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Prevalence and Significance of Perivascular Soft Tissue Surrounding the Hepatic Artery After Liver Transplantation

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Abstract

Objective—The objective of this study was to determine the prevalence and significance of perivascular soft tissue surrounding the hepatic artery on computed tomography (CT) after liver transplantation.

Materials and Methods—A total of 119 consecutive patients who underwent liver transplantation were retrospectively identified from a search of electronic medical records. Fourteen patients had histologic proof of posttransplant lymphoproliferative disease (PTLD). For each patient, the initial CT scan after transplantation, and the most recent CT scan if available, was analyzed for the presence of soft tissue in the porta hepatis region, particularly surrounding the transplanted hepatic artery. The hepatic artery was identified, and the maximum diameter of the soft tissue surrounding the vessel was measured and classified using the following scale: grade 0, none; grade 1, mild; grade 2, moderate; grade 3, moderate-large; and grade 4, large.

Results—Prevalence of perivascular soft tissue was 93% in the initial CT scans and follow-up studies. Comparing the initial and follow-up soft tissue measurements, 34% decreased, 62% were unchanged, and 4% increased. Using the Fisher exact test and a Mann-Whitney test, there was no statistically significant difference in the prevalence or diameter of perivascular soft tissue when comparing patients with pathologically proven PTLD and patients with no PTLD. Twenty-nine of the 119 patients underwent 68 positron emission tomography/CT scans in the time interval analyzed. Ninety percent of these patients had no abnormal fluorodeoxyglucose activity in the porta hepatis and portacaval regions.

Conclusions—The presence of isolated perivascular soft tissue in patients after liver transplantation is a common finding and is not associated with lymphoproliferative disease.

Keywords

liver transplantation; postoperative; hepatic artery

Approximately 5000 liver transplantations are performed annually in the United States,¹ adding to a growing number of patients who had undergone organ transplant in the healthcare system. At large tertiary care centers, patients are frequently imaged for routine

surveillance after their transplant or for other unrelated medical reasons. As the number of imaging studies increases in this population, it becomes even more important to recognize normal postsurgical changes from more concerning pathology. In our clinical experience, there has been particular uncertainty regarding the significance of the presence of perivascular soft tissue surrounding the hepatic artery. This finding can cause clinical confusion and may raise the suspicion for early posttransplant lymphoproliferative disease (PTLD), transplant rejection, or recurrent tumor. To our knowledge, this has not been previously described in the literature. The uncertainty and clinical concern for these findings may prompt additional imaging, extended medical workups, and increased patient anxiety. The purpose of this study was to determine the prevalence and clinical significance of soft tissue surrounding the hepatic artery in the porta hepatis region after liver transplantation.

MATERIALS AND METHODS

A total of 119 consecutive patients who underwent liver transplant were retrospectively identified from an electronic medical database of computed tomography (CT) scans performed from January 2005 to December 2009 at a single institution. Each patient included in the study had 1 or more contrast-enhanced CT examinations of the abdomen/pelvis after their liver transplantation. Fourteen of these patients had documented histologic proof of PTLD.

The patient population was 77% male (92/119) and 23% female (27/119). Patient age at the time of the initial CT scan ranged from 27 to 78 years with a mean age of 58.8 years. The most common indications for liver transplantation included liver disease from hepatitis C virus (68/119), hepatitis B virus (17/119), alcohol (10/119), primary sclerosing cholangitis (9/119), hepatocellular carcinoma (62/119), and more than 1 indication (47/119). For all patients, the initial CT examination after transplantation and the most recent follow-up CT scan that was available were analyzed in the study. Thirty-three of the 119 patients did not have follow-up scans to date. The initial CT examinations were conducted at an average of 3.1 years (range of 8 days to 16 years) after transplantation. The most current follow-up CT scan was performed at an average of 2.8 years (range of 22 days to 11 years) from the initial study.

Initially, 150 patients were selected from the database. Thirty-one patients were excluded. Exclusion criteria included the following: partial/lobar liver transplants, focal postoperative fluid collections in the periportal region, and large-volume ascites. Partial liver transplants were excluded to limit potential variation in the hepatic artery anatomy. Examinations limited by poor image quality, surgical clip artifacts, or motion were also excluded. Each patient's medical record was reviewed including clinical, surgical, and pathological reports. The diagnosis of PTLD and rejection were confirmed with pathology. Twenty-one of the 119 patients in this study had biopsy confirmation of transplant rejection.

The prevalence and diameter of the perivascular soft tissue were compared in the patient subgroups with PTLD ($n = 14$) and without PTLD ($n = 105$) as well as in the patient subgroups with pathologically proven liver transplant rejection ($n = 21$). Group differences in binary (yes/no) outcomes were compared using the Fisher exact test. Binomial estimates

and confidence intervals are reported for the risks in each group, and Z-test of proportions was used to generate estimates and confidence intervals for risk differences. Group differences in ordinal and continuous variables were compared using the Mann-Whitney test. For all statistical analyses, a *P* value less than 0.05 was considered a statistically significant difference.

Computed Tomographic Technique

Only patients with contrast-enhanced studies of the abdomen/pelvis were included. All patients were imaged with multidetector-row CT (4, 16, or 64 detectors; HighSpeed or LightSpeed; General Electric, Milwaukee, Wis) using 1.25- or 5-mm slice thickness. Scans performed at 1.25-mm collimation were reconstructed to 5-mm slice thickness. The peak tube voltage was 120 kilovolt (peak) and the milliamperage was automatically adjusted to attain a noise index of 12 Hounsfield units (HUs). A total of 150 mL of intravenous iohexol (Omnipaque 350; Nycomed Amersham, Princeton, NJ) was injected at a rate of 3 to 5 mL/s. Computed tomographic scans were obtained using either a liver protocol with both arterial phase and portal venous phases using SmartPrep or a single-phase protocol with an 80-second scan delay.

Positron emission tomography (PET)/CT examinations were performed on either a Siemens Biograph HiRez 16-detector model (Siemens Medical Systems, Iselin, NJ) or a GE Discovery VCT 64 detector with intravenous administration of 18F-fluorodeoxyglucose (FDG).

Image Analysis

All examinations were retrospectively reviewed by a board-certified radiologist (S.W.) with more than 5 years of experience in abdominal imaging and a radiology resident doing a year of research (E.J.). A final consensus read was performed. Both readers were blinded to those patients with a diagnosis of PTLT. The initial post transplantation CT and the most current CT scan available were analyzed for the presence of soft tissue surrounding the transplanted hepatic artery. The hepatic artery was analyzed from the celiac trunk to the porta hepatis using primarily axial images with coronal reconstructions to supplement evaluation. When present, perivascular soft tissue (density greater than 20 HU) surrounding or tracking along the course of the artery was measured in its maximum diameter using electronic calipers. The hepatic artery was included in the measurement when the soft tissue was found to be present on both sides of the vessel (Fig. 1). On the follow-up examinations, a measurement of the soft tissue was made in the same area as that of the initial CT to maintain consistency. The presence of a “periportal collar,”² or “halo,”³ which has been previously described in the literature in patients with transplant rejection, was also noted. This periportal low attenuation surrounding the portal veins was noted as either *central* at the liver hilum or *peripheral*, tracking into the liver along the intrahepatic portal venous branches.

Any available PET-CT scans were reviewed for the presence of increased FDG uptake with particular attention to the porta hepatis and portacaval regions. A total of 68 PET examinations were reviewed in the 29 patients who had liver transplant. Indications for PET-CT scans included recurrent hepatocellular carcinoma or cholangiocarcinoma, or staging for

newly diagnosed nonliver malignancy. One patient specifically underwent a PET-CT scan with the indication “rule out PTLT” because of the increased soft tissue prominence in the porta hepatis noted on routine CT examinations (Fig. 2).

The perihepatic arterial soft tissue was classified into 5 groups on the basis of the maximum diameter of the soft tissue: group 0, none; group 1, mild (1–10 mm); group 2, moderate (11–20 mm); group 3, moderate-large (21–30 mm); and group 4, large (greater than 30 mm) (Figs. 3, 4). The measurements from the initial and follow-up CT were compared and classified as *decreased*, *stable*, or *increased*. The *decreased group* was defined as a reduction of more than 3 mm from the initial CT; the *stable group*, as a change of 3 mm or less; and the *increased group*, as a growth of more than 3 mm from the initial examination. The 3-mm cutoff was selected to account for potential small differences within measurement error.

All data were compiled into an electronic spreadsheet, and a statistical analysis was performed. The institutional review board before the initiation of the investigation approved this retrospective study.

RESULTS

The presence of perivascular soft tissue surrounding the hepatic artery was a common finding, visualized in 93% of the initial CT scans (111/119) and 93% of the follow-up studies (80/86). The distribution of soft tissue diameter in the initial and follow-up scans is represented in Table 1. When the initial and follow-up soft tissue measurements were compared, it was noted that 33.7% (29/86) decreased in size, that 61.6% (53/86) remained stable, and that 4.7% (4/86) increased in size (Table 2). Of those 4 follow-up studies that increased, the maximum increase in the size of the perivascular soft tissue was 12 mm, which was seen on a 5-year follow-up CT examination in a patient who had active PTLT and also had a contiguous intrahepatic mass. Thirty-three patients have not had a follow-up CT examination to date.

The prevalence and diameter of the perivascular soft tissue were compared in the patient subgroups with PTLT ($n = 14$) and without PTLT ($n = 105$) as well as in the patient subgroups with pathologically proven liver transplant rejection ($n = 21$). When comparing the patients with and without PTLT or the patients with or without transplant rejection, there was no significant difference in the prevalence or diameter of the perivascular soft tissue (Tables 3, 4). Using the Fisher exact test, there was no statistical difference in the percentage of the patients with or without perivascular soft tissue on the initial CT scans ($n = 119$) in either of the groups with PTLT ($n = 105$) or without PTLT (14) ($P = 1.00$) or in the groups with ($n = 21$) or without transplant rejection ($n = 98$) ($P = 1.00$). On the follow-up CTs ($n = 86$), there was an unexpected statistically significant difference between the groups with PTLT ($n = 11$) and without PTLT ($n = 75$) in that there was actually a higher proportion of patients without soft tissue (27.3%, [3/11]) in the group with PTLT when compared with the group without PTLT (4% [3/75]) ($P = 0.026$).

Using the presence of perivascular soft tissue as a predictor for PTLT on initial CT resulted in a sensitivity of 11.7% (95% confidence interval, 0.064–0.192) and a specificity of 87.5%

(95% confidence interval, 0.473–0.997). For the 14 patients who had PTLT, the soft tissue was analyzed regardless of the timing of the imaging relative to PTLT disease activity because the reader was blinded to the diagnosis.

A periportal collar was seen in 26.9% (32/119) of the patients. Of these, 69% (22/32) had central involvement only, 3% (1/32) had peripheral involvement, and 28% (9/32) had both central and peripheral periportal low attenuation. The presence of a periportal collar was therefore not related to the presence of perihepatic arterial soft tissue. Of the 21 patients with rejection, 70% (14/20) had no evidence of a periportal collar, 10% (2/20) had central, and 20% (5/20) had both central and peripheral periportal low attenuation.

Twenty-nine patients underwent a total of 68 PET-CT examinations in the time interval analyzed, and 90% (26/29) of these patients had no abnormal FDG activity in the porta hepatis and portacaval regions. Two of the 3 patients with abnormal FDG activity had pathologically proven PTLT, and the other had a cholangiocarcinoma metastasis. One patient with pathologically proven PTLT had no significant FDG uptake in the region of the perivascular soft tissue but did have FDG-avid perihepatic masses and peritoneal implants (Fig. 5). The other patient with PTLT had an FDG-avid intrahepatic mass contiguous with the large amount of perivascular soft tissue (Figs. 6A, B). This patient also had the maximum increase in perivascular soft tissue on follow-up CT scan. The patient with cholangiocarcinoma had an FDG activity corresponding to an enlarged portacaval lymph node; however, the perihepatic arterial soft tissue itself was not FDG-avid (not shown).

DISCUSSION

Postsurgical changes after liver transplantation have been infrequently described in the literature. However, postsurgical findings in patients, after a Whipple procedure, have been thoroughly covered in the literature and similar perivascular soft tissue to what we observed in patients who had liver transplant has been noted.^{4,5} Mortelé et al^{4,5} performed a retrospective cohort study of 43 patients after Whipple with a total of 84 examinations where “perivascular cuffing” was noted in 50% of the examinations (42/84) and in 60% of the patients (26/43). We believe that the underlying etiology is similar in both patient cohorts and that it is likely to represent granulation tissue or fibrosis related to inflammatory change.

The major concern of this perivascular tissue is the potential association with the development of PTLT. To directly assess this possibility, we searched all 119 patients who underwent liver transplant for the development of PTLT in the time frame for which we had available CT scans. Statistical analysis failed to demonstrate a correlation between PTLT and the presence of perivascular soft tissue or the thickness of the soft tissue (Tables 3 and 4). The only statistically significant difference, which was seen in the patients on follow-up examinations only, was in the PTLT subset, which actually had a higher percentage of patients without perivascular soft tissue. Therefore, it is inappropriate to use the presence of this soft tissue alone to predict the development of PTLT or to suggest that the soft tissue represents lymphomatous infiltration.

Recent studies^{6,7} have promoted the utility of PET-CT imaging in patients with PTLT. Because of the hypermetabolic nature of PTLT, PET is useful for diagnosis, assessment of chemotherapy response, and surveillance. We retrospectively reviewed any PET-CT scans available in our study population. Ninety percent (26/29) of the patients with PET examinations showed normal metabolic activity in the perihepatic and periportal region. Of the 3 patients with a positive finding in the PET examination, only 1 had a hypermetabolic activity corresponding to the perivascular soft tissue (Fig. 6). This patient had an FDG-avid perivascular soft tissue contiguous with a large FDG-avid hepatic mass, a biopsy-proven PTLT (Figs. 6A, B). The large mass significantly decreased in size after chemotherapy (Fig. 6C). A second patient had strongly hypermetabolic perihepatic masses and peritoneal implants, also a biopsy-proven PTLT but no FDG uptake in the region of the perivascular soft tissue (Fig. 5). The third patient with a positive PET examination had an isolated hypermetabolic portacaval lymph node, separate from the perivascular soft tissue, consistent with metastatic cholangiocarcinoma (not shown).

Follow-up scans were also reviewed to track changes over time and to better understand the natural progression of this soft tissue. On the follow-up examinations, 90.9% of the patients with PTLT and 96% of patients without PTLT showed a stable or a decreased amount of the perivascular soft tissue. In the few cases of increased soft tissue growth on follow-up, the change was never greater than 12 mm during a 5-year period. Follow-up scans were conducted at an average of almost 3 years after the initial CT. The long length of follow-up showing predominance of stability or decrease in the size of the perivascular soft tissue is a good predictor of benignity. Furthermore, the surprisingly high overall prevalence of soft tissue surrounding the hepatic artery implies that this tissue is an expected finding after liver transplantation. In contrast, PTLT is a relatively rare disease in adult patients who had liver transplant with a prevalence range of 2% to 3.5% and an incidence of 1.1% at 18 months.^{9,10}

Limitations of the study include its retrospective nature, the fact that the images were only reviewed by 1 board-certified radiologist and a radiology resident, and the small cohort of patients with PTLT. Posttransplant lymphoproliferative disease, however, is a relatively uncommon malignancy, and our cohort size is similar to other studies that have examined PTLT.^{11,12} Another limitation is the lack of confirmatory histology of the perivascular soft tissue. We have not been able to obtain tissue from our transplant surgeons and pathologists during autopsy. Routine autopsy in our institution does not include the sampling of this region. A biopsy would also be a high-risk and technically challenging procedure. Therefore, we have relied on PET-CT and long-term follow-up imaging in predicting benignity. This is another limitation of the study, however, because of the low number of PET/CT scans, available in only 29 patients. In conclusion, perivascular soft tissue around the hepatic artery in patients after liver transplantation is a common postoperative finding and, in isolation, is more likely a benign, expected postoperative finding and should not raise the suspicion for lymphoproliferative disease.

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FIGURE 1.

Arterial-phase axial CT image demonstrates a mild (1–10 mm) amount of perivascular soft tissue surrounding the transplant hepatic artery (black arrows). After 10 years, there was no change in density or amount of soft tissue (not shown).

FIGURE 2.

Arterial-phase axial CT and PET images 9 months after the transplant show soft tissue density in the porta hepatis adjacent to surgical clips, primarily around the hepatic artery without FDG avidity (black arrows). Figure 2 can be viewed online in color at www.jcat.org.

FIGURE 3.

Arterial-phase axial CT image from a patient with a moderate (11–20 mm) amount of perivascular soft tissue (black arrow). Note the close relationship to the hepatic artery. There was no change on a follow-up CT 18 months later (not shown).

FIGURE 4.

Arterial-phase CT image demonstrates a large amount (>3 cm) of tissue surrounding the hepatic artery and within the porta hepatis. Hounsfield unit attenuation is consistent with soft tissue density. This patient did not have PTLT.

FIGURE 5.

Contrast-enhanced PET-CT image through the level of the perivascular soft tissue (black arrows) in a patient who had a pathologically proven PTLT. There are multiple FDG-avid perihepatic masses and peritoneal implants (white arrows) but no increased FDG activity corresponding to the perivascular soft tissue. Figure 5 can be viewed online in color at www.jcat.org.

FIGURE 6.

A, Consecutive axial CT images through a large central intrahepatic mass contiguous with a large amount of perivascular soft tissue along the hepatic artery, which was a biopsy-proven PTLN (black arrows). B, Whole-body coronal PET image demonstrates an FDG uptake within this mass (white arrow). C, Follow-up contrast-enhanced CT and PET images show marked decrease in the amount of perivascular soft tissue and FDG activity at background levels after treatment for PTLN (black arrows). Figure 6 can be viewed online in color at www.jcat.org.

TABLE 1

Prevalence and Diameter of Perivascular Soft Tissue

Initial CT Postoperative (n = 119)	Initial CT of All Patients (n = 119)	Initial CT of Patients Without PTLTLD (n = 105)	Initial CT PTLTLD* (n = 14)	Most Recent CT of All Patients (n = 86)	Most Recent CT of Patients Without PTLTLD (n = 75)	Most Recent CT of Patients with PTLTLD (n = 11)
Grade	No.	No.	No.	No.	No.	No.
0 (none)	6.7% (8)	6.6% (7)	7.1% (1)	7.0% (6)	4% (3)	27.2% (3)
1 (1–10 mm)	40.3% (48)	40% (42)	28.6% (4)	47.7% (41)	50.7% (38)	18.2% (2)
2 (11–20 mm)	35.2% (42)	35.2% (37)	42.8% (6)	32.6% (28)	33.3% (25)	27.2% (3)
3 (21–30 mm)	10.9% (13)	11.4% (12)	14.2% (2)	9.3% (8)	8% (6)	27.2% (3)
4 (>30 mm)	6.7% (8)	6.7% (7)	7.1% (1)	3.5% (3)	4% (3)	0% (0)
Total	93%	93%	93%	93%	96%	73%

TABLE 2

Stability of Perivascular Soft Tissue in all Patients

Change	No. All Patients (n = 86)	No. Patients Without PTLD (n = 75)	No. Patients With PTLD (n = 11)
Decreased (decrease of more than 3 mm)	33.7% (29)	33.3% (25)	36.4% (4)
Stable (within 3 mm)	61.6% (53)	62.7% (47)	54.5% (6)
Increased (increase of more than 3 mm)	4.7% (4)	4% (3)	9.1% (1)

TABLE 3

Summary of Variables of Interest by PTLT

Variable	PTLT Dx = No (N = 105)	PTLT Dx = Yes (N = 14)	P
Initial CT soft tissue, mean (SD) [N]	1.37 (0.989) [105]	1.41(0.888) [14]	0.67 [*]
Follow up CT soft tissue, mean (SD) [N]	1.19 (0.788) [75]	1.16 (0.982)	0.94
Grade initial, mean (SD) [N]	1.69 (0.984) [105]	1.86 (1.03) [14]	0.46
Grade follow-up CT, mean (SD) [N]	1.55 (0.843) [75]	1.55 (1.21)	0.91
Stability, mean (SD) [N]	-0.293 (0.54) [75]	-0.273 (0.647) [11]	0.98
Grade initial			
Grade 0	7 (6.7%)	1 (7.2%)	0.83 [†]
Grade 1	44 (41.9%)	4 (28.6%)	
Grade 2	36 (34.3%)	6 (42.9%)	
Grade 3	11 (10.5%)	2 (14.3%)	
Grade 4	7 (6.7%)	1 (17.1%)	
Total	105	14	
Summary of Variables of Interest by Rejection			
Variable	Rejection N = No (N = 98)	Rejection N = Yes (N = 21)	P
Initial CT soft tissue, mean (SD) [N]	1.41 (1.02) [98]	1.17 (0.721) [21]	0.32
Follow-up CT soft tissue, mean (SD) [N]	1.25 (0.854) [69]	0.941 (0.546) [17]	0.34
Grade initial, mean (SD) [N]	1.76 (1.01) [98]	1.48 (0.873) [21]	0.18
Grade Follow-up CT, mean (SD) [N]	1.61 (0.927) [69]	1.29 (0.686)	0.32
Stability, mean (SD) [N]	-0.304 (0.577) [69]	-0.235 (0.437) [17]	0.54

^{*} Based on the Mann-Whitney test.

[†] Based on the Fisher exact test.

Dx, diagnosis.

TABLE 4

Risk Estimates Comparing Proportion of Soft Tissue on Initial CT = 1 in PTLD = NO Versus PTLD = YES

PTLD	Risk	95% Confidence Limits ^{*†‡} (Asymptotic)
No	0.9333	0.8809–0.9858
Yes	0.9286	0.7580–1.0000
Difference	0.0048	–0.1788 to 0.1883

* The asymptotic confidence limits include a continuity correlation.

† Data from the Z-test.

‡ Difference is [(Row1 (No) – Row 2 (yes))].