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A new diagnostic approach for bilious pleural effusion

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ABSTRACT

Background: Bilious pleural effusion is an extremely rare condition associated with liver diseases, subphrenic or subhepatic abscess formation, biliary peritonitis, and invasive procedures (i.e., percutaneous biliary drainage or liver biopsy). The current diagnostic test is based on the measurement of the ratio of pleural total bilirubin to serum total bilirubin, which is greater than 1 in patients with bilious pleural effusion. Given the low incidence of bilious pleural effusion, the precise diagnostic yield of this ratio based test has not been evaluated.

Methods: We retrospectively reviewed the medical records of our institution and searched the PubMed database for reports of bilious pleural effusion.

Results: We identified a total of 12 cases of bilious pleural effusion (9 from 8 Pubmed reports and 3 from our institutional records). The factors causing this condition were broadly classified into three categories based on the pathophysiology: 1) liver diseases (echinococcosis, tuberculosis and amebiasis); 2) subhepatic/subphrenic abscess or biliary peritonitis, with or without biliary tract obstruction; and 3) iatrogenic disease after percutaneous biliary drainage and/or liver biopsy. The sensitivity of detection was 76.9% when the ratio of pleural total bilirubin to serum total bilirubin was greater than 1. The sensitivity increased to 100% when a combination test including pleural glycoholic acid was adopted.

Conclusions: This study demonstrates the high diagnostic yield for bilious pleural effusion using a combination of two test criteria; a ratio of pleural total bilirubin to serum total bilirubin greater than 1 and the presence of pleural glycoholic acid.

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1. Introduction

Bilious pleural effusion is an unusual clinical event that is considered to be one of the causes of black pleural effusions. Saraya et al. [1] and Koide et al. [2] reported on the utility of pleural glycoholic acid in the differentiation of bilious pleural effusion from other causes of black pleural effusion. In 1988, Strange et al. [3] demonstrated that bilious green fluid, with a pleural fluid total bilirubin (T-Bil) to serum T-Bil ratio of >1 indicated the presence of a biliopleural fistula. However, there are no reports on the diagnostic yield of a test for bilious pleural effusion combining these two criteria; presence of pleural glycoholic acid and a pleural T-Bil/serum T-Bil ratio of >1. We conducted a case review of 12 patients (13 episodes) with bilious pleural effusion for whom pleural data were available, and examined the clinical significance of these two tests.

2. Patients and methods

We searched the Pubmed database (http://www.ncbi.nlm.nih.gov/pubmed), using the search term "bilious pleural effusion", and the medical records of Kyorin University between January 2006 and June 2014. Only the cases for which pleural data were available were included in the present study. This study was approved by the ethics committee of Kyorin University (Approval number H26-033 dated July 17, 2014).

3. Results

3.1. *Patient characteristics*

We identified a total of 12 cases (13 episodes) of bilious pleural effusion. There were 9 cases from 8 published reports in the Pubmed data base [3–10] and 3 cases from our institutional medical records between the years 2013 and 2015 (Table 1). Among the 12 patients identified, the male to female ratio was 3:1 and the median age was 61.5 years (interquartile range, 53.5–75.5 years). Various underlying diseases, such as cancer (pancreas, breast, gastric), cholecystitis with gallbladder stones and polyps, were noted. Diverse clinical symptoms, including dyspnea, fever, pleuritic chest pain (mostly on the right side) or right sided abdominal pain, jaundice, and cough were observed. Bilious pleural effusion was observed on the right side in 10 patients, on the left side in 1 patient, and on both sides in 1 patient. Based on the published literature and review of our records, we broadly classified the possible pathophysiology for bilious pleural effusion into three categories: 1) liver diseases (echinococcosis [11], tuberculosis [12], amebiasis [13]); 2) subhepatic/subphrenic abscess or biliary peritonitis, with [7] or without [4,10,14–18] biliary tract obstruction; and 3) iatrogenic disease after percutaneous biliary drainage [3,5,8,9,19] and/or liver biopsy [6] (Fig. 1). Within each pathologic pathway, the transition of bile acid from the abdominal cavity into the pleural space may occur via: 1) diaphragmatic fistula; 2) congenital diaphragmatic defects [15]; or 3) through the natural (aortic and esophageal) hiatus [1].

3.2. *The clinical significance of the pleural T-Bil to serum T-Bil ratio of >1.0 and presence of pleural glycoholic acid*

The bilious pleural effusions showed various colors such as yellow (Fig. 2A, case 10) or greenish yellow or dark brown (Fig. 2B, case 11). It was difficult to discern the source of the effusions at first glance. The elevation of T-Bil in the pleural fluid is a clinical indicator of the presence of a bilious pleural effusion. Our review showed that the median value of pleural T-Bil was 9.1 (IU/L) (interquartile range, 2.1–27.5 IU/L). The ratio of pleural T-Bil to serum T-Bil ranged from 0.83 to 52.2 (median 2.0, interquartile range 1.3–6.6) (Table 2). The sensitivity of detection of bilious pleural effusion, when the ratio of pleural T-Bil to serum T-Bil was >1, was 76.9%. Importantly, all 3 cases of bilious pleural effusion identified at our institution (4 episodes in cases 10, 11, and 12) tested positive for pleural glycoholic acid. Pleural glycoholic acid concentration in these patients was in the range of 5.4–53 μg/dL. Of these 3 cases, 2 (cases 11 and 12) did not satisfy the criteria of a pleural T-Bil to serum T-Bil ratio of >1. The combination of two tests (presence of pleural glycoholic acid and the ratio of pleural T-Bil to serum T-Bil is >1) showed 100% sensitivity in the diagnosis of bilious pleural effusion. Six patients (7 episodes) for whom the pleural data were available (cases 1, 4, 5, 10, 11, and 12) satisfied Light's criteria for exudative pleural effusion [20].

4. Discussion

Bilious pleural effusions have been reported under various conditions. In 1988, Strange et al. [3] reported on three patients with bilious pleural effusions. They used a rabbit model of bilious pleural effusion, generated using intrapleural bile injection, to study the effects of bile in the pleural space. Although Strange et al. [3] reported that a ratio of pleural fluid T-Bil to serum total T-Bil of greater than 1 could be a sign for bilious pleural effusion, the precise diagnostic yield was not determined. The present study demonstrates that the sensitivity of detection, when using pleural T-Bil to serum T-Bil ratio >1 as the test criteria, was 76.9%. This can be enhanced to 100% by adopting a combination test that also includes the presence of pleural glycoholic acid (the main component of bile acid) as the second test criteria. However, this result is limited in that it is dependent on a small sample of 3 patients at our hospital who tested' positive for pleural glycoholic acid. This might overestimate the real value of this test for bilious pleural effusion. Therefore, evaluation of more cases with bilious pleural effusion is required for assessing the diagnostic significance accurately.

Since Peacock's [21] earliest description of bronchobiliary fistula in a 20-year-old woman with hepatic echinococcosis in 1850, the most common cause of acquired pleurobiliary and bronchobiliary fistula has been thoracoabdominal trauma [17]. As described in Fig. 1, with regard to other possible pathophysiologies, the collection of bile acid in the abdominal cavity, with or without biliary tract obstruction, can