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Original contribution

Evaluation of histologic changes in the livers of patients with early and late hepatic artery thrombosis☆,☆☆

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Summary Hepatic artery thrombosis (HAT) following orthotopic liver transplantation (OLT) can cause hepatic parenchymal necrosis and ischemic cholangiopathy. This study investigates additional histologic features that may suggest HAT in post-OLT liver specimens. For 94 liver specimens (explanted allografts and biopsies) from patients with a clinical or pathologic diagnosis of HAT, we recorded length of time between OLT and procedure, categorizing cases into early HAT (;≤30 days since OLT) and late HAT (>30 days since OLT). Common histologic findings in HAT included lobular necrosis (60 cases, 64%), portal inflammation (68 cases, 72%), ductular reaction (73 cases, 78%), lobular cholestasis (70 cases, 74%), and bile-tinged macrophages (40 cases, 43%). Ductular cholestasis was seen in 30 cases (32%); 10 of those patients were clinically septic. Bile in veins was seen in 16 (17%) cases and arteritis in 6 (6%) cases. Findings more common in resection than biopsy specimens included lobular necrosis ($P < .0001$), hemorrhage ($P = .0044$), ductular cholestasis ($P = .0003$), and bile-tinged macrophages ($P < .0001$). Lobular necrosis was more common in early HAT ($P = .0002$), and ductular reaction ($P = .006$) and bile in veins ($P = .03$) were more common in late HAT. Histologic changes in HAT vary based on specimen type and whether HAT is early or late. In late HAT, biliary injury might occur after a prolonged period of ischemia, with subsequent bile duct necrosis, bile in veins, and remodeling (eg, ductular reaction). Bile in veins is an unusual finding that may occur in HAT, although it can be seen in bile infarcts from other causes.

1. Introduction

Organ transplantation is a relatively new field, with the first successful liver transplant performed in the 1960s [1]. The 1-year survival rate was less than 30% during this decade [2] because of post–liver transplant complications such as preservation/reperfusion injury, vascular compromise (hepatic artery thrombosis [HAT], portal vein thrombosis, hepatic vein thrombosis), acute and chronic rejection, and recurrence of the original disease [3].

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However, with growing medical knowledge and improvements in the management of postoperative complications, preservation techniques, imaging modalities, and immunosuppressive therapy (eg, the introduction of cyclosporine), the 5- and 10-year survival rates have improved to 70% and 50%, respectively [4-6].

Studies have shown that half of transplanted livers with graft failure within a month had ischemic injury [7,8]. This is generally caused by either arterial insufficiency (stenosis, splenic arterial steal syndrome, sepsis) or HAT. HAT following orthotopic liver transplantation (OLT) is a common vascular postoperative complication, with several known risk factors [9]. Many cases occur shortly after transplantation, although some patients develop "late" HAT more than 30 days after OLT [10]. Radiologic studies and ultrasound imaging are considered the criterion standard for diagnosis [11].

The histopathologic changes of HAT have received little attention in the literature aside from their broad strokes [11]. Early HAT is primarily characterized by geographic areas of hepatocellular necrosis. The centrilobular areas are more sensitive to ischemic insults, and as such, portal tracts and zone 1 hepatocytes may be spared. Chronic HAT can lead to ischemic cholangiopathy with biliary strictures, necrosis, abscess formation, bacterial overgrowth, and bile infarcts [12].

A diagnosis of HAT is usually established clinically via Doppler sonography to detect a vascular flow abnormality and angiography to confirm the diagnosis [13]. However, it sometimes is not evident until explanted allograft evaluation; we have occasionally encountered explanted livers that contained grossly observable HAT, yet HAT had not been diagnosed (or sometimes even suspected) preoperatively. Additionally, rare HAT patients do not demonstrate symptoms [14].

Given the patchy distribution of ischemic injury, changes related to HAT could be missed on a liver biopsy specimen because of sampling issues. Still, knowledge of the full spectrum of possible pathologic changes in HAT could help suggest the diagnosis in posttransplant patients who undergo a liver biopsy for hepatic dysfunction of uncertain etiology. This study therefore investigated histopathologic features in biopsy and resection specimens of early and late HAT.

2. Materials and methods

This study was a collaborative effort between the surgical pathology departments at the University of Rochester Medical Center and Columbia University Medical Center. With appropriate institutional research board approval, the pathology archives of both institutions were searched for biopsy and surgical resection specimens carrying a tissue diagnosis of HAT in a donor liver allograft from January 1996 to April 2017. Biopsy specimens were excluded if inadequate for evaluation (shorter than 1.0 cm in aggregate and/or fewer than 6 portal tracts).

In total, 94 cases were identified with available hematoxylin and eosinE)-;–stained slides and clinical information. All biopsy cases and most resection cases were diagnosed with HAT prior to tissue procurement. For each, we recorded the length of time between OLT and the tissue-sampling procedure, categorizing cases into early HAT (;≤30 days since OLT) and late HAT (>30 days since OLT). We also recorded whether the patient was clinically deemed to have HAT and/or sepsis, and we recorded the most recent preprocedure alanine aminotransferase (ALT), aspartate transaminase (AST), and alkaline phosphatase (AlkPhos) levels when available. All E;hematoxylin and eosin slides were reviewed for 20 histologic findings: lobular necrosis, lobular inflammation, acidophil bodies, lobular hemorrhage, portal tract inflammation, arteritis, artery wall vacuoles, fibrin in vascular spaces, vein abnormalities, ductitis, duct disarray, vacuoles in duct epithelium, duct necrosis, ductular reaction, lobular cholestasis, ductular cholestasis, large duct injury, large duct stasis (ie, luminal bile), flecks of bile within portal/central veins, and bile-tinged macrophages. Histologic features were compared between biopsy and resection specimens and between early and late HAT. These subgroups were compared using Fisher exact test and the unpaired *t* test in GraphPad Software online (http://graphpad.com/quickcalcs; GraphPad Software, San Diego, CA; last accessed April 18, 2019), with a $P < .05$ considered statistically significant.

A comparison group of 7 explanted livers was reviewed for the presence of bile in veins and bile-tinged macrophages to evaluate the specificity of these findings.

3. Results

The 94 cases in the study included 25 biopsy specimens and 69 explant hepatectomy specimens from 69 patients. The specimens overall accounted for 73 transplanted livers (as 12 livers each represented more than 1 sample in the series [range: 2-5 samples]). Most patients overall were clinically known or highly suspected to have HAT, although this was more common in patients undergoing resection (94% versus 72%, $P = .007$).

The 69 patients included 51 males and 18 females, with a mean age of 50 years (range: 10 months–71 years). The most common reason for liver transplantation was alcoholic steatohepatitis (n = 21); other common reasons included chronic hepatitis C infection (n = 16), cryptogenic cirrhosis (n = 8), primary sclerosing cholangitis (n = 6), chronic hepatitis B infection (n = 4), and primary biliary cholangitis (n = 3). Overall median time to diagnosis of HAT was 26 days (range: 1-4015 days). Forty of the 73 livers experienced early HAT (41 specimens overall), and the other 33 livers only experienced late HAT (53 specimens overall). Preprocedure laboratory values were available for 59 specimens; mean ALT value was 152 IU/L (range: 11-1918), mean AST value was 292 IU/L (range: 9-5536), and mean AlkPhos value was 230 IU/L (range: 40-1436). Laboratory values did not significantly differ between early and late HAT cases for any of these enzymes ($P = .39$ for ALT, $P = .39$ for AST, and $P = .52$ for AlkPhos).

Histologically, the most common findings in the 94 cases included lobular necrosis (60 cases, 64%, Figure A), lobular hemorrhage (43 cases, 46%), portal inflammation (68 cases, 72%), ductular reaction (73 cases, 78%), lobular cholestasis (70 cases, 74%), and bile-tinged macrophages (40 cases, 43%) (Figure B). Bile in veins (typically portal veins but sometimes central veins) was seen in 16 (17%) cases (Figure C), portal/central vein fibrin in 8 cases (9%) (Figure D), and arteritis in 6 (6%) cases (Figure E). Ductular cholestasis was seen in 30 cases (32%) (Figure F), each from a different patient; 10 of those 30 patients were clinically septic. Artery wall vacuoles were seen in 12 (13%) cases (Figure G). The portal tract changes could reliably be categorized as focal or diffuse in 85 cases; they were focal in 25 (29%) and diffuse in 60 (71%).

There were 27 cases (9 resections, 18 biopsies) that showed neither lobular necrosis nor acidophil bodies. Histologic features suggesting biliary-pattern injury were somewhat common among these cases, including ductular reaction (7 resections [78%], 13 biopsies [87%]), lobular cholestasis (6 resections [67%], 13 biopsies [72%]), and large duct injury/stasis (6 resections [67%], 0 biopsies [0%]).

Findings in biopsy (n = 25) and resection (n = 69) cases are compared in Table 1. Several findings were more commonly seen in resection than biopsy cases, including lobular necrosis (83% versus 12%, P <0; .0001), lobular hemorrhage (55% versus 20%, P = .044), artery wall vacuolization (17% versus 0%, P = .03), ductular cholestasis (42% versus 4%, P = .0003), and bile-tinged macrophages (42% versus 4%, P < .0001). No finding was significantly more common in biopsy specimens, although duct disarray tended to be seen more commonly in biopsies than in resections (32% versus 14%, P = .08).

Findings in early and late HAT cases are compared in Table 2. Tissue from livers experiencing early HAT were significantly more likely to show lobular necrosis (85% versus 47%, P = .0002) and artery wall vacuolization (22% versus 6%, P = .03), and they tended to show bile-tinged macrophages more frequently (54% versus 34%, P = .06). In contrast, findings more common in late HAT included ductular reaction (89% versus 63%, P = .006), large duct injury (73% versus 36%, P = .004), large duct stasis (67% versus 33%, P = .008), and bile in veins (25% versus 7%, P = .03).

The comparison group of 7 explanted livers included 5 from patients with primary sclerosing cholangitis (PSC), 1 with fulminant liver failure, and 1 with cryptogenic cirrhosis and a bile infarct. Only the case with the bile infarct showed bile in veins microscopically. Five of the 7 cases showed lobular bile-tinged macrophages; the 2 that did not were both from PSC patients.

4. Discussion

Biopsy of the postallograft liver is challenging, with the main diagnostic considerations being recurrent disease and organ rejection [15]. HAT is not often considered as a potential diagnosis in these situations, as pathologic examination is rarely the factor that establishes a previously unknown diagnosis of HAT. Still, this phenomenon can occur; in 28% of our biopsy cases, the diagnosis was not established prior to biopsy. Therefore, recognizing the spectrum of histologic changes in early and late HAT can facilitate suggesting the diagnosis based on biopsy findings, and expeditious diagnosis of HAT can improve clinical outcomes for patients [16]. In contrast, fewer HAT patients (6%) underwent liver explant prior to their diagnosis, and in such specimens, HAT can be confirmed grossly rather than inferred histologically.

For those uncommon cases where HAT has not been previously established, pathologists need to recognize both overt and subtle histologic clues to the diagnosis. These histologic changes vary based on whether HAT is early or late. In early HAT, there is decreased perfusion to the liver. The hepatic arteries branch off into progressively smaller vessels before becoming a small artery in the portal tract. The hepatocytes farthest from the portal tract are most susceptible to ischemic injury. Furthermore, collateral blood supply has not had time to form between the hepatic artery and portal vein, which also perfuses the liver [17]. This explains why the most striking finding during early HAT is lobular necrosis. In chronic ischemic injury, there are collateral blood flow and vascular remodeling within the liver's dual blood supply [18,19], which explain the decreased frequency of hepatocellular necrosis compared to early HAT.

On the other hand, the biliary tree is primarily perfused by the hepatic artery [20]. Prolonged ischemia, as occurs in late HAT, leaves the liver susceptible to ischemic cholangiopathy [12]. This process can manifest dramatically as large duct injury [21] and also explains the remodeling (ie, ductular reaction) seen in late HAT. Other related findings in late HAT include bile-tinged macrophages and bile in vein lumens. The exact mechanism by which bile gains access to the adjacent vascular system is unclear, but injury of the biliary tree and subsequent architectural aberrancy likely play a role. These changes occur less often during the window of early HAT but readily persist in cases of late HAT [22].

Histologic vascular changes are uncommon in HAT specimens; only a few cases in our series showed arteritis or fibrin thrombi. Arterial wall vacuoles were seen in 13% of our cases and were more common in early HAT, although the overall relevance of this finding to the diagnosis is unclear.

Another study has suggested that increased mitotic figures and acidophil bodies are indicative of posttransplant hepatic arterial flow abnormalities [23]. We observed acidophil bodies in 17% of our cases; we did not observe increased mitotic figures but did not specifically evaluate them as part of our study design.

The patchy nature of the changes we observed in HAT is emphasized by the fact that several findings (including lobular necrosis, lobular hemorrhage, ductular cholestasis, and bile-tinged macrophages) were more commonly seen in resection than biopsy specimens. As a liver biopsy represents

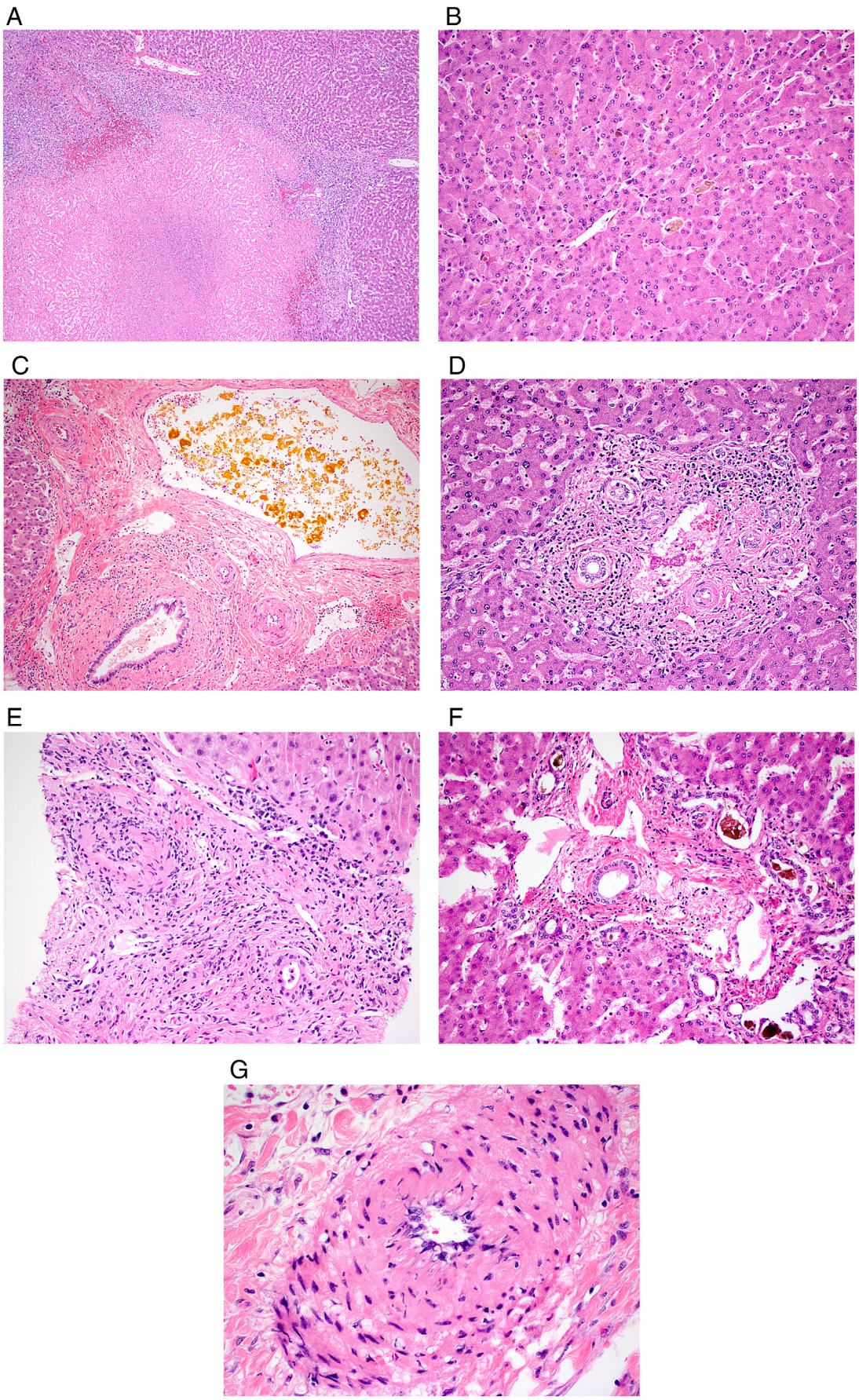
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Table 1 Comparative clinicopathological findings in biopsy and resection cases of HAT

	Biopsy cases (n = 25)	Resection cases (n = 69)	*P*
Clinical HAT	18 (72%)	65 (94%)	.007
Clinical sepsis	1 (4%)	19 (28%)	.02
Lobular necrosis	3 (12%)	57 (83%)	<.0001
Lobular inflammation	3 (12%)	14 (20%)	.54
Acidophil bodies	6 (24%)	10 (14%)	.35
Lobular hemorrhage	5 (20%)	38 (55%)	.044
Portal inflammation	15 (60%)	53 (77%)	.12
Arteritis	1 (4%)	5 (7%)	1.0
Artery wall vacuoles	0 (0%)	12 (17%)	.03
Vein fibrin	2 (8%)	6 (9%)	1.0
Vein abnormalities	1 (4%)	3 (4%)	1.0
Ductitis	2 (8%)	16 (23%)	.14
Duct disarray	8 (32%)	10 (14%)	.08
Duct epithelium vacuoles	0 (0%)	3 (4%)	.56
Duct necrosis	0 (0%)	1 (1%)	1.0
Ductular reaction	19 (76%)	54 (78%)	.79
Lobular cholestasis	19 (76%)	51 (%74)	1.0
Ductular cholestasis	1 (4%)	29 (42%)	.0003
Large duct injury	N/A	37 (54%)	N/A
Large duct stasis	N/A	34 (49%)	N/A
Bile in veins	1 (4%)	15 (22%)	.06
Bile-tinged macrophages	2 (8%)	38 (55%)	<.0001

Abbreviation: N/A, not available.

Table 2 Comparative clinicopathological findings in early and late cases of HAT

	Early HAT (n = 41)	Late HAT (n = 53)	*P*
Clinical HAT	38 (93%)	45 (85%)	.34
Clinical sepsis	6 (15%)	14 (26%)	.21
Lobular necrosis	35 (85%)	25 (47%)	.0002
Lobular inflammation	5 (12%)	12 (23%)	.28
Acidophil bodies	8 (20%)	8 (15%)	.59
Lobular hemorrhage	18 (44%)	25 (47%)	.84
Portal inflammation	31 (76%)	37 (70%)	.64
Arteritis	2 (5%)	4 (8%)	.69
Artery wall vacuoles	9 (22%)	3 (6%)	.03
Vein fibrin	6 (15%)	2 (4%)	.08
Vein abnormalities	2 (5%)	2 (4%)	1.0
Ductitis	8 (20%)	10 (19%)	1.0
Duct disarray	8 (20%)	10 (19%)	1.0
Duct epithelium vacuoles	1 (2%)	2 (4%)	1.0
Duct necrosis	0 (0%)	1 (2%)	1.0
Ductular reaction	26 (63%)	47 (89%)	.006
Lobular cholestasis	34 (86%)	36 (68%)	.15
Ductular cholestasis	16 (39%)	14 (26%)	.26
Large duct injury	13/36 (36%)	24/33 (73%)	.004
Large duct stasis	12/36 (33%)	22/33 (67%)	.008
Bile in veins	3 (7%)	13 (25%)	.03
Bile-tinged macrophages	22 (54%)	18 (34%)	.06

approximately 1/50,000 of the entire organ [24], such sampling error is inherent to the procedure, not the diagnosis.

Bile in veins and bile-tinged macrophages are unusual findings that we observed in HAT, although they are not specific to the diagnosis. They can be seen in bile infarcts from other causes, and the latter in particular was seen in most cases in our small comparison group. We also observed ductular cholestasis in several cases; this is generally linked to sepsis [25,26], but it is not specific for that diagnosis, and indeed, most of our patients with this finding were not clinically septic. Frank bile duct necrosis with fibrosis and inflammation of the wall has also been described [3], but this was a rare occurrence in our series.

As discussed in a review article by Adeyi et al [15], several pathologic processes in the posttransplant liver can cause hemorrhagic and/or biliary-type histologic changes similar to those of HAT. These include acute viral hepatitis, fibrosing cholestatic hepatitis, large duct obstruction, and recurrent PSC. As noted above, biliary-type changes were somewhat common in our HAT cases that lacked microscopic evidence of necrosis. Ischemic-type changes can also be seen in preservation-reperfusion injury, in primary graft dysfunction, and in unexplained massive hemorrhagic graft necrosis [27]. Although most microscopic changes we observed in livers with HAT are unfortunately nonspecific, we note that the combination of hemorrhagic and biliary injury should raise concern for HAT, and the absence of hemorrhagic change in the presence of biliary injury does not exclude the possibility of HAT. Additionally, the finding of bile in veins should lead to HAT being considered in the differential diagnosis.

Although HAT is generally diagnosed based on clinical features, this study reports the spectrum of histologic findings in early and late disease and highlights potential diagnostic pitfalls. In particular, sampling issues on biopsy may show

Figure 1 A, A region of lobular necrosis from a hepatectomy performed for early HAT. This finding was significantly more common in early HAT than in late HAT, and in resection specimens than in biopsy specimens. B, Focal bile-tinged macrophages in the lobular parenchyma of a liver resected for late HAT. This finding was somewhat more common in early HAT and was rarely encountered in biopsy samples. C, Flecks of bile in the portal vein of a liver resected for early HAT. This finding, seen in 17% of cases, was generally encountered in resection specimens and was more common in late HAT. D, Fibrin in the portal vein of a liver resected for early HAT. This uncommon finding was most commonly encountered in liver specimens taken during early HAT. E, Hepatic artery inflammation (arteritis) from a biopsy specimen in a patient with late HAT. This finding was only encountered in 6% of cases. F, Ductular cholestasis from the resected liver of a nonseptic patient with late HAT. This finding was much more common in resection than biopsy specimens; only one-third of the patients with this finding had been clinically diagnosed as septic. G, Artery wall vacuoles were an uncommon and typically focal finding, seen only in resection specimens.

a paucity of hepatocellular necrosis, and the histologic features of chronic HAT overlap with a biliary pattern of injury. Biopsy sampling should certainly not be relied upon to make the diagnosis of HAT [12], but certain features (including bile-tinged macrophages and bile in portal veins) should prompt the inclusion of HAT in a differential diagnosis.

References

[1] Starzl TE, Groth CG, Brettschneider L, et al. Orthotopic homotransplantation of the human liver. Ann Surg 1968;168:392-415.

[2] Starzl TE, Iwatsuki S, Van Thiel DH, et al. Evolution of liver transplantation. Hepatology 1982;2:614-36.

[3] Washington K. Update on post-liver transplantation infections, malignancies, and surgical complications. Adv Anat Pathol 2005;12:4221-6.

[4] Pomfret EA, Fryer JP, Sima CS, Lake JR, Merion RM. Liver and intestine transplantation in the United States, 1996-2005. Am J Transplant 2007;7:1376-89.

[5] Barber K, Blackwell J, Collett D, Neuberger J. UK Transplant Liver Advisory Group. Life expectancy of adult liver allograft recipients in the UK. Gut 2007;56:279-82.

[6] Dawwas MF, Gimson AE, Lewsey JD, Copley LP, van der Meulen JHP. Survival after liver transplantation in the United Kingdom and Ireland compared with the United States. Gut 2007;56:1606-13.

[7] Hübscher SG. Transplant pathology of the liver. Curr Diagn Pathol 1994;1:59-69.

[8] Quiroga J, Colina I, Demetris AJ, Starzl TE, Van Thiel DH. Cause and timing of first allograft failure in orthotopic liver transplantation: a study of 177 consecutive patients. Hepatology 1991;14:1054-62.

[9] Yang Y, Zhao JC, Yan LN, et al. Risk factors associated with early and late HAT after adult liver transplantation. World J Gastroenterol 2014;20:10545-52.

[10] Gunsar F, Rolando N, Pastacaldi S, et al. Late hepatic artery thrombosis after orthotopic liver transplantation. Liver Transpl 2003;9:605-11.

[11] Clouston AD, Hübscher SG. Transplantation pathology. In: Burt AD, Ferrell LD, Hübscher SG, editors. MacSween's pathology of the liver. 7th ed. Philadelphia: Elsevier; 2018. p. 880-965.

[12] Deltenre P, Valla DC. Ischemic cholangiopathy. Semin Liver Dis 2008;28:235-46.

[13] Horrow MM, Blumenthal BM, Reich DJ, Manzarbeitia C. Sonographic diagnosis and outcome of hepatic artery thrombosis after orthotopic liver transplantation in adults. AJR Am J Roentgenol 2007;189:346-51.

[14] Krajicek E, Sherman S, Lacerda M, Johnson MS, Vuppalanchi R. Ischemic cholangiopathy 11 years after liver transplantation from asymptomatic chronic hepatic artery thrombosis. ACG Case Rep J 2018;5:e75.

[15] Adeyi O, Fischer SE, Guindi M. Liver allograft pathology: approach to interpretation of needle biopsies with clinicopathological correlation. J Clin Pathol 2010;63:47-74.

[16] Mourad MM, Liossis C, Gunson BK, et al. Etiology and management of hepatic artery thrombosis after adult liver transplantation. Liver Transpl 2014;20:713-23.

[17] Brittain RS, Marchioro TL, Hermann G, Waddell WR, Starzl TE. Accidental hepatic artery ligation in humans. Am J Surg 1964;107:822-32.

[18] Bhattacharjya S, Gunson BK, Mirza DF, et al. Delayed hepatic artery thrombosis in adult orthotopic liver transplantation-a 12-year experience. Transplantation 2001;71:1592-6.

[19] O'Connor PJ, Buhac I, Balint JA. Spontaneous hepatic artery thrombosis with infarction of the liver. Gastroenterology 1976;70:599-601.

[20] Douglass TC, Cutter WW. Arterial blood supply of the common bile duct. Arch Surg 1948;57:599-612.

[21] Valente JF, Alonso MH, Weber FL, Hanto DW. Late hepatic artery thrombosis in liver allograft recipients is associated with intrahepatic biliary necrosis. Transplantation 1996;61:61-5.

[22] Chen J-W, Chen D-Z, Lu G-Z. Asymptomatic process of hepatic artery thrombosis in a patient after orthotopic liver transplantation. HBPD INT 2004;3:149-51.

[23] Liu TC, Nguyen TT, Torbenson MS. Concurrent increase in mitosis and apoptosis: a histological pattern of hepatic arterial flow abnormalities in post-transplant liver biopsies. Mod Pathol 2012;25:1594-8.

[24] Lefkowitch JH. General principles of biopsy assessment. Lefkowitch JH. Scheuer's liver biopsy interpretation. 8th ed. Philadelphia: Saunders; 2010. p. 1-10.

[25] Lefkowitch JH. Bile ductular cholestasis: an ominous histopathologic sign related to sepsis and "cholangitis lenta". Hum Pathol 1982;13:19-24.

[26] Torous VF, De La Cruz AL, Naini BV, Wang HL. Cholangitis lenta: a clinicopathologic study of 28 cases. Am J Surg Pathol 2017;41:1607-17.

[27] Clouston AD, Hübscher S. Transplantation pathology. In: Burt AD, Ferrell LD, Hübscher S, editors. MacSween's pathology of the liver, seventh edition. Philadelphia: Elsevier; 2018. p. 910.