Diagnostic Laparoscopy in Patients with Acute Leukemia and Suspected Hepatic Candidiasis


To assess the value of laparoscopy in the diagnosis of suspected hepatosplenic candidiasis in patients with acute leukemia, a retrospective analysis of 28 laparoscopies was conducted. In all but two cases, imaging of the liver showed focal lesions before laparoscopy. Diagnosis of hepatic candidiasis was established significantly more often when the biopsy was targeted at white nodules (in 12 of 22 laparoscopies) than when targeted randomly or at scars (0 of 6 laparoscopies) (p = 0.017, chi-square test). Yeast was detected more often if the laparoscopy was performed during the three-week period after recovery from neutropenia (in 8 of 12 laparoscopies) than when performed later (in 4 of 16 laparoscopies) (p = 0.028, chi-square test). In addition to the 12 laparoscopically diagnosed patients, eight (29%) patients were diagnosed with disseminated Candida infection by other methods. In another eight (29%) patients the causative agent was not identified. No bleeding or other problems occurred after the laparoscopy. Laparoscopy-guided liver biopsy is most useful if biopsies are targeted to macroscopic lesions and if laparoscopy is performed soon after recovery from neutropenia.

During the last few decades, deep fungal infections have emerged as a significant problem in patients with cancer (1). A distinct form of deep Candida infection, hepatic or hepatosplenic candidiasis manifesting after recovery from chemotherapy-induced neutropenia, has been a major problem in patients with acute leukemia (2-9). The definite diagnosis of hepatosplenic candidiasis has proved to be a major challenge. Clinical suspicion may be elicited by persistently elevated liver enzyme levels, especially alkaline phosphatase, or by signs compatible with infection, such as fever or elevated serum C-reactive protein concentration (4, 5, 8). The focal lesions, usually manifesting in the liver, are commonly small and may be demonstrated by ultrasonography, computed tomography, or magnetic resonance imaging (MRI) (10-13).

The definitive confirmation of hepatosplenic candidiasis by microbiological means usually requires an invasive procedure, such as ultrasound-guided fine-needle aspiration or laparoscopy-guided liver biopsy (8, 14). Diagnostic laparoscopy has been shown to be a safe and accurate procedure in patients with liver disease and also in immunocompromised patients infected with the human immunodeficiency virus (15, 16). Although laparoscopy has been reported to be diagnostically useful in a few individual cases of hepatic candidiasis, its role in patients with acute leukemia and focal liver lesions has not been systematically evaluated (14, 17). Therefore, we analyzed the findings of diagnostic laparoscopies over a ten-year period in patients with acute leukemia and suspected hepatic candidiasis.

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Patients and Methods

Patients. Adult patients with acute leukemia and focal hepatic lesions on whom a diagnostic laparoscopy was performed between 1985 and 1995 at the Helsinki University Central Hospital were included in the study. The registry of laparoscopy procedures performed by the gastrointestinal division was screened retrospectively for leukemia patients. All patients had multiple focal lesions and had received cytotoxic treatment inducing a period of severe neutropenia; all had recovered from the neutropenia.

Laparoscopy. Peritoneoscopy was performed using a standard technique under local anesthesia. Pneumoperitoneum was created with nitrous oxide, using Storz equipment (Storz, Germany). Focal lesions were biopsied with a biopsy forceps or by biopsy needle, and purulent material was aspirated and collected. Samples were collected for histology and cytology and for bacterial, mycobacterial, and fungal cultures. If macroscopic focal lesions (white nodules) were not seen on the surface of the liver, the biopsy was taken randomly or targeted at scars. Macroscopic findings were classified as positive if focal lesions, usually white nodules, were seen on the surface of the liver (Figure 1) and as negative if no lesions at all (2 cases) or only scars (4 cases) were detected (Table 1).

Microscopy. Liver biopsies were stained with hematoxylin-eosin or Herovici stain and with periodic acid-Schiff stain and/or silver methenamine techniques (Figure 2). Air-dried smears for cytological examinations were examined by microscopy after Calcofluor White, May-Grünwald-Giemsa, and/or periodic acid-Schiff, and/or Gomori’s silver methenamine staining. Gram staining was used for the detection of bacteria and Ziehl-Neelsen or acidine orange acid-fast stain for the detection of mycobacteria.

Culture. The samples were cultured on Sabouraud dextrose agar (LabM, UK) with penicillin (200 U/ml) and streptomycin (250 µg/ml) and in Sabouraud dextrose broth (Difco, USA) containing 40 µg/ml gentamicin. If the sample volume was sufficient, the samples were cultured on Sabouraud dextrose agar slants without antibiotics, on brain heart infusion (BHI) agar plates (Difco), and on mycobiotic agar slants (Difco). Sabouraud dextrose agar plates and BHI plates were incubated at 35°C, Sabouraud dextrose broths and mycobiotic agar slants at 30°C, and Sabouraud dextrose agar slants without antibiotics at room temperature, for a total of 30 days. For bacteriological diagnosis the samples were cultured on chocolate agar plates (Becton Dickinson, USA), blood agar plates or colistin-oxolinic acid blood agar plates, on fastidious anaerobe agar plates (LabM), neomycin-vancomycin chocolate agar plates, and in thioglycolate broth (Oxoid, UK). Chocolate agar, blood agar and colistin-oxolinic acid blood agar plates were incubated at 35°C in ambient atmosphere, and fastidious anaerobe agar and neomycin-vancomycin chocolate agar plates at 35°C in anaerobic jars, for a total of 10 to 14 days.

For mycobacteriological diagnosis the samples were cultured on modified Jensen slants: mycobacterium-1 medium containing glycerol and mycobacterium-2 medium containing pyruvate (Orion Diagnostica, Finland), and, in some cases, in Bac-tect 12B mycobacteria medium vials (Becton Dickinson). Jensen slants and Bactec 12B bottles were incubated at 35°C for a total of six to eight weeks.

Statistical Analysis. The chi-square test was used for comparison of differences in rates. P values < 0.05 were regarded as statistically significant.

Results

From 1985 to 1995, 440 adult patients with acute leukemia (311 patients with acute myeloid leukemia and 129 patients with acute lymphatic leukemia) were treated at the Helsinki University Central Hospital. Twenty-five patients underwent a total of 28 diagnostic laparoscopies to confirm the diagnosis of focal lesions in the liver. In all but two cases imaging of the liver had shown focal lesions before laparoscopy. In one patient focal lesions were detected in the liver during appendectomy, but the lesions were not biopsied (Table 1, patient 24), and in one further patient laparoscopy was performed because of persistently elevated levels of serum alkaline phosphatase and serum C-reactive protein although computed tomography and ultrasonography did not show any focal lesions in the liver. In this patient focal lesions were detected in the liver during laparoscopy (Table 1, patient 6).

In three patients diagnostic laparoscopy was performed twice. In one of these patients a second