. At this endoscopy, there was also diffuse mucosal edema and erosions in the gastric antrum and duodenum. Histology showed acute GVHD of the stomach. The patient was treated with prednisone 2 mg/kg/d, but died of infection on day 56.

Figure 2: Histological findings in an esophageal biopsy taken adjacent to the deep ulceration, showing the desquamating epithelium (a) and edema and apoptosis of the basal layer and suprabasal keratinocytes (b) (hematoxylin-eosin).

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