Clinical characteristics and the usefulness of the QuantiFERON-TB Gold In-Tube test in hematologic patients with hepatic or splenic lesions

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Background/Aims: Hepatic or splenic lesions in hematologic patients are not defined well because they are not easy to evaluate due to limitations of invasive procedures. Management typically depends on the clinical diagnosis with few microbiological data.

Methods: We reviewed the medical records of consecutive hematologic patients with hepatic or splenic lesions in the infectious diseases unit from April 2009 to December 2010 at the Catholic Hematopoietic Stem Cell Transplantation Center in Korea.

Results: Twenty-six patients were identified. Their mean age was 46.0 ± 14.7 years, and 16 (61.5%) were male. Underlying diseases were acute myelogenous leukemia (n = 15, 57.7%) and myelodysplastic syndrome (n = 6, 23.1%). Among the nine nontuberculous infectious lesions, two bacterial, six fungal, and one combined infection were identified. The numbers of confirmed, probable, and possible tuberculosis (TB) cases were one, three, and four, respectively. Two patients had concurrent pulmonary TB. QuantiFERON-TB Gold In-Tube (QFT-GIT, Cellestis Ltd.) was positive in seven cases, among which six were diagnosed with TB. The sensitivity and specificity of QFT-GIT were 75% and 81.3%. Nine (34.6%) were defined as noninfectious causes.

Conclusions: Causes of hepatic or splenic lesion in hematologic patients were diverse including TB, non-TB organisms, and noninfectious origins. TB should be considered for patients not responding to antibacterial or antifungal drugs, even in the absence of direct microbiological evidence. QFT-GIT may be useful for a differential diagnosis of hepatosplenic lesions in hematologic patients.

Keywords: Hematology; Liver abscess; Tuberculosis; Diagnosis

INTRODUCTION

Patients with fever and hepatic or splenic lesions should have an abscess ruled out. Traditionally, amebic and pyogenic infections are the two most common causes of liver abscess and the former has decreased with improved public and individual hygiene [1,2]. Hepatosplenic fungal infection is another possible diagnosis, particularly in patients with hematologic malignancies such as acute leukemia [3,4] or tuberculosis.
(TB) in Korea where pulmonary and extrapulmonary TB are still common [5].

A diagnosis of hepatosplenic lesions usually depends on invasive procedures such as sonography-guided biopsy or aspiration with subsequent microbiological confirmation. However, invasive diagnostic procedures are not easy to perform in hematologic patients because of the increased bleeding risk and marked neutropenia following intensive chemotherapy. Therefore, management is largely dependent on clinical diagnosis when few microbiological data are available.

QuantiFERON-TB Gold In-Tube (QFT-GIT, Cellestis Ltd., Victoria, Australia) is one of two interferon-γ release assays (IGRAs) that have been approved by the U.S. Food and Drug Administration and recommended by the U.S. Centers for Disease Control and Prevention as an aid to detection of latent TB infection among patients at risk [6]. Several studies have investigated the diagnostic performance of IGRAs for extrapulmonary TB (E-TB) with some promising results [7-9].

In this retrospective study, we investigated the clinical characteristics, causes, and outcomes of hepatic or splenic lesions and evaluated the usefulness of the QFT-GIT for the diagnosis of TB in febrile patients with hematologic diseases.

**METHODS**

**Study patients and data collection**

We identified all consecutive cases of hepatic or splenic lesions in patients with hematologic diseases who were admitted to the infectious diseases (IDs) unit or who consulted with the hematologic unit from April 2009 to December 2010 at the Catholic Hematopoietic Stem Cell Transplantation (HSCT) Center in Korea. The following data were collected from all cases; demographic information (e.g., age and sex), underlying diseases, medical history, microbiological data, radiological findings, site of infection, medical and surgical treatment, laboratory findings including QFT-GIT results, and other important clinical parameters at the time of infection and follow-up. The QFT-GIT test and interpretation were performed according to the manufacturer’s instructions (Cellestis Ltd.). Serum detection of galactomannan (GM) by Platelia Aspergillus assay (Bio-Rad Laboratories, Marennes-La-Couquette, France) and blood chemistry were performed at least twice weekly at our institution, and other examinations were conducted as clinically indicated. The endpoint of the study was April 2011 or time of death or follow-up loss. This study was approved by the Institutional Review Board at Seoul St. Mary’s Hospital with a waiver of informed consent (Project No. KC11RISI0366).

**Evaluation of hepatosplenic lesions**

All patient medical records and images were reviewed by two IDs specialists, the attending hematologist, and one radiologist. Infectious lesions were classified as TB or non-TB infections. When infections were suspected without identifying a causative organism, the decision was based on the response to empirical antibacterial or antifungal drugs. Invasive fungal disease (IFD) was defined according to the European Organization for Research and Treatment of Cancer/Mycosis Study Group (EORTC/MSG) definition criteria [10]. We made a final clinical diagnosis for noninfectious lesions based on a combination of the response to anticancer chemotherapy, underlying disease status, serial radiological findings, and laboratory results.

The categories of diagnostic certainty for TB were classified as “confirmed,” “probable,” and “possible.” They were defined as described in previous studies [7,11]. A confirmed case was defined as positive for *Mycobacterium tuberculosis* in culture or by the *M. tuberculosis* polymerase chain reaction in any clinical specimen. A probable case was defined as clinical suspicion of TB and one of the following: histological finding of biopsy tissue showing granulomatous inflammation with caseating necrosis or positive acid fast bacilli stain results in a clinical specimen. A possible case was defined as successful clinical and radiological response to empirical anti-TB therapy when antibacterial and antifungal drugs were ineffective. The QFT-GIT results did not influence the certainty of diagnosis.

**Assessment of response to therapy and outcome**

We assessed the clinical response to therapy for the infectious lesions as described in a previous study with modifications [12]. Follow-up computed tomography (CT) was required for at least 4 weeks after treatment...