Prevalence of Anti-gp210 and Anti-sp100 Antibodies in Patients under Evaluation for Primary Biliary Cholangitis

Troy D. Jaskowski[1], Carri Craig[2], and Anne E. Tebo[1,2,3]

[1]Associated Regional and University Pathologists (ARUP) Institute for Clinical and Experimental Pathology, Salt Lake City, UT, USA, [2]Autoimmune Immunology Laboratory I, ARUP Laboratories, Salt Lake City, UT, USA, [3]Department of Pathology, University of Utah School of Medicine, Salt Lake City, UT, USA

Presented at the 33nd AMLI Annual meeting August - 2020

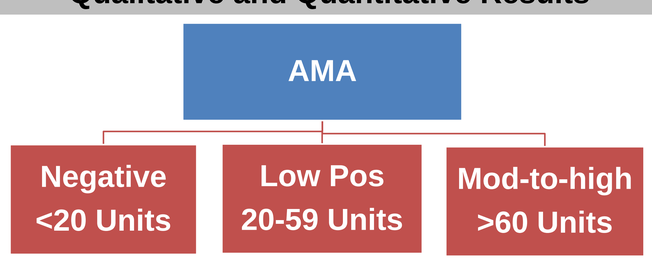
INTRODUCTION AND OBJECTIVE

Primary biliary cholangitis (PBC) is a chronic autoimmune liver disease characterized by the destruction of the small intrahepatic bile ducts. The serological hallmark of PBC is the presence of anti-mitochondrial antibody (AMA) characterized by reticular cytoplasmic staining pattern on HEp-2 substrate indirect fluorescent antibody (IFA) test. Some HEp-2 IFA patterns such as multiple nuclear dots (MND) and rim-like patterns are known to be associated with PBC. These markers have been reported in a subset of patients with PBC who are seronegative for AMA. The corresponding nuclear antigens are the components of the nuclear pore complex (gp210 for rim-like pattern), and sp100 and promyelocytic leukemia (PML) factor proteins (for MND pattern), which can be detected in a number of immunoassays such as ELISA, and line immunoassay. Anti-sp100 antibodies are found in some patients who test negative for AMA, and anti-gp210 antibodies may identify a subgroup of patients with a more severe disease course. The main objective of this study was to evaluate the prevalence and associations of both biomarkers in patients under evaluation for PBC based on the presence or absence of AMA.

MATERIALS AND METHODS

One hundred and ninety patient sera (76 males, age 21-76; mean 52 and 114 females, age 17-83; mean 53) submitted to ARUP Laboratories for AMA testing, and 50 healthy adults were assessed for the presence of anti-gp210 and anti-sp100 by ELISA (INOVA Diagnostics, San Diego, CA). The 190 patient samples were separated into three groups: AMA strong positive (≥60 Units; n=29), AMA low-moderate positive (20-59 Units; n=47) and AMA negative (<20 Units; 114).

Figure 1. Categorization of AMA based on Qualitative and Quantitative Results



Legend: AMA: anti-mitochondrial, Pos: positive, Mod: moderate

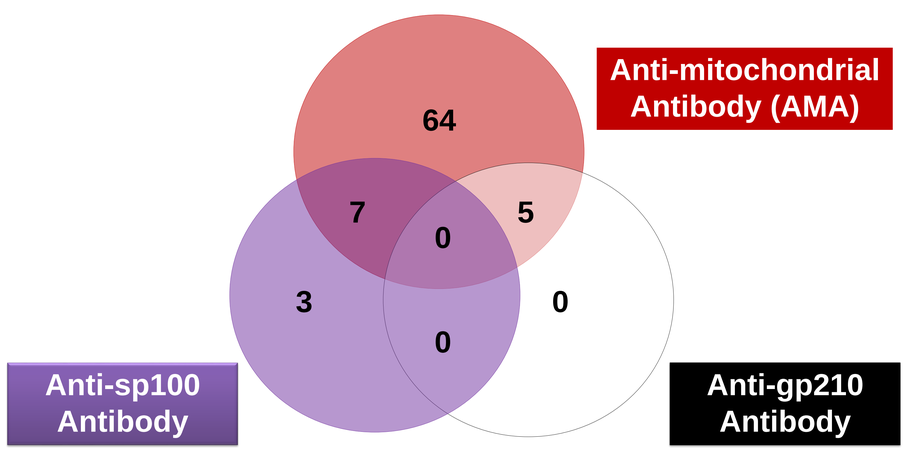
RESULTS

The prevalence of anti-sp100 and anti-gp210 antibodies were evaluated based on the presence or absence of AMA as well as the level of AMA (Figure 1). Elevated anti-sp100 antibodies were more common in AMA-negative than anti-gp210 (Table 1). In AMA positive patients, both markers were mutually exclusive (Figure 2). However, the prevalence of anti-sp100 was higher than that of anti-gp210. The mean antibody level for anti-gp210 was 99.0 (71-117) Units, and anti-sp100 77.2 (40-130) Units. The prevalence and association in the different groups of AMA tested patients and healthy controls are shown in Table 1.

Table 1. Anti-gp210 and Anti-sp100 Antibodies in Patients Under Evaluation for PBC and Controls

Groups	Anti-gp210 Number, n (%) positive	Anti-sp100 Number, n (%) positive
AMA >60 Units (n=29)	4 (13.8)	6 (20.7)
AMA 20-59 Units (n=47)	1 (2.1)	1 (2.1)
AMA <20 Units (n=114)	0 (0.0)	3 (2.6)
Healthy Adults (n=50)	0 (0.0)	0 (0.0)

Figure 2. Association Between PBC-specific Antibodies in Seropositive Patients



Numbers in the Venn diagram represent positive patients for the indicated markers

DISCUSSION

- The estimated prevalence of anti-gp210/sp100 in this single center cohort (15.8% [AMA >20 Units; 12/76] to 34.5% [AMA >60 Units; 10/29]) is comparable to that in published studies (25%).
- Only anti-sp100 was positive in AMA negative patients (Table 1 and Figure 2). This observation has also reported in a limited number of published studies. It is unknown if this phenomenon is limited to specific patient demographics. Given the limited number of patients in this cohort, it is likely future studies are needed to address this issue.
- Based on the healthy controls, both antibody tests are highly specific for PBC.

CONCLUSION

- In AMA positive patients, both anti-sp100 and anti-gp210 were mutually exclusive.
- Given the limited size of this cohort, future studies are needed identify specific populations outside AMA negative patients that may benefit from additional testing for these biomarkers.
- Overall, results from our preliminary analyses demonstrate that anti-sp100 antibodies may add to the diagnostic outcome of at-risk patients for PBC.
- Patients charts are currently under review to evaluate the use of these biomarkers in risk stratification.

ACKNOWLEDGMENTS

Anti-gp210 and Anti-sp100 ELISA kits were provided free-of-charge by INOVA Diagnostics for this study. This study was funded by the ARUP Institute for Clinical and Experimental Pathology and the Department of Pathology, University of Utah School of Medicine, Salt Lake City, UT.

REFERENCES

1. Vergani D, Bogdanos DP. Am J Gastroenterol. 2003; 98: 241-3.
2. Yang WH et al. Clin Gastroenterol Hepatol. 2004; 2: 1116-22.
3. Romero-Gomez M et al. Am J Gastroenterol. 2004; 99: 2150-7.
4. Czaja AJ, Norman GL. J Clin Gastroenterol. 2003; 37: 315-29.