

The presence and significance of lymphadenopathy detected by CT in primary sclerosing cholangitis

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Abstract. Patients with primary sclerosing cholangitis (PSC) are at increased risk of developing cholangiocarcinoma, which adversely affects their survival, especially after orthotopic liver transplantation. All CT scans of patients with PSC referred to the Liver Unit at the Queen Elizabeth Hospital since 1992 were reviewed. The location of any lymph node with a short axis diameter greater than normal was documented. The incidence of lymphadenopathy and cholangiocarcinoma was also documented. 36 scans are reviewed, including eight with cholangiocarcinoma as well as PSC. Abdominal lymphadenopathy was present in 26 cases (66%) and 45 separate lymph node groups were involved in these patients. There were eight cases of cholangiocarcinoma; five were detectable on CT, but only four had significant lymphadenopathy. The remaining three cases of cholangiocarcinoma were not detectable on CT and only one of these had lymphadenopathy. Follow-up of the remaining patients has not demonstrated the development of cholangiocarcinoma. Lymphadenopathy is commonly demonstrated by CT in PSC patients, but does not imply malignancy and should not exclude a patient from undergoing liver transplantation. Conversely cholangiocarcinoma may develop without significant lymphadenopathy.

Primary sclerosing cholangitis (PSC) is a disease of unknown aetiology, resulting in inflammation and fibrosis of the biliary tree. It is a predisposing factor for the development of cholangiocarcinoma [1] in about 10% of cases. The initial clinical signs of malignancy are not dissimilar to those of PSC, namely jaundice, pruritis and general malaise. Cholangiocarcinoma can be difficult to detect radiologically when it occurs in cases of PSC [2, 3]. The presence of lymphadenopathy and its association with malignancy may therefore be an important discriminator in cases of PSC.

We describe the findings on CT of lymphadenopathy in patients with PSC, detailing the location of enlarged lymph nodes and the presence of or absence of cholangiocarcinoma.

Methods

36 patients with PSC referred to the Liver Unit at The Queen Elizabeth Hospital, Birmingham since 1992, who had undergone abdominal CT, were reviewed. There were 22 male and 14 female patients with a mean age of 41 years (range 29–59). In all cases, the diagnosis of PSC had been made prior to CT by either liver biopsy or endoscopic retrograde cholangiography. Two CT scanners were used: a Somatom CR (Siemens Medical System, Erlangen, Germany) or a Pro speed 200 (General Electric Medical Systems, Milwaukee,

WI, USA). Each patient underwent a dynamic scan using a 100 ml intravenous bolus of Ultravist 300 (iopromide 300 mgI ml⁻¹, Schering AG, Berlin Germany) or Omnipaque 300 (iohexol 300 mgI ml⁻¹, Nycomed, Oslo, Norway). 10 mm contiguous slices from the dome of the diaphragm to the pelvic inlet were obtained. All images were reviewed by at least two of the three authors and agreement reached by consensus. The presence and location of any lymph node with a short axis diameter greater than 10 mm, or 8 mm for those in the region of the stomach [4, 5] were recorded. The medical records of all patients were reviewed to determine if they had undergone liver transplantation or had developed cholangiocarcinoma.

Results

Abdominal lymphadenopathy was demonstrated in 26 of the 36 patients (66%). A total of 45 sites of enlarged lymph nodes were identified (Figures 1–3) in the 26 cases of lymphadenopathy. 12 patients had only a single site involved. Five patients had two involved sites and eight patients had multiple involved sites. The different lymph node sites are summarised in Table 1.

Eight patients had orthotopic liver transplantation during the study period. Six of the transplanted cases had abdominal lymphadenopathy on CT. In one case an incidental cholangiocarcinoma was detected in the explanted liver. This patient had no radiological evidence of a cholangiocarcinoma or any enlarged lymph nodes on pre-operative

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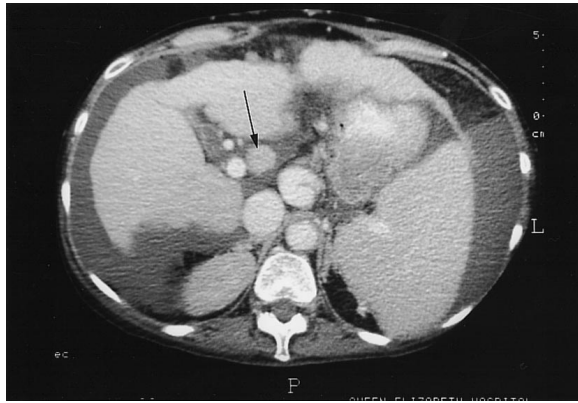


Figure 1. An enlarged lymph node (arrow) at the porta hepatis. There is also marked ascites in a patient with portal hypertension.

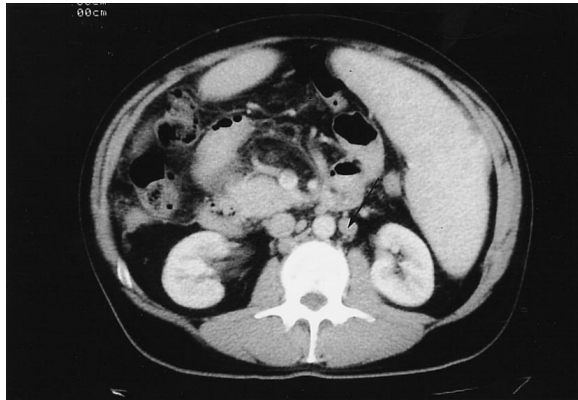


Figure 2. An enlarged paraortic node (arrow).



Figure 3. An enlarged supra pyloric node (arrow).

Table 1. The distribution and number of lymph node groups involved

Lymph node group	Number of patients with group involved
Coeliac axis	14
Paraortic	6
Left gastric	5
Pyloric	5
Porta hepatis	5
Peripancreatic	4
Superior mesenteric	3
Aortocaval	3

CT 4 months prior to transplantation. There was no evidence of malignancy at surgery or on histology in the other seven transplanted cases.

There were eight cases of cholangiocarcinoma in the study. Five of the cholangiocarcinomas were detectable on CT, but only four had significant lymphadenopathy. The remaining three cases of cholangiocarcinoma were not detectable on CT and only one of these cases had lymphadenopathy. Cholangiocarcinoma was diagnosed in one of these following transplant surgery, as previously mentioned, in the second by an ultrasound guided biopsy of the common hepatic duct origin when there were dilated intrahepatic ducts but no identifiable mass, and from endoscopic cytological brushings in the third.

In the five cases where there was lymphadenopathy and a cholangiocarcinoma, the porta hepatis was the involved site in two cases, the coeliac axis was involved twice, and in one case there was paraaortic lymphadenopathy.

None of the remaining 28 patients has developed cholangiocarcinoma to date. The patients have been followed for up to 5 years (mean 2 years 6 months). Eight of the 28 patients have had subsequent imaging of the abdomen, six have had an MRI scan and the remaining two have had repeat CT between 4 and 14 months following the original CT. In all patients there is persisting lymphadenopathy, which does not appear to have altered significantly. One patient previously had a bowel resection for colonic carcinoma and developed liver metastases, in addition to PSC, but there was no associated lymphadenopathy.

There were six patients with associated inflammatory bowel disease and in all there was no radiological or clinical evidence of active bowel disease. Four of these cases had lymphadenopathy involving all the different lymph node groups except the pyloric and left gastric.

Discussion

PSC is a disease of unknown aetiology but with a known association with inflammatory bowel disease and with an increased risk of developing cholangiocarcinoma. The initial diagnosis of PSC is made from the cholangiographic appearances of multiple strictures and dilatations in both the intrahepatic and extrahepatic biliary tree [6]. The patients are usually between 20 and 50 years old and have symptoms of jaundice, pruritis and fatigue. The treatment options for the disease are limited and disease progression means that most patients will develop hepatic failure. Patients with advanced PSC are therefore considered for hepatic transplantation. The survival for these patients is good and is improving; recent studies have shown a survival rate of around 70% at four years [7].

The outlook is considerably worse in cases where transplantation is performed on patients with an undetected cholangiocarcinoma. The survival rate for transplantation for all cases of PSC, including those with undetected cholangiocarcinoma, falls from 85% at 1 year to 27% at 5 years [8]. Cholangiocarcinoma has an adverse effect on survival after transplantation and investigation is therefore required to exclude patients with cholangiocarcinoma from the transplantation programme. The detection of cholangiocarcinoma may be very difficult as PSC can have a very similar appearance at endoscopic cholangiography. Cross-sectional imaging is poor in its detection unless there is a well defined mass [2, 3]. Mass lesions at the porta hepatis can be detected and characterized with contrast enhanced MRI [9] but those cholangiocarcinomas that diffusely infiltrate the bile ducts remain a diagnostic challenge.

We found that enlarged lymph nodes occur in 66% of cases of PSC, their distribution is varied but all the lymph node groups draining the liver and bile duct can be involved. We are not aware of any correlation between disease severity and the degree of lymphadenopathy.

Eight patients in the study were known to have developed cholangiocarcinoma. In three cases there was no radiological evidence of cholangiocarcinoma and two of these three cases had no detectable lymphadenopathy, demonstrating the difficulties in detecting malignant change by cross-sectional imaging. Three cases of cholangiocarcinoma had no significant lymph node enlargement and malignant change may therefore occur without any lymph node enlargement. Conversely, the presence of lymphadenopathy is not associated with the development of a cholangiocarcinoma. No new cases of cholangiocarcinoma developed over the study period in those patients with documented lymphadenopathy. A previous review of patients undergoing transplantation for PSC found an incidence of malignancy of 10.6%, with tumour unrecognized in over half [10]. Hilar lymph nodes were found to be positive for tumour at surgery in only 16.7%. The presence of benign lymph nodes at surgery and biopsy in cases of PSC has previously been reported [11, 12]. In these studies, the lymph nodes have been described on pathological examination as reactive hyperplasia or sinus histiocytosis. Sclerosing cholangitis has been associated with diseases that cause benign lymphadenopathy including angioimmunoblastic lymphadenopathy and histiocytosis X [13, 14]. PSC is also known to co-exist with other conditions that cause widespread abdominal lymphadenopathy such as sarcoidosis [15], lymphoma [16] and autoimmune hepatitis [17]. None of the patients in our study had evidence of any these diseases.

Whatever size criterion is chosen for determining

significant lymphadenopathy, the problem remains that a malignant node may be normal size and a benign node may be enlarged. At present there is no imaging test that can perfectly detect malignant lymph nodes.

PSC is a serious disease with relatively disabling symptoms, and an association with cholangiocarcinoma. The presence of lymphadenopathy neither indicates nor predicts malignant change. Malignancy may not be associated with enlarged lymph nodes. The presence of lymphadenopathy should not be regarded as an exclusion criteria for referral for transplantation.

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