



## Liver News Elsewhere

# Gallbladder disease in patients with primary sclerosing cholangitis\*

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## Abstract

**Background/Aims:** Gallbladder abnormalities may be part of the spectrum in primary sclerosing cholangitis (PSC). The aim of the present study was to evaluate the occurrence and prognostic importance of gallbladder abnormalities in patients with PSC. **Methods:** Presence of gallbladder abnormalities was assessed in 286 patients with PSC treated at the Liver Unit, Karolinska University Hospital, Huddinge, between 1970 and 2005. **Results:** One or more gallbladder abnormalities were found in 41% of the patients. Gallstones were found in 25% and cholecystitis in 25%. Cholecystitis among patients with extrahepatic involvement of PSC [30% (65/214)] was significantly higher than among those with intrahepatic involvement [9% (6/70)] ( $P < 0.0001$ ). A gallbladder mass lesion with a mean size of 21 ( $\pm 9$ ) mm (S.D.) was found in 18 (6%) patients, in 56% (10/18) of whom it constituted gallbladder carcinoma. In 9 patients without a gallbladder mass lesion, histological re-evaluation disclosed epithelial dysplasia of the gallbladder. **Conclusions:** Gallbladder disease is common in patients with PSC. Dysplasia and carcinoma are commonly found in gallbladder epithelium, suggesting that regular examination of the gallbladder in PSC patients could be of value for early detection of a gallbladder mass lesion. Cholecystectomy is recommended when such a lesion is detected, regardless of its size.

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## Comment

We have read an interesting article in which Said *et al*<sup>1</sup> assessed the prevalence and clinical relevance of gallbladder sonographic abnormalities in 286 patients with confirmed Primary Sclerosing Cholangitis (PSC). They found that gallbladder disease; especially gallstones, cholecystitis and epithelial dysplasia are common manifestations in PSC; furthermore, it seems that cholecystitis is a marker for extrahepatic involvement; supporting the hypothesis that gallbladder epithelium is affected in the inflammatory process of PSC. In regard to the evidence presented, we consider this article of great clinical importance in addressing the importance of hepatobiliary sonographic follow-up in patients with PSC in order to detect premalignant lesions.

Although the precise prognostic implications of gallbladder abnormalities in PSC remain unknown, it seems to be that the only ones clinically relevant are the presence of gallbladder polyps<sup>2</sup> or metaplasia.<sup>3</sup> Gallbladder polyps have been subject of study since the 19<sup>th</sup> century, but only recently recognized as lesions of increased risk for malignancy, specially those greater than 1 cm in diameter, sessile and rapidly growing even in less than 1 cm, in patients with concurrent gallstones and in patients older than 50 years.<sup>4</sup> Buckles *et al*<sup>2</sup> found that 13.7% of the patients with PSC that underwent cholecystectomy had a gallbladder mass, 57% of them being malignant, suggesting that in patients with PSC gallbladder polyps must be considered having a greater probability of malignancy; whereas prevalence in patients without PSC ranges from 4.3<sup>5</sup> to 9.5.<sup>6</sup> Leung *et al*<sup>7</sup> described 4 cases of patients with PSC with gallbladder polyps, all of them presented with adenocarcinoma regardless of size, even when no other «malignancy markers» were found in any of them.

The abnormalities of the biliary tree epithelium in PSC (metaplasia-dysplasia) extend to the gallbladder epithelium<sup>1,3</sup> and seems to be a marker for extrahepatic involvement.<sup>1</sup> Therefore, for patients whose sonography demonstrates a gallbladder polyp cholecystectomy is warranted, as 60% of those lesions will be malignant.<sup>2,4</sup> This evidence raises a question whether or not a dysplastic gallbladder polyp should be considered as a marker to prioritize liver transplantation, since the detection of cholangiocarcinoma (CC) before Orthotopic Liver Transplantation (OLT) worsens the 5-year survival rate from 90% to 33%.<sup>8</sup>

To the date, biliary dysplasia, instead of gallbladder polyps is an indication for liver transplantation,<sup>9,10</sup> but since epithelial alterations of PSC are shared by the gallbladder epithelium, we consider that gallbladder polyps should be considered as premalignant lesions, and therefore should be considered as an equivalent to dysplasia regarding the decision to perform a liver transplantation. Since CC is difficult to diagnose in PSC by the current methods available (brush cytology, endobiliary biopsy, CT or MRI scanning, and serum tumor markers)<sup>11</sup> gallbladder polyps detected by sonography would be a feasible detection method.

In conclusion, gallbladder abnormalities are frequent in patients with PSC and gallbladder polyps and dysplasia should be considered of mayor clinical significance. These abnormalities should warrant a sonographic follow up in this particular population.

## References

1. Said K, Glaumann H, Bergquist A. Gallbladder disease in patients with primary sclerosing cholangitis. *J Hepatol* 2008; 48(4): 598-605.
2. Buckles DC, Lindor KD, Larusso NF, Petrovic LM, Gores GJ. In primary sclerosing cholangitis, gallbladder polyps are frequently malignant. *Am J Gastroenterol* 2002; 97(5): 1138-42.
3. Lewis JT, Talwalkar JA, Rosen CB, Smyrk TC, Abraham SC. Prevalence and risk factors for gallbladder neoplasia in patients with primary sclerosing cholangitis: evidence for a metaplasia-dysplasia-carcinoma sequence. *Am J Surg Pathol* 2007; 31(6): 907-13.
4. Karlsten TH, Schrumpf E, Boberg KM. Gallbladder polyps in primary sclerosing cholangitis: not so benign. *Curr Opin Gastroenterol* 2008; 24(3): 395-9.
5. Jorgensen T, Jensen KH. Polyps in the gallbladder. A prevalence study. *Scand J Gastroenterol* 1990; 25(3): 281-6.
6. Lin WR, Lin DY, Tai DI, Hsieh SY, Lin CY, Sheen IS, Chiu CT. Prevalence of and risk factors for gallbladder polyps detected by ultrasonography among healthy Chinese: Analysis of 34 669 cases. *J Gastroenterol Hepatol* 2007.
7. Leung UC, Wong PY, Roberts RH, Koea JB. Gall bladder polyps in sclerosing cholangitis: does the 1-cm rule apply? *ANZ J Surg* 2007; 77(5): 355-7.
8. Goss JA, Shackleton CR, Farmer DG, Arnaout WS, Seu P, Markowitz JS, Martin P, Stribling RJ, Goldstein LI, Busuttil RW. Orthotopic liver transplantation for primary sclerosing cholangitis. A 12-year single center experience. *Ann Surg* 1997; 225(5): 472-81; discussion 81-3.
9. Gow PJ, Chapman RW. Liver transplantation for primary sclerosing cholangitis. *Liver* 2000; 20(2): 97-103.
10. Cullen SN, Chapman RW. Review article: current management of primary sclerosing cholangitis. *Aliment Pharmacol Ther* 2005; 21(8): 933-48.
11. Tung BY. *Clinical manifestations and diagnosis of primary sclerosing cholangitis*. In: Angulo P, ed. Up To Date. Waltham: Up To Date; 2008.