Reviewer 1 (00074737)

Major comments:

1. The authors presented that AMA was positive in 90.9% in their patients with PBC. How was the patients with negative AMA diagnosed as PBC? In these patients, was liver biopsy performed to confirm PBC?

Reply: In this study, all patients satisfied the diagnostic criteria for PBC (*Hepatology* 2009;50:291-308.PMID:19554543). According to these criteria, patients without positive AMAs were diagnosed as PBC only if they had elevated ALP/γ-GT and also showed typical histological features of PBC on liver biopsy. Liver biopsies were preformed on 29 patients with negative AMA.

2. How can you confirm that patients without CTDs really did not have CTDs? Did you perform all evaluations for diagnosis of CTDs in all patients with PBC?

Reply: The medical histories of all patients who were diagnosed with PBC and registered in our database were extensively reviewed, along with any clinical data regarding autoantibody profile, in order to determine whether CTDs were present.

3. How many patients were performed the liver biopsy? Was there any difference in the degree of inflammation or fibrosis between patients with CTD and those without CTD?

Reply: Seventy-two patients (22.4%) underwent liver biopsy. Most of them were AMA-negative or had incomplete responses to UDCA. The limited number of liver biopsies precluded our ability to perform statistical analysis of the differences between pathologic features of patients with CTDs and those without. This limitation has been clarified in the Discussion section.

4. Could you suggest the indication for the evaluation of CTDs in patients with PBC? Which tests should be performed in these patients to diagnose the CTDs? Do you think that all patients with PBC should be performed the evaluation of all kinds of CTDs?

Reply: Yes, we recommend CTDs screening for PBC patients, especially for those

who have RP, renal disease, or signs of involvement of other organ systems. A detailed medical history and autoantibodies profile (including ANA and anti-ENA) should be obtained from PBC patients as part of the CTDs screening process. Moreover, we recommend that the CTD screening include the common disease forms, such as SS, SS, SLE, and PM.

Minor comments:

1. Following part in the RESULTS should be moved to the DISCUSSION: 'The data [16] from a geographically-based PBC patient cohort (n=160) in the UK showed that 53% of patients had at least one additional autoimmune condition. The prevalence of these CTDs in the PBC population were SS (40 cases, 25%), autoimmune thyroid disease (37 cases, 23%), RA (27 cases, 17%), and SSc (12 cases, 8%). None had PM or DM.A study from Bach et al [17]in the USA reported that about 72%of PBC patients were combined with SS, and 20% of PBC patients had joint disease. In an Italian study [18], 170 PBC cases were included, of which 54 had Raynaud's phenomenon (RP). The highest-frequency CTD in these PBC patients was SSc (21 cases, 12.3%).The numbers of overlap cases of SS and PBC, SLE and PBC, RA and PBC, and PM and PBC were: 6 cases (3.5%), 3 cases (1.8%), 3 cases (1.8%), and 1 case (0.6%), respectively (Table 3).'

Reply: Thank you for this insightful suggestion. The text has been moved to the Discussion section.

Reviewer 2 (00006992)

Major concerns:

1. The discussion should be supported by explaining or speculating about the pathophysiological mechanisms underlying the co-incidence of PBC and CTD.

Reply: The pathophysiological mechanisms underlying the co-incidence of PBC and CTD have been clarified in the Discussion section.

2. In a second step limitations of the studiy should be included in the discussion.

Reply: We have outlined the limitations of the study in the Discussion section.

3. The statistical analysis should be recalculated by a testing appropriate for not normally distributed data. Alternatively the authors should show a normal distribution before using the Students t test. A non-parametric alternative to this test can be used such as Kruskal-Wallis one-way analysis of variance.

Reply: The statistical analyses were re-performed. To this end, the distribution was first assessed to determine whether the data was normally distributed. Then, an appropriate test method was chosen to analyze the variance: Student's *t*-test for normally distributed data, and Wilcoxon's two-sample test for non-normally distributed data.

Minor concerns:

1. A lot of blanks between words are missing.

Reply: We have revised the manuscript and these errors have been removed.

2. Were positive AMA patients positive for AMA M2? This information should be included in Table 1.

Reply: Among the AMA-positive patients, 90.3% also showed positivity for AMA-M_2 antibody. These data have been added to Table 1.

Reviewer 3(02462197)

GENERAL COMMENTS The results of the present manuscript are interesting due to the opportunity to compare the percentage of CTDs overlapping PBC in a cohort of Chinese patients in respect to previous large studies coming from US and Europe. The present study is not innovative, and several large studies on the same argument have been performed worldwide; however, it is interesting to underline that the current research is performed on a relatively large cohort (n=322) and that it investigates an ethnic group not already investigated in previous studies. The paper is well written, however a minor language polishing is required.

Reply: We apologize for our lack of proficiency in the English language. The manuscript has been carefully edited by a professional English editing service to correct the grammatical and typographical errors.