



HAL
open science

Inflammatory Pseudotumours of the Liver: A Spectrum of Presentation and Management Options

P Goldsmith, A Loganathan, M Jacob, N Ahmad, Gj Toogood, Jpa Lodge, Kr Prasad

► **To cite this version:**

P Goldsmith, A Loganathan, M Jacob, N Ahmad, Gj Toogood, et al.. Inflammatory Pseudotumours of the Liver: A Spectrum of Presentation and Management Options. *EJSO - European Journal of Surgical Oncology*, 2009, 35 (12), pp.1295. 10.1016/j.ejso.2009.04.003 . hal-00556298

HAL Id: hal-00556298

<https://hal.science/hal-00556298>

Submitted on 16 Jan 2011

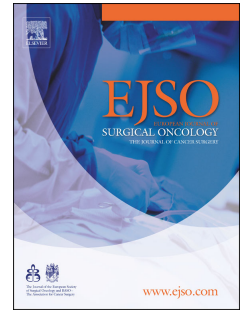
HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Accepted Manuscript

Title: Inflammatory Pseudotumours of the Liver: A Spectrum of Presentation and Management Options

Authors: P Goldsmith, A Loganathan, M Jacob, N Ahmad, GJ Toogood, JPA Lodge, KR Prasad



PII: S0748-7983(09)00122-X

DOI: [10.1016/j.ejso.2009.04.003](https://doi.org/10.1016/j.ejso.2009.04.003)

Reference: YEJSO 2825

To appear in: *European Journal of Surgical Oncology*

Received Date: 13 December 2008

Revised Date: 23 March 2009

Accepted Date: 2 April 2009

Please cite this article as: Goldsmith P, Loganathan A, Jacob M, Ahmad N, Toogood GJ, Lodge JPA, Prasad KR. Inflammatory Pseudotumours of the Liver: A Spectrum of Presentation and Management Options, *European Journal of Surgical Oncology* (2009), doi: 10.1016/j.ejso.2009.04.003

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Original Article

Inflammatory Pseudotumours of the Liver: A Spectrum of Presentation and Management Options

P Goldsmith, A Loganathan, M Jacob, N Ahmad, GJ Toogood, JPA

Lodge, KR Prasad

Department of Hepatobiliary & Transplant Surgery, St James's University Hospital,
Beckett Street, Leeds, LS9 7TF

Correspondence author:

Mr K R Prasad

Consultant Hepatobiliary & Transplant Surgeon

St James University Hospital

Beckett Street

Leeds

LS9 7TF

Telephone: (+44) 113 206 5921

Fax: (+44) 113 244 8182

Email: raj.prasad@leedsth.nhs.uk

Abstract**Purpose**

To review the current management options in inflammatory pseudotumours via analysis of ten cases from this unit the largest experience of this pathology in a Western series. To assess the medical and operative options available for this condition and the varying outcomes and the lessons learned in this unit over the time period.

Results

Data from the ten cases were analysed and a comprehensive review of the published literature to date has detailed 128 case reports with 215 cases of inflammatory pseudotumour of the liver. Data analysed included patient demographics, diagnostic modalities, details of treatment and eventual outcome. The data was tabulated using an Excel spreadsheet (Microsoft ® Excel 2004 for Mac 2004 .Version 11.0). Categorical variables were compared using Pearson's χ^2 test and a p values <0.05 were defined as statistically significant. Statistical analysis was performed using SPSS for Windows (Version 9.0, SPSS Inc., Chicago, IL).

Conclusion

Emphasis is placed on a preferred medical management initially for this tumour with a good prognosis coupled with regular follow up. There may be a need for surgical resection cases where diagnosis is unclear or the patient is not responding to medical treatment with progression of disease or symptoms.

Keywords

Inflammatory pseudotumour, cholangiocarcinoma, management options, jaundice, steroids

Introduction

Inflammatory Pseudotumour (IPT) of the liver is a benign condition of unknown aetiology. IPTs are rare well circumscribed benign tumour-like masses with similar morphological characteristics, occurring throughout the body with the most common site being the lung. Other documented sites include the central nervous system, major salivary glands, kidney, liver, omentum, ovary, larynx, bladder, breast, pancreas, spleen, lymph nodes, skin, soft tissues and the orbit. Inflammatory pseudotumours have also been called inflammatory myofibroblastic tumour, plasma cell granuloma, histiocytoma and fibroxanthoma. Someren histologically classified inflammatory pseudotumours into three groups, namely (1) xanthogranuloma-type pseudotumours, (2) plasma cell granuloma-type pseudotumours and (3) sclerosing pseudotumours^{1,2}.

It has been reported to be rare, however recent reports suggest it may be more common than previously thought. One retrospective review of 403 patients who underwent liver resection for focal liver lesions demonstrated an incidence of IPT of one percent³.

Management remains controversial. IPT involving the bile ducts may mimic cholangiocarcinoma (CC). If the diagnosis can be established pre-operatively, extensive and radical surgery can be avoided or at best less radical, thus reducing the morbidity and mortality. There are however a number of authors who advocate a radical approach with hepatic resection⁴⁻⁶. This institute reviews the literature and presents its cases on this condition and how management has changed from previous lessons learned.

Patients and Methods

A systematic search of Medline, Embase and Cochrane to date was undertaken using the keywords “Liver”, “Pseudotumour”. This produced 185 papers from Medline, 115 papers from Embase and no papers from Cochrane. There was an overlap of 79 papers between Medline and Embase. This produced a total of 221 papers. 93 papers were excluded as they did not relate to IPT of the liver, no case reports were presented, or if an English translation of the report was not available. The paper also presents ten cases in our own unit over a period of fourteen years, with an annual incidence of less than one percent.

Data was tabulated using Excel (Microsoft ® Excel 2004 for Mac 2004 .Version 11.0). Categorical variables were compared using Pearson’s χ^2 test and a p values <0.05 were defined as statistically significant. Statistical analysis was performed using SPSS for Windows (Version 9.0, SPSS Inc., Chicago, IL).

Cases on this unit

Table 1

Case	Age	Sex	Imaging	Surgery	Outcome
1	57	M	CT- mass porta hepatis, USS – dilated ducts	Right hepatic trisectionectomy	Portal vein thrombosis, sepsis -died
2	65	F	CT + MRI mass in hilar region, narrowing of CHD and CBD	Right hepatic trisectionectomy	Massive GI haemorrhage, MOF - died
3	62	M	CT- tumour of CHD and at confluence	Right hemi-hepatectomy + Whipples	Renal failure, sepsis, refusal of further treatment - died
4	7	M	MRI- Mass hilum of the liver extended into segments 4 and 8	Left trisectionectomy	Portal vein thrombosis – liver transplant. Alive 5years post-operation
5	73	M	CT – mass in hilum compressing PV and IVC	Attempted right hepatectomy – no resection as involvement of right and left hepatic arteries and PV	Oral steroids – asymptomatic and disease free CT at 3yrs
6	54	M	MRI – mass in hilum + left lobar structures	None	Maintenance steroids, disease free at 4 years
7	65	F	USS – intrahepatic duct dilatation MRCP – CHD stricture	Right hepatectomy	Disease free at 4 years
8	70	F	MRCP - dilatation of peripheral sectral ducts, abnormal tissue involving peri-portal tissues	None	URSO Symptom free at 3 years
9	47	F	USS- dilated ducts CT – mass involving porta	None	URSO and oral steroids – asymptomatic at 6 months. Stable CT appearances
10	24	F	USS – liver abscesses	None	Initial improvement with stroids, methotrexate + azathioprine, then regression. Ongoing treatment with Interleukin treatment

PC – Presenting complaint, LFT- Liver function tests, Obstruct – Obstructive,

USS- Ultrasound, ERCP – Endoscopic Retrograde Cholangiopancreatography

CHD – Common hepatic duct, CBD - Common bile duct, MRI – Magnetic resonance imaging, GI – Gastrointestinal, MOF – Multi-organ failure, PV – Portal vein
IVC – Inferior vena cava, RUQ – Right upper quadrant, URSO – Ursodeoxycholic acid

Results

One hundred and twenty eight reports were published from 1975 to date, with a total of 215 patients with IPT of the liver. Median age of the patients was 47 years (range 4 months to 85 years). 129 were male (gender not stated in 12 cases).

Symptoms

One hundred and ninety one of two hundred and ten patients were symptomatic at presentation (No data for 5 cases). The commonest presenting symptoms were fever (49%), abdominal pain (48%) and fatigue/weight loss (37%). Other symptoms included gastrointestinal upset, jaundice, weakness and myalgia. A small percentage were completely asymptomatic

Blood Tests

The most common inflammatory markers measured were CRP, erythrocyte sedimentation rate (ESR) and WCC. 37 % were reported to have either raised WCC or raised ESR and CRP, while 15% had deranged LFT's.

Diagnostic liver biopsy

Seventy-four patients underwent a diagnostic liver biopsy. Patients that underwent a liver biopsy were more likely to be managed conservatively as a histological diagnosis was available. Consequently almost three quarters of the patients who had a

diagnostic liver biopsy were managed conservatively in comparison to a quarter patients who had a liver resection ($p < 0.001$, χ^2).

Management

Data was available for 188 out of the 215 cases. 106 out of 188 cases had a liver resection versus 76 of 188 cases managed medically. Five patients were initially managed conservatively then subsequently underwent a liver resection. One patient underwent liver transplantation.

Of the 106 patients who underwent a liver resection, operative data was available in 91 patients. The commonest operation was a hemi-hepatectomy in 68% of cases followed by segmentectomy in twenty-one percent. Of the remaining there were 7 wedge resections, 1 trisectionectomy and 4 others who underwent combinations of procedures .

Of the 76 patients managed medically, details were available in 53 patients. Almost half were treated with antibiotics, A third received no treatment and 15% received steroids. There were 5 patients in whom initial medical management failed.

Outcomes

Outcomes were compared between patients who underwent liver resection and those that underwent medical management. Data was available in 75 of the 106 patients who underwent a resection. The average follow up was 31 months. Of these, 65 patients were reported to have a good outcome without major complications. 4 patients were reported to have developed major complications with an eventual good outcome. Complications reported included sepsis, acute renal failure, myocardial

infarction, portal vein stenosis, bile leak, deep venous thrombosis and hepatic artery thrombosis. There were 6 reported deaths

Outcome data was available for 69 of the 76 patients managed medically with an average follow up of 14 months. 60 patients were reported to have a good outcome without major complications. There were 5 deaths related to the disease process and 3 unrelated deaths. In addition, 40 patients were reported to have undergone spontaneous resolution or regression of the IPT.

Comparison of mortality rates between patients managed medically and those who underwent liver resection did not demonstrate any significant difference. ($p > 0.5$, χ^2 test).

Discussion

IPT was first described in 1953⁷ as circumscribed benign tumour-like masses with areas of haemorrhage and necrosis, occurring throughout the body with the commonest site being the lung.

Aetiology

The exact aetiology and pathogenesis is unclear. It is generally regarded as a non-neoplastic reactive/inflammatory condition. Pathologically, its reactive nature is supported by the polyclonality of the infiltrating plasma cells and lymphocytes. Causes postulated include an infective aetiology based on symptoms and findings of elevated acute phase proteins. Microorganisms from the gut gain access to the hepatic parenchyma via the portal vein and subsequently elicit an inflammatory reaction. Bacteria found include *Bacteroides caccae* and mixed bacteria/*Actinomyces*⁸, *Klebsiella*⁹, *Escherichia coli*¹⁰, Gram-positive cocci¹¹ and β -haemolytic streptococcus¹². This may explain why in some cases resolution of IPT occurs following treatment with antibiotics. Some suggest an autoimmune aetiology such as IgG4 sclerosing cholangitis¹³. IgG4-related sclerosing disease is a systemic disease characterised by extensive IgG4-positive plasma cells and T-lymphocyte infiltration. Histological findings are similar to that found in autoimmune pancreatitis. In these cases patients often respond well to steroids¹⁴.

Incidence

Published data suggests that IPT is being recognized with increased frequency predominantly in the Far East¹⁵ and this paper has the largest number of patients from

a Western series. A study by Torzilli *et al* evaluated outcomes of 403 consecutive patients undergoing liver resection for a focal liver lesion³. Patients with IPT accounted for 20 % of the patients where a pre-operative diagnosis proved incorrect and 33% of cases wrongly assigned to a surgical procedure.

History & Histology

IPT tends to affect younger patients with a median age of 47 years (Median age of this case series 61 years). A majority are symptomatic at presentation, with fever abdominal pain and weight loss the most common. Where reported a third of patients have elevated serum inflammatory markers and some have deranged LFT's. In our series all were symptomatic. These clinical findings and associated rise in inflammatory markers may point towards a diagnosis of liver abscess. However differentiation can be made on histology, IPT is characterised by hyalinized collagenous tissue with chronic inflammatory infiltrates whilst a liver abscess will reveal liquefactive necrosis with acute inflammatory cells¹.

Radiology

There is still some doubt as to the specificity of CT and MRI in differentiating between IPT and other focal liver lesions. Sakai *et al*¹⁶ reported on a series of five patients with IPT. CT appearances were of low-density lesions with irregular delayed enhancement as also described by other authors^{4,12,16,18,19}. Seki *et al*²⁰, demonstrated peripheral enhancement of IPT in the early phases of dynamic CT in three patients. This however, was not specific to IPT. Enhancement may occur when a CT is performed with contrast but this is variable, between none at all to heterogeneous or homogenous enhancement¹⁵. IPT sometimes mimics hypovascular tumours secondary

to the abundant fibrosis and show a delayed enhancement on dynamic CT, similar appearances to those patients with metastatic liver deposits and CC¹⁹. MRI again reveals varying images, appearing hypointense on T1 weighted images and hyperintense on T2³.

Outcomes

Four cases presented in this study demonstrate a successful outcome when managed medically and illustrate how the correct diagnosis was made using pre-operative biopsy and radiological evidence. However in six of the cases this was not possible because of the malignant looking nature of the MRI , a difficulty when managing this condition and subsequently underwent surgical procedures.

In our series the first 3 cases died as diagnosis prior to surgical intervention was thought to be that of CC and the patients went on to require extensive resections

The next seven cases were all managed with added experience within the unit from previous lessons learned. Case 10 has shown further evolution in the management of this condition, where input from the surgical team has been minimal.

Based on the findings of the review, an initial medical approach should be considered for IPT of the liver, when histology and/or radiology point to IPT. Clinicians should be alert that in spite of its rarity, IPT of the bile duct remains a possibility in patients presenting with hilar mass and obstructive jaundice. In terms of medical treatment options there was no evidence of any difference in overall outcome between patients receiving antibiotics, steroids or no treatment. There may though be a role for steroids in symptom control.

There appears however, to be a subgroup of patients in whom IPT is more aggressive where conservative treatment may be ineffective, the exact reasoning behind this is

unknown, but could be related to the position of the IPT and the external compression on adjacent structures. These patients may experience progressive symptomatology with failure of tumour regression or even enlargement of the IPT. From the evidence available surgical resection may provide the best possible long-term outcome in this subgroup.

Acknowledgments

Dr A Baird for reviewing the histology. Mr KR Wedgewood for allowing access to information regarding patient information.

Conflict of interest

The authors state that they have no conflict of interest.

References

1. Fukuya T, Honda H, Matsumata T, Kawanami T, Shimoda Y, Muranka T Hayashi T, Maeda T. Diagnosis of inflammatory pseudotumour of the liver: value of CT. *AJR Am J Roentgenol* 1994; **163**(5):1087-1091.
2. Someren A. "Inflammatory pseudotumour" of liver with occlusive phlebitis: report of a case in child and review of the literature. *AM J Clin Pathol* 1978;69(2): 176-181.
3. Torzilli G, Inoue K, Midorikawa Y, Hui AM, Takayama T, Makuuchi M. Inflammatory pseudotumours of the liver: prevalence and clinical impact in surgical patients. *Hepatogastroenterology* 2001; **48**(40):1118-1123.
4. Materne R. Inflammatory pseudotumour of the liver: MRI with mangafodipir trisodium. *Journal of Computer Assisted Tomography* 1998; **22**(1):82-84.
5. Li GH, Li JQ, Lin YZ. Inflammatory pseudotumour of the liver. *J Surg Oncol* 1989; **42**(4):244-248.
6. Kaneko K, Ando H, Watanabe Y, Seo T, Nagino M, Kamiya J, Nimura Y. Aggressive preoperative management and extended surgery for inflammatory pseudotumour involving the hepatic hilum in a child. *Surgery* 2001; **129**(6):757-760.
7. Pack GT, Baker HW. Total right hepatic lobectomy; report of a case. *Ann Surg* 1953; **138**(2):253-258.
8. White JE, Chase CW, Kelley JE, Brock WB, Clark MO. Inflammatory pseudotumour of the liver associated with extrahepatic infection. *South Med J*. 1997; **90**: 23–9.
9. Kafeel G, Telesinghe PU. Inflammatory pseudotumour of the liver. *J.Clin. Pathol* 1997; **50**: 352–3.

10. Standiford SB, Sobel H, Dasmahapatra KS. Inflammatory pseudotumour of the liver. *J Sur. Oncol* 1989; **40**: 283–7.
11. Lupovitch A, Chen R, Mishra S. Inflammatory pseudotumour of the liver. Report of the fine needle aspiration cytologic findings in a case initially misdiagnosed as malignant. *Acta Cytol* 1989; **33**: 259–62.
12. Lim JH, Lee JH. Inflammatory pseudotumour of the liver. Ultrasound and CT features. *Clin. Imaging* 1995; **19**: 43–6
13. Anthony PP. Inflammatory pseudotumour (plasma cell granuloma) of the lung, liver and other organs. *Histopathology* 1993; **23**(5):501-503.
14. Kamisawa T, Okamoto A. IgG4-related sclerosing disease. *World J Gastroenterol*. 2008 Jul 7; **14**(25):3948-55.
15. Levy S, Sauvanet A, Diebold M, Marcus C, Da Costa N, Thiéfin G. Spontaneous regression of an inflammatory pseudotumour of the liver presenting as an obstructing malignant biliary tumour. *Gastrointest Endosc* 2001; **53**:371-4.
16. Horiuchi R. Inflammatory pseudotumour of the liver. Clinicopathologic study and review of the literature. *Cancer* 1990; **65**(7):1583-1590.
17. Sakai T, Shiraki K, Yamamoto N, Kawakita T, Ohmori S, Itoh I Nakano T, Yasuda M, Yamakado K, Takeda K, Yagi S, Yamagiwa K, Yokoi H, Noguchi T, Uemoto S. Diagnosis of inflammatory pseudotumour of the liver. *Int J Mol Med* 2002; **10**(3):281-285.
18. Ishida H, Tatsuta M, Furukawa H, Ohta H, Hashimoto K, Hayashi N Morimoto O, Ikeda M, Miya A, Masutani S, Kawasaki T, Satomi T, Yoshioka H, Hanai J. Multiple inflammatory pseudotumours mimicking liver metastasis from the colon: report of a case. *Surg Today* 2000; **30**(6):530-533.

19. Yamaguchi J, Sakamoto Y, Sano T, Shimada K, Kosuge T. Spontaneous Regression of Inflammatory Pseudotumour of the Liver: Report of Three Cases. *Surg Today* 2007; **37**:525–529
20. Seki S, Kitada T, Sakaguchi H, Iwai S, Hirohashi K, Higaki I, Nakamura K, Wakasa K, Kinoshita H. A clinicopathological study of inflammatory pseudotumours of the liver with special reference to vessels. *Hepatogastroenterology* 2004; **51**(58):1140-1143.

ACCEPTED MANUSCRIPT