Figure 1 - 795

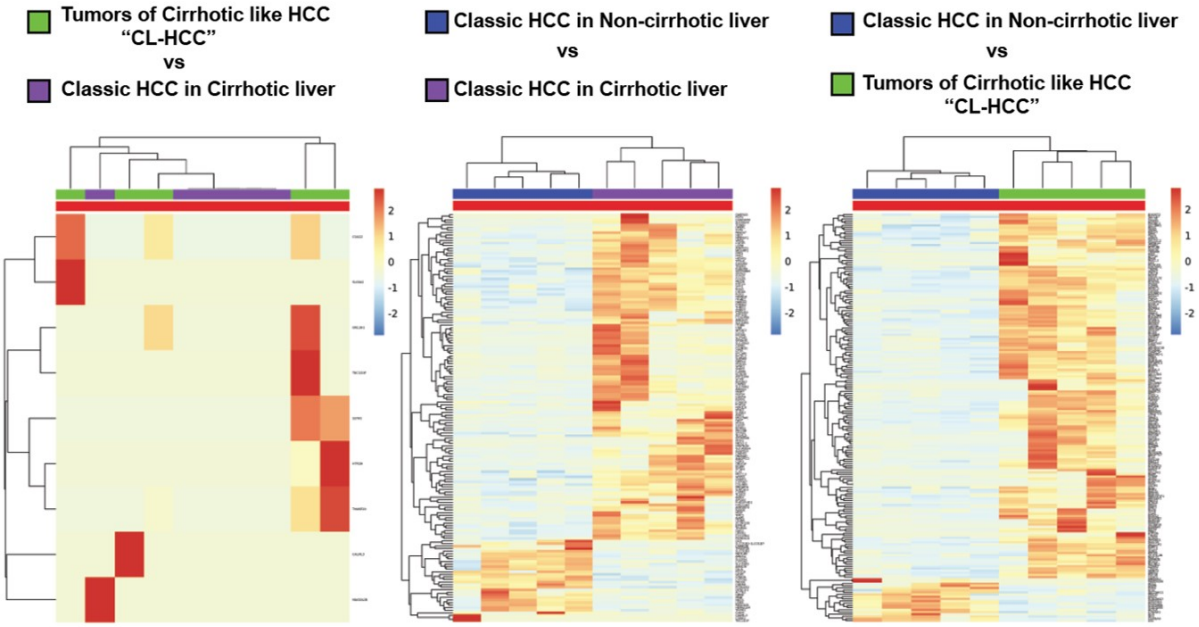

Figure: Heat map of significant differentially-expressed genes in all three tumor comparison groups. (adjusted p-value<0.05)

Conclusions: These findings suggest that GSS, SSTR5, CDC42EP1, HTR3A, and ACRC gene expression profiles, after further validation, may serve as diagnostic biomarkers of CL-HCC. Further, somatostatin or its analogues should be evaluated as targeted therapies for CL-HCC.

796 Will the Real "Hepatobiliary Cystadenocarcinoma" Please Stand Up? True Malignancy is Exceedingly Rare in Cystic Liver Lesions; Implications for Pathologic Evaluation and Pre-Operative Decision Making

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Background: Concern for hepatic cysts being "hepatobiliary cystadenocarcinoma" along with the allegedly high frequency of its occurrence in the literature (up to 30% of the hepatic cysts) remains a major driver for the management of cystic lesions in this organ.

Design: 260 resected hepatic cysts (all > 1 cm) from 2 separate continents were pathologically analyzed and classified based on the WHO 2019 criteria.

Results: Among all 260 cases, only 27 (10%) had ovarian type stroma (OTS) and thus would have qualified for the previous definition of “hepatobiliary cystadenoma/cystadenocarcinoma”, a term that WHO-2019 advocates discarding, and instead defines mucinous cystic neoplasms (MCN) as cysts with OTS as in pancreas. Moreover, only 7/260 (2.5%) hepatic cysts had invasive malignancy: 1 mucinous cystic neoplasm (MCN with OTS) that had a microscopic focus (6 mm) of invasive carcinoma, 1 intraductal papillary neoplasm of bile duct (IPNB) with invasive carcinoma, 1 ordinary cystic cholangiocarcinoma, and 4 cystic metastasis (2 colonic carcinoma, 1 ovarian granulosa cell, 1 neuroendocrine tumor)[Fig 1]. 3 additional cases had high grade dysplasia (HGD)/in-situ carcinoma (CIS), bringing the total number of carcinomatous cysts (HGD/CIS and/or invasive; so called hepatobiliary cystadenocarcinoma) to 10 (3.8 %): The non-invasive HGD/CIS-only group comprised 1 MCN with focal HGD/CIS, 1 IPNB with extensive HGD/CIS, and 1 intraductal oncocytic papillary neoplasm. However, a significant proportion of cysts resected with pre-operative radiologic diagnosis of “hepatobiliary cystadenoma/cystadenocarcinoma” proved to be non-neoplastic (including 7 abscesses presumed malignant pre-operatively). Of 23 echinococcal cysts, 2 were alveolaris type, and both had complex cystic lesions and thought radiologically (and grossly) malignant [Fig 2].

Figure 1 - 796

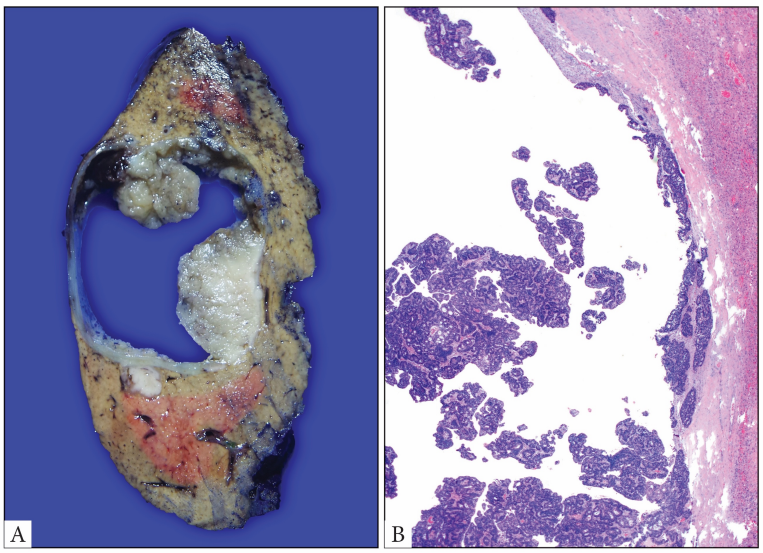
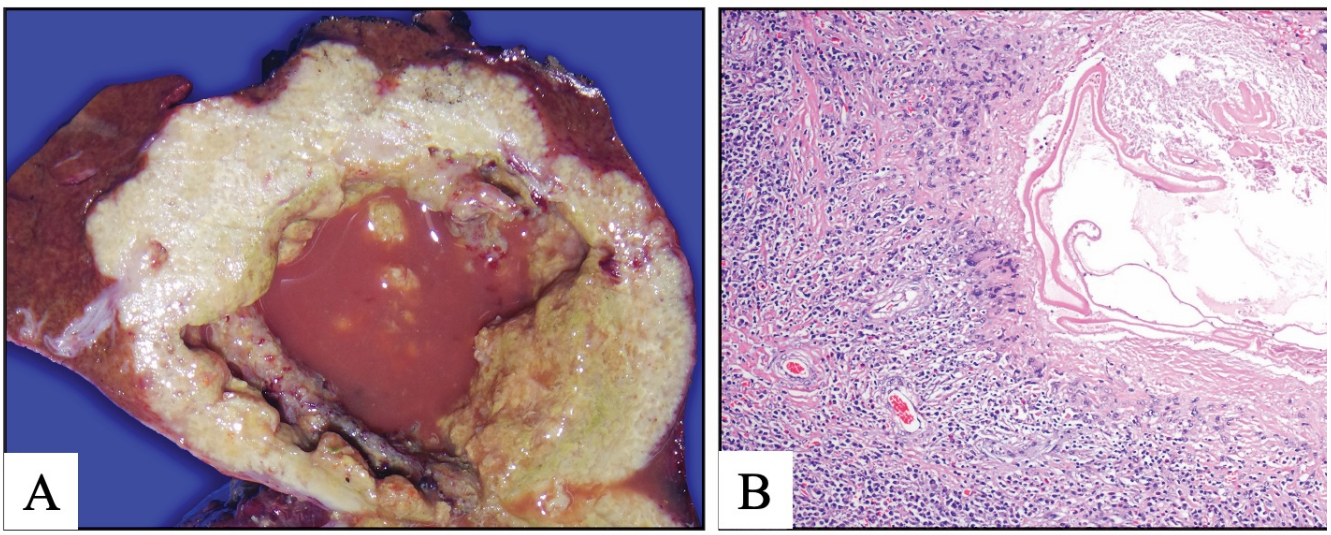


Figure 2 - 796



Conclusions: <5 % of hepatic cysts harbor carcinomatous changes, and, invasive malignancy occurs in only 2.5 %. Moreover, the few cysts that have malignancy are classifiable as specific entities other than “HB cystadenoma/cystadenocarcinoma” (WHO-2019 criteria). Considering that “cystadenoma”(MCN) is now defined by

OTS (only 10% of hepatic cysts), and that they are diagnosable only by full pathologic examination, it is advisable to revise current radiologic classification of hepatic cysts in which the cystadenoma/cystadenocarcinoma terms are still widely employed but often conflict with final pathology report as highlighted here. Accordingly, we propose the following pre-operative terminology until further analysis: 1) “Non-complex cyst (favor benign)”, 2) “Complex” (in three subsets, as 2a. favor benign, 2b. cannot rule out malignancy, or 2c. favor malignancy) 3) “Malignant features” (with the understanding that many in this category will prove benign).

797 Impact of HLA Anti-Donor Antibody (DSA) on Treatment Response and Graft Loss in Early Liver Allograft Rejection

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Background: Antibody-mediated rejection (AMR) in liver transplant (LT) patients has recently been recognized as an important cause of graft injury. While AMR appears to impact long-term graft survival, its impact in the early period remains unclear especially its impact on treatment. More specifically, it is unclear if AMR co-existing with T cell-mediated rejection (TCMR) impacts response to treatment versus TCMR only. Other questions exist such as when to consider additional treatment: at the start of rejection treatment (RX) or after failure of standard therapy? The aim of this study was to evaluate the impact of DSA on treatment response and graft failure in LT recipients with TCMR.

Design: All LT recipients treated for biopsy-confirmed rejection between 2009-2019 were identified (n=166). Of these 38 had complete data of DSA (MFI >500) and biopsy (LBX) materials. We reviewed LBX and calculated RAI (Rejection Activity Index) score for each; extracted clinical and immunosuppression data; post-RX outcome; DSA profile [de novo versus preformed] and HLA specificity. Analysis was directed at identifying factors that predicted nonresponse and graft loss in DSA+ and DSA- patients. RX nonresponse was defined as failure of steroid treatment requiring thymoglobulin (ATG) and/or other rescue therapies.

Results: 38 patients treated for rejection had post-LT DSA & LBX data. 20/38 (53%) were DSA+ vs 18 (47%) DSA-. 8/20 (40%) DSA+ vs 2/18 (11%) DSA- required rescue RX (p=0.002). There was no significant difference in age, gender, peak ALT/AST, bilirubin, or time from transplant among DSA+ and DSA- patients, or between patients that responded or failed steroid RX. RAI was significantly higher in DSA+/nonresponders vs DSA+/responders (median RAI=7 [6.75, 7.25] vs 4.5 [4.00, 5.25])(p=0.002). 5/8 (63%) DSA+/nonresponders developed graft loss (all due to alloimmune factors) vs 3/12 (25%) DSA+/responders (none from alloimmune factors)(p=0.002). C4d data showed no significant difference between these DSA+ groups.

Table 1. Demographic and Laboratory data among different sub-groups.

	DSA+ N=12	DSA+ steroid non-responder N=8	DSA- N=16	DSA- steroid non-responder N=2
Age at LT (median [IQR])	50.44 [38.25, 59.46]	37.54 [31.61, 57.43]	49.14 [36.30, 55.06]	41.11 [30.30, 51.91]
Male Gender (%)	7 (58.3)	6 (75.0)	7 (43.8)	2 (100.0)
AST 6mo post-RX (median [IQR])	51.00 [24.00, 95.00]	41.00 [31.25, 156.50]	26.00 [21.00, 56.00]	32.00 [32.00, 32.00]