

Ectopic liver tissue (choristoma) on the gallbladder: A comprehensive literature review

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Abstract

BACKGROUND

Liver tissue situated outside the liver with a hepatic connection is usually called an accessory liver, and that without a connection to the mother liver, is called ectopic liver tissue.

AIM

To identify studies in the literature on ectopic liver tissue located on the gallbladder surface or mesentery.

METHODS

We present two patients and review published articles on ectopic liver tissue located on the gallbladder surface accessed *via* PubMed, MEDLINE, Google Scholar, and Google databases. Keywords used included accessory liver lobe, aberrant liver tissue, ectopic liver tissue, ectopic liver nodule, heterotopic liver tissue, hepatic choristoma, heterotopic liver tissue on the gallbladder, and ectopic liver tissue on the gallbladder. The search included articles published before June 2020 with no language restriction. Letters to the editor, case reports, review articles, original articles, and meeting presentations were included in the search. Articles or abstracts containing adequate information on age, sex, history of liver disease, preliminary diagnosis, radiologic tools, lesion size, surgical indication, surgical procedure, and histopathological features of ectopic liver tissue were included in the study.

RESULTS

A total of 72 articles involving 91 cases of ectopic liver tissue located on the

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gallbladder surface or mesentery were analyzed. Of these 91 patients, 62 were female and 25 were male (no gender available for 4 patients), and the age range was 5 d to 91 years. Forty-nine patients underwent surgery for chronic cholecystitis or cholelithiasis, and 14 patients underwent surgery for acute cholecystitis. The remaining 28 patients underwent laparotomy for other reasons. Cholecystectomy was laparoscopic in 69 patients and open in 11 patients. The remaining 19 patients underwent various other surgical procedures such as autopsy, liver transplantation, living donor hepatectomy, Whipple procedure, and liver segment V resection. Histopathologically, hepatocellular carcinoma was detected in the ectopic liver tissue of one patient.

CONCLUSION

Ectopic liver tissue is a rare developmental anomaly which is usually detected incidentally. Although most studies suggest that ectopic liver located outside the gallbladder has a high risk of hepatocellular carcinoma, this is not reflected in statistical analysis.

Key Words: Liver; Gallbladder; Ectopic liver tissue; Hepatic choristoma; Histopathological features; Hepatocellular carcinoma

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Core Tip: Ectopic liver tissue is a rare developmental anomaly usually detected incidentally. While it is often asymptomatic, there is a risk of malignant transformation and other complications such as bleeding and torsion. In this review, we present two cases of ectopic liver tissue located on the gallbladder surface and review published studies on ectopic liver tissue located on the gallbladder surface accessed *via* the PubMed, MEDLINE, Google Scholar, and Google databases. Although most studies suggest that ectopic liver located outside the gallbladder has a higher risk of hepatocellular carcinoma, this is not reflected in the statistical analysis.

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INTRODUCTION

Ectopic liver tissue is a rare developmental anomaly in which the liver tissue is situated outside the liver. It is usually asymptomatic and is discovered incidentally during surgery or autopsy, but there are potential complications. Torsion, malignant transformation, compression of adjacent organs, and intra-peritoneal bleeding are among the possible complications^[1-72].

Liver tissue situated outside the liver with a hepatic connection is usually called an accessory liver, and that without a connection to the main liver, is called ectopic liver tissue. Accessory liver and ectopic liver tissues were first described by Morgagni in 1767 and by Corsy in 1922, respectively^[1,20,36,72]. Subsequent reports showed that the accessory liver lobe most commonly occurs in the gallbladder wall, under the surface of the liver, at the gastrohepatic ligament, umbilical cord, adrenal glands, pancreas, pylorus, diaphragm, and the splenic capsule if a portion of the pars hepatica is displaced^[28,31,34,44,36]. The histological architecture of the ectopic tissue resembles normal liver, although it does not have a complete functional architecture, is metabolically handicapped, and is more prone to carcinogenesis^[2,6,36,40,62,72]. In this article, we report two cases of ectopic liver tissue and review the literature for articles published on ectopic liver tissue on the gallbladder surface or gallbladder mesentery^[1-72]. The clinical and pathological characteristics are described in addition to an analysis of the possible clinical implications including malignant transformation.

MATERIALS AND METHODS

The primary aim of this study was to review the articles published in the literature on ectopic liver tissue on the gallbladder surface or gallbladder mesentery. To achieve this aim, a literature search was conducted on PubMed, MEDLINE, Google Scholar, and Google databases using the following keywords: Accessory liver lobe, aberrant liver tissue, ectopic liver tissue, ectopic liver nodule, heterotopic liver tissue, hepatic choristoma, liver, gallbladder, heterotopic liver tissue on the gallbladder, ectopic liver tissue on the gallbladder, accessory liver lobe on the gallbladder, accessory liver tissue on the gallbladder alone or in different combinations. Language restrictions were not applied in this literature review. All documents published on ectopic liver tissue related to the gallbladder before June 2020 were reviewed. Patients with ectopic liver tissue found in the gallbladder lumen incidentally were excluded from the study. As a result, articles without an accessible full-text version, those without adequate information in the abstract, and those that did not include comprehensive information compared to other studies were excluded. The following information was collected: Publication year, country, type of article available (full-text, abstract), age, sex, clinical presentation, diagnostic modalities, indication for surgery, surgical approach, postoperative complications, and histopathologic features of specimens. The details of the literature search are provided in [Table 1](#). The secondary aim of this study was to present two cases of ectopic liver tissue attached to the gallbladder wall that was discovered during living donor hepatectomy and recipient hepatectomy.

RESULTS

Review of the literature

Using the PubMed, MEDLINE, Google Scholar, and Google databases, 72 articles involving 91 patients published between January 1925 and August 2020 were compatible with the above-mentioned criteria. The four countries with the highest numbers of published articles were Turkey ($n = 13$), the United States ($n = 12$), India ($n = 8$), and Japan ($n = 7$). Sixty-two articles were written in English, three in Turkish, two in Japanese, one in French, one in German, one in Chinese, one in Russian, and one in Spanish. The full text was obtained for 69 of the 72 articles, whereas only abstracts were available for three articles. Of the 91 patients, 62 were female and 25 male; no gender data were available for the remaining four patients. The age of these 87 patients ranged from five days to 91 years; this information was unavailable for the remaining four patients.

Eleven patients had a history of various liver diseases, while 12 patients had no liver disease. No data could be obtained on whether the remaining 68 patients had any liver disease. Forty-nine patients underwent surgery for chronic cholecystitis and/or cholelithiasis, while 14 patients underwent surgery for a presumed diagnosis of acute cholecystitis. The remaining 28 patients underwent laparotomy for unrelated reasons. Sixty-one patients underwent laparoscopic cholecystectomy and 11 underwent open cholecystectomy. The remaining 19 patients underwent cholecystectomy and various surgical procedures such as autopsy, liver transplantation, living donor hepatectomy, Whipple procedure, and liver segment V resection. Demographic, clinical, and histopathological characteristics of the 91 patients with ectopic liver tissue are summarized in [Tables 1 and 2](#).

Case presentations

Case 1: A 25-year-old woman [body mass index (BMI): 27 kg/m², A Rh (+), graft volume: 600 cc, remnant liver: 29%] was admitted to our liver transplant institute to donate a part of her liver to her 33-year-old sister with cryptogenic liver cirrhosis. Radiological and biochemical examinations were completed using the preoperative donor evaluation algorithm available in our liver transplant institute. The donor candidate underwent laparotomy using a modified Makuuchi incision (reversed L-shaped incision). The exploration showed ectopic liver tissue approximately 15 mm × 5 mm in size, located in the gallbladder corpus, and had no association with the liver ([Figure 1](#)). Cholecystectomy was performed to include the ectopic liver tissue, and cholangiography was carried out *via* the cystic duct, and the biliary tract anatomy was found to be normal (Choi Type I). Right lobe donor hepatectomy was performed as previously described in our transplant institute. The donor was discharged without any postoperative complications. Macroscopically, the gallbladder specimen was 70 mm in length, 50 mm in diameter, and 3 mm in wall thickness. Histopathologically,

Table 1 Summary of the demographic and clinicopathological characteristics of 91 patients published in the literature between 1925 and 2020

Ref.	Year	Country	Language	Age	Sex	History of liver disease	Preliminary diagnosis	Radiologic tools
Kachi et al ^[1]	2020	Lebanon	English	44	F	No	CC	US
				62	F	No	CC	NA
Avdaj et al ^[2]	2020	Kosovo	English	47	F	No	CC	US
Baral et al ^[3]	2019	United States	English	67	F	No	CC	US
Yuksel et al ^[4]	2019	Turkey	English	34	F	NA	CC	US
Mannan et al ^[5]	2019	S. Arabia	English	38	F	NA	AC	US
Isa et al ^[6]	2019	Bahrain	English	42	F	No	CC	US
Pandit et al ^[7]	2019	Nepal	English	30	F	NA	Biliary pancreatitis	US + MRCP
Granek et al ^[8]	2019	Australia	English	36	M	NA	AC	US
Lodha et al ^[9]	2018	India	English	50	M	NA	Kidney tumor	CT
Topcu et al ^[10]	2018	Turkey	English	64	F	NA	AC	US
				70	F	NA	Icterus	US + CT + MR
Burke et al ^[11]	2018	Ireland	English	30	F	NA	CC	US
Greenberg et al ^[12]	2018	United States	English	52	F	FLD	AP	US + CT
Termos et al ^[13]	2017	Kuwait	English	73	F	NA	GBC	US + CT
Weber-Alvarez et al ^[14]	2017	Mexico	English	37	F	NA	AC	US
Galimov et al ^[15]	2017	Russia	Russian	70	M	NA	AC	US
Handra-Luca et al ^[16]	2016	France	English	68	F	NA	CC	US
				56	F	NA	CC	US
Mani et al ^[17]	2016	United States	English	56	M	FLD	AC	CT
Ito et al ^[18]	2016	Japan	English	59	F	NA	CC	MR + CT
Leena et al ^[19]	2016	India	English	25	M	NA	Cadaver	Autopsy
Karaca et al ^[20]	2016	Turkey	English	43	F	NA	CC	US
Jaboury et al ^[21]	2016	Australia	English	22	F	NA	CC	NA
Yahya et al ^[22]	2016	Libya	English	35	F	NA	CC	US
				45	F	NA	CC	US
				45	F	NA	CC	NA
				20	F	NA	Penetrating injury	NA
Aslan et al ^[23]	2016	Turkey	English	49	F	NA	CC	US
Longjam et al ^[24]	2016	India	English	42	F	NA	CC	US
Kostov et al ^[25]	2016	Bulgaria	English	49	M	RCLM	RCLM	NA
Bal et al ^[26]	2015	Turkey	English	51	F	NA	CC	US
Smyth et al ^[27]	2015	Australia	English	77	F	NA	CC	US
Abhilash et al ^[28]	2015	India	English	45	F	NA	AC	US
Hussein et al ^[29]	2015	Lebanon	English	49	F	NA	AC	CT
Yankol et al ^[30]	2015	Turkey	English	30	M	No	Living donor	US + CT + MRCP
Arslan et al ^[31]	2014	Turkey	English	59	F	NA	CC	US
Pulle et al ^[32]	2014	India	English	43	F	NA	CC	US
Terakawa et al ^[33]	2014	Japan	Japanese	33	F	NA	CC	US + MRCP

Sirasanagandla <i>et al</i> ^[34]	2013	India	English	62	M	NA	Cadaver	NA
Hassan <i>et al</i> ^[35]	2013	India	English	32	F	NA	CC	US
Martinez <i>et al</i> ^[36]	2013	Brazil	English	37	F	NA	AC	US
Ozturk <i>et al</i> ^[37]	2013	Turkey	Turkish	35	F	No	CC	US
Yajima <i>et al</i> ^[38]	2013	Japan	Japanese	73	F	NA	CC	US + CT
Khan <i>et al</i> ^[39]	2013	India	English	32	F	NA	CC	NA
Karaman <i>et al</i> ^[40]	2012	Turkey	English	63	M	NA	CC	US
Patel <i>et al</i> ^[41]	2012	United Kingdom	English	21	F	NA	CC	US
Sozen <i>et al</i> ^[42]	2012	Turkey	Turkish	40	F	NA	CC	US
Catani <i>et al</i> ^[43]	2011	Italy	English	72	F	NA	AC	US
				83	F	No	CC	US
Dettmer <i>et al</i> ^[44]	2011	Switzerland	English	91	F	NA	AC	CT
Nagar <i>et al</i> ^[45]	2011	United States	English	25	F	NA	AP + Cystic mass	US + CT + MRCP
Ates <i>et al</i> ^[46]	2010	Turkey	Turkish	64	F	NA	AC	NA
				49	M	NA	CC	US
Triantafyllidis <i>et al</i> ^[47]	2009	Greece	English	56	F	NA	CC	US
Guzman <i>et al</i> ^[48]	2009	Mexico	Spanish	36	M	NA	CC	US
Kyeong <i>et al</i> ^[49]	2008	S. Korea	English	66	F	NA	CC	CT
Koh <i>et al</i> ^[50]	2007	Australia	English	60	F	NA	AC	NA
Malhas <i>et al</i> ^[51]	2007	United Kingdom	English	42	M	FLD	CC	US
				39	F	NA	CC	US
Soto <i>et al</i> ^[52]	2007	United States	English	32	F	NA	CC	US
Beltran <i>et al</i> ^[53]	2007	Chile	English	47	M	NA	CC	US
				33	F	NA	CC	US
				27	M	NA	Gastric cancer	US + CT
				35	M	NA	Pancreatic pseudocyst	US + CT
Wang <i>et al</i> ^[54]	2006	China	Chinese	38	M	NA	Gallbladder polyps	US
Ikeda <i>et al</i> ^[55]	2006	Japan	English	70	M	No	HCC + Cirr	US + CT
Ngowe <i>et al</i> ^[56]	2006	Cameroon	French	46	F	NA	CC	US
Lundy <i>et al</i> ^[57]	2005	United States	English	38	F	FLD	Liver tumor	US + CT
Leone <i>et al</i> ^[58]	2004	Italy	English	54	F	NO	GBC	US + CT
Griniatsos <i>et al</i> ^[59]	2002	United Kingdom	English	39	F	NA	CC	US
				49	M	NA	CC	US
Acar <i>et al</i> ^[60]	2002	Turkey	English	55	F	NA	CC	US
Sakarya <i>et al</i> ^[61]	2002	Turkey	English	NA	NA	NA	NA	NA
Arakawa <i>et al</i> ^[62]	1999	Japan	English	48	M	ALD	ALD	Autopsy
Hamdani <i>et al</i> ^[63]	1994	United States	English	49	M	Cirr	PSC	US + CT
Boyle <i>et al</i> ^[64]	1992	United States	English	44	F	No	AC	US
Tejada <i>et al</i> ^[65]	1989	United States	English	43	M	NA	CC + HS	US
Watanabe <i>et al</i> ^[66]	1989	Japan	English	37	M	CLL	CLL	CT
				54	M	Cirr	ALD	Laparoscopy
				64	F	Cirr	Cirr	CT

				71	F	Cirr	Cirr	Laparoscopy
Fellbaum et al ^[67]	1987	Austria	German	34	F	NA	CC	NA
Natori et al ^[68]	1986	Japan	English	56	F	NA	CC	CT
Ashby et al ^[69]	1969	United Kingdom	English	42	M	NA	Duodenal ulcer	NA
BASSIS et al ^[70]	1956	United States	English	NA	NA	NA	CC	NA
				NA	NA	NA	CC	NA
				NA	NA	NA	CC	NA
				5d	M	NA	Cadaver	No
Thorsness et al ^[71]	1941	United States	English	63	F	NA	Cadaver	No
Cullen et al ^[72]	1925	United States	English	33	F	No	Jaundice	NA

CC: Chronic cholecystitis ± cholelithiasis; US: Ultrasound; NA: Non-available; AC: Acute cholecystitis; MRCP: Magnetic resonance cholangiopancreatography; CT: Computed tomography; MR: Magnetic resonance; FLD: Fatty liver disease; GBC: Gallbladder cancer; RCLM: Rectum cancer liver metastasis; ALD: Alcoholic liver disease; PSC: Primary sclerosing cholangitis; Cirr: Cirrhosis; HS: Hereditary spherocytosis; CLL: Cystic liver lesion; AP: Abdominal pain.

the tissue (15 mm × 3 mm × 2 mm) located in the gallbladder corpus was ectopic liver tissue (Figure 2A and B).

Case 2: A 45-year-old female patient with cryptogenic liver cirrhosis [BMI: 37.2 kg/m², A Rh (-), MELD-Na: 16, Child: 10/C] presented to our liver transplant institute for live-donor liver transplantation. Both the liver recipient and the 40-year-old male [BMI: 25.5 kg/m², A Rh (+), graft volume: 940 cc, remnant liver: 31%] living liver donor candidate were evaluated according to an algorithm consisting of radiological and biochemical analyses. Laparotomy was performed using a reversed L-shaped incision. During exploration, it was revealed that the liver had a macronodular appearance and a relatively small size. Ectopic liver tissue associated with the gallbladder mesentery was seen on the corpus of the gallbladder without an association with the liver. The ectopic liver tissue showed a cirrhotic appearance similar to the main liver tissue (Figure 3A and B). The gallbladder was removed *en-bloc* with the liver without recipient cholecystectomy as described previously (recipient hepatectomy). The recipient was discharged on postoperative day 15 without complications. The ectopic liver tissue, located in the gallbladder was also seen in the retrospective examinations of computed tomography sections (Figure 4).

DISCUSSION

Ectopic liver tissue is a rare developmental anomaly in which the liver tissue is situated outside the liver^[9,19,28,60]. Four main types are described in the literature: Ectopic liver, which is not connected to the mother liver, and is usually attached to the gallbladder or intra-abdominal ligaments; microscopic ectopic liver found in the gallbladder wall; a large accessory liver lobe attached to the mother liver by a stalk; and a small accessory liver lobe, 10-30 g, attached to the mother liver^[73]. However, this classification may not apply to all cases^[60].

The real incidence of ectopic liver tissue attached to the gallbladder wall is difficult to assess; most cases are asymptomatic and are diagnosed at laparotomy, laparoscopy, or during an autopsy^[1,2,14]. However, the incidence of ectopic liver tissue has been reported to range from 0.24% to 0.47%^[2,31]. A review of 5500 autopsies showed that only 0.05% had ectopic liver tissue in which only three cases were attached to the gallbladder wall^[74]. A review of 1060 laparoscopic procedures found ectopic liver tissue attached to the gallbladder wall in three patients (0.28%)^[10]. To date, we detected only two (0.04%) patients with ectopic liver tissue among 4500 patients who underwent living donor hepatectomy or recipient hepatectomy.

Different theories have been proposed to explain the development of an ectopic liver at various sites: Development of an accessory lobe of the liver with atrophy or regression of the original connection to the main liver; migration or displacement of a portion of the pars hepatica to other sites, entrapment of a nest of cells in the region of the foregut following closure of the diaphragm or umbilical ring and trapping of

Table 2 Summary of the surgical and histopathological characteristics of 91 patients published in the literature between 1925 and 2020

Ref.	Lesion sizes (mm)	Surgical indication	Surgical procedure	Histopathological findings of ELT	Histopathological findings of GB
Kachi <i>et al</i> ^[1] , 2020	10	CC	LC	ELT	NA
	5	CC	LC	ELT	NA
Avdaj <i>et al</i> ^[2] , 2020	NA	CC	LC	ELT	NA
Baral <i>et al</i> ^[3] , 2019	30	CC	LC	ELT	NA
Yuksel <i>et al</i> ^[4] , 2019	17	CC	LC	ELT	CC
Mannan <i>et al</i> ^[5] , 2019	5	AC	LC	ELT	NA
Isa <i>et al</i> ^[6] , 2019	NA	CC	LC	ELT	NA
Pandit <i>et al</i> ^[7] , 2019	35	CC	LC	ELT	NA
Granek <i>et al</i> ^[8] , 2019	19	AC	LC	ELT	NA
Lodha <i>et al</i> ^[9] , 2018	20	Kidney tumor	Lap nephrectomy	ELT (no excised)	NA
Topcu <i>et al</i> ^[10] , 2018	15	CC	OC	ELT	NA
	80	Pancreatic tumor	Whipple procedure	ELT	NA
Burke <i>et al</i> ^[11] , 2018	NA	CC	LC	ELT	NA
Greenberg <i>et al</i> ^[12] , 2018	30	CC	LC	ELT	NA
Termos <i>et al</i> ^[13] , 2017	30	Diag lap	LC	ELT	NA
Weber-Alvarez <i>et al</i> ^[14] , 2017	10	AC	LC	ELT	AC + CC
Galimov <i>et al</i> ^[15] , 2017	6	AC	LC	ELT	Phlegmonous cholecystitis
Handra-Luca <i>et al</i> ^[16] , 2016	5	CC	LC	ELT	CC
	11	CC	LC	ELT	CC
Mani <i>et al</i> ^[17] , 2016	NA	CC	LC	ELT	NA
Ito <i>et al</i> ^[18] , 2016	15	CC	LC	ELT	NA
Leena <i>et al</i> ^[19] , 2016	15	Autopsy	Autopsy	ELT	NA
Karaca <i>et al</i> ^[20] , 2016	15	CC	LC	ELT	NA
Jaboury <i>et al</i> ^[21] , 2016	NA	CC	LC	ELT	NA
Yahya <i>et al</i> ^[22] , 2016	60	CC	LC	ELT	NA
	NA	CC	LC	ELT	NA
	NA	CC	LC	ELT	NA
	NA	Penetrating injury	Diag lap	ELT	NA
Aslan <i>et al</i> ^[23] , 2016	8	CC	LC	ELT	NA
Longjam <i>et al</i> ^[24] , 2016	15	CC	LC	ELT	CC
Kostov <i>et al</i> ^[25] , 2016	35	RCLM	OC	ELT	Hydatid cyst on gallbladder wall
Bal <i>et al</i> ^[26] , 2015	20	CC	LC	ELT	NA
Smyth <i>et al</i> ^[27] , 2015	20	CC	LC	ELT	CC
Abhilash <i>et al</i> ^[28] , 2015	10	AC	LC	ELT	CC
Hussein <i>et al</i> ^[29] , 2015	NA	AC	LC	ELT	NA
Yankol <i>et al</i> ^[30] , 2015	15	Donor hepatectomy	LDH	ELT	Accessory gallbladder tissue
Arslan <i>et al</i> ^[31] , 2014	20	CC	LC	ELT	NA
Pulle <i>et al</i> ^[32] , 2014	20	CC	LC	ELT	CC
Terakawa <i>et al</i> ^[33] , 2014	12	CC	LC	ELT	NA

Sirasanagandla <i>et al</i> ^[34] , 2013	20	Autopsy	Autopsy	ELT	NA
Hassan <i>et al</i> ^[35] , 2013	10	CC	LC	ELT	CC
Martinez <i>et al</i> ^[36] , 2013	30	CC	LC	ELT	Chronic inflammation
Ozturk <i>et al</i> ^[37] , 2013	20	CC	LC	ELT	NA
Yajima <i>et al</i> ^[38] , 2013	6	CC	LC	ELT	NA
Khan <i>et al</i> ^[39] , 2013	NA	CC	LC	ELT (Fatty change)	CC
Karaman <i>et al</i> ^[40] , 2012	11	CC	LC	ELT	NA
Patel <i>et al</i> ^[41] , 2012	26	CC	LC	ELT	NA
Sozen <i>et al</i> ^[42] , 2012	7	CC	LC	ELT	NA
Catani <i>et al</i> ^[43] , 2011	15	AC	LC	ELT	NA
	14	CC	LC	ELT	NA
Dettmer <i>et al</i> ^[44] , 2011	15	AC	LC	ELT	Acute cholecystitis
Nagar <i>et al</i> ^[45] , 2011	45	AP + Cystic mass	LC	ELT	CC
Ates <i>et al</i> ^[46] , 2010	5	AC	LC	ELT	NA
	6	CC	LC	ELT	NA
Triantafyllidis <i>et al</i> ^[47] , 2009	15	CC	LC	ELT	CC
Guzman <i>et al</i> ^[48] , 2009	30	CC	LC	ELT	NA
Kyeong <i>et al</i> ^[49] , 2008	10	CC	LC	ELT	CC
Koh <i>et al</i> ^[50] , 2007	15	AC	LC	ELT	NA
Malhas <i>et al</i> ^[51] , 2007	NA	CC	LC	ELT	NA
	NA	CC	LC	ELT	NA
Soto <i>et al</i> ^[52] , 2007	8	CC	LC	ELT	NA
Beltran <i>et al</i> ^[53] , 2007	12	CC	LC	ELT	CC
	17	CC	LC	ELT	NA
	7	Gastric cancer	OC + Gastrectomy	ELT	NA
	18	Pancreatic pseudocyst	OC + Gastrectomy	ELT	NA
Wang <i>et al</i> ^[54] , 2006	11	Gallbladder polyps	LC	ELT	CC + Polyps
Ikeda <i>et al</i> ^[55] , 2006	NA	HCC	OC + Segment V Resection	NASH	NA
Ngowe <i>et al</i> ^[56] , 2006	30	CC	LC	ELT	CC
Lundy <i>et al</i> ^[57] , 2005	30	Diag lap	LC	ELT	NA
Leone <i>et al</i> ^[58] , 2004	90	GBC	OC	ELT + HCC	NA
Griniatsos <i>et al</i> ^[59] , 2002	10	CC	LC	ELT	NA
	15	CC	LC	ELT	NA
Acar <i>et al</i> ^[60] , 2002	14	CC	OC	ELT	Papillary epithelial hyperplasia
Sakarya <i>et al</i> ^[61] , 2002	NA	NA	LC	NA	NA
Arakawa <i>et al</i> ^[62] , 1999	15	Autopsy	Autopsy	ELT	NA
Hamdani <i>et al</i> ^[63] , 1994	30	PSC	LT	ELT	NA
Boyle <i>et al</i> ^[64] , 1992	20	AC	OC	ELT	CC
Tejada <i>et al</i> ^[65] , 1989	11	CC	OC + Splenectomy	ELT	CC
Watanabe <i>et al</i> ^[66] , 1989	5	Cystic lesion of the liver	Diag lap	Biliary hamartoma	NA

	8	Cirr	Diag lap	NA	NA
	10	Cirr	Diag lap	NA	NA
	6	Cirr	Diag lap	NA	NA
Fellbaum <i>et al</i> ^[67] , 1987	NA	NA	NA	NA	NA
Natori <i>et al</i> ^[68] , 1986	12	CC	OC + Excision	ELT	Chronic inflammation
Ashby <i>et al</i> ^[69] , 1969	10	Duodenal ulcer	OC + Excision	ELT	NA
BASSIS <i>et al</i> ^[70] , 1956	15	CC	OC	ELT	CC
	10	CC	OC	ELT	CC
	6	CC	OC	ELT	CC
	8	Autopsy	Autopsy	ELT	NA
Thorsness <i>et al</i> ^[71] , 1941	5	Autopsy	Autopsy	ELT	NA
Cullen <i>et al</i> ^[72] , 1925	12	Jaundice	Excision	NA	NA

NA: Non-available; LC: Laparoscopic cholecystectomy; AC: Acute cholecystitis; CC: Chronic cholecystitis ± cholelithiasis; RCLM: Rectum cancer liver metastasis; PSC: Primary sclerosing cholangitis; GBC: Gallbladder cancer; LDH: Lactate dehydrogenase; OC: Open cholecystectomy; Diag lap: Diagnostic laparoscopy; ELT: Ectopic liver tissue; HCC: Hepatocellular cancer.

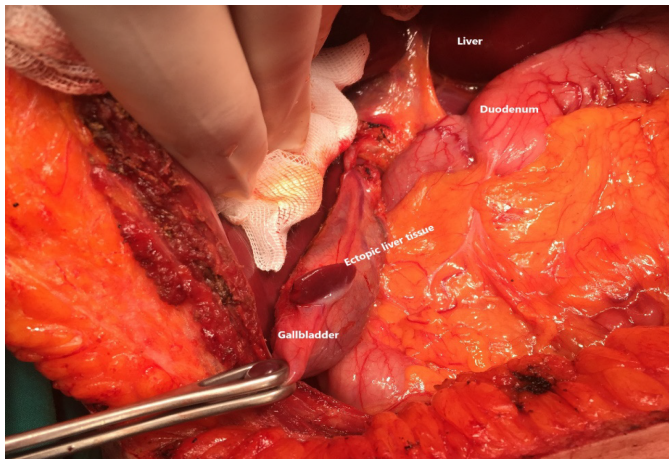


Figure 1 Intraoperative view of the ectopic liver tissue located in the gallbladder.

hepatocyte-destined mesenchyma in several areas thus budding hepatic tissue before the closure of the pleuroperitoneal canal^[23,28]. Ectopic and accessory liver may occur at different sites, including sites close to the liver, such as the gallbladder and hepatic ligaments or sites far from the liver, for example, omentum, retroperitoneum, and thorax, with the most common location on the gallbladder^[66,75,76].

Ectopic liver tissue varies considerably in size^[60,62]. Based on 72 reports reviewed in this study, the average size of the ectopic liver tissue was found to be 17.8 mm. In the literature, the reported size of ectopic livers (without hepatocellular carcinoma) ranges from a few millimeters to several centimeters^[24,44,58].

No detailed reports on the vascular supply of ectopic liver tissue were given in most of the papers reviewed. In general, three different vascular supply patterns have been described for gallbladder-associated ectopic liver tissue: An artery arising from the cystic artery^[50], a vascular pedicle arising from the liver parenchyma substance^[26], and vascular structures embedded in a mesentery lying from the hepatic site to ectopic liver tissue^[43]. The identification of vascular supply requires surgery to avoid bleeding during the main surgery^[3,4,26]. Extensive traction of the gallbladder should be avoided in cases with direct vascular supply from the liver substance. Biliary drainage was not described in detail or was not evident intraoperatively in most reports. In general, accessory liver lobes are classified into three types based on biliary drainage: In type I, the duct of the accessory liver lobe drains into an intrahepatic bile duct of the native liver; in Type II, it drains into an extrahepatic bile duct of the native liver, and if both the accessory lobe and the main liver have a common capsule and the bile duct of the

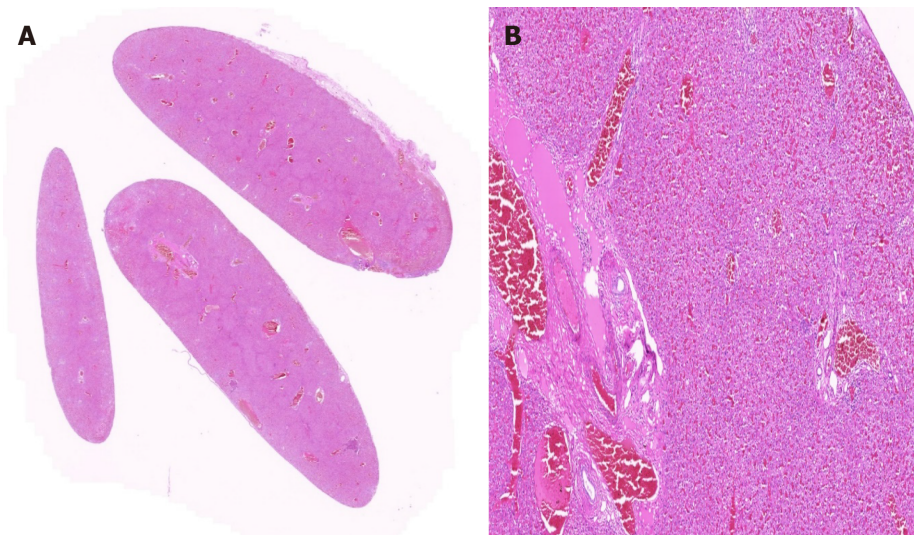


Figure 2 Encapsulated liver tissue with normal histological features. A: HE $\times 1$; B: HE $\times 2.5$.

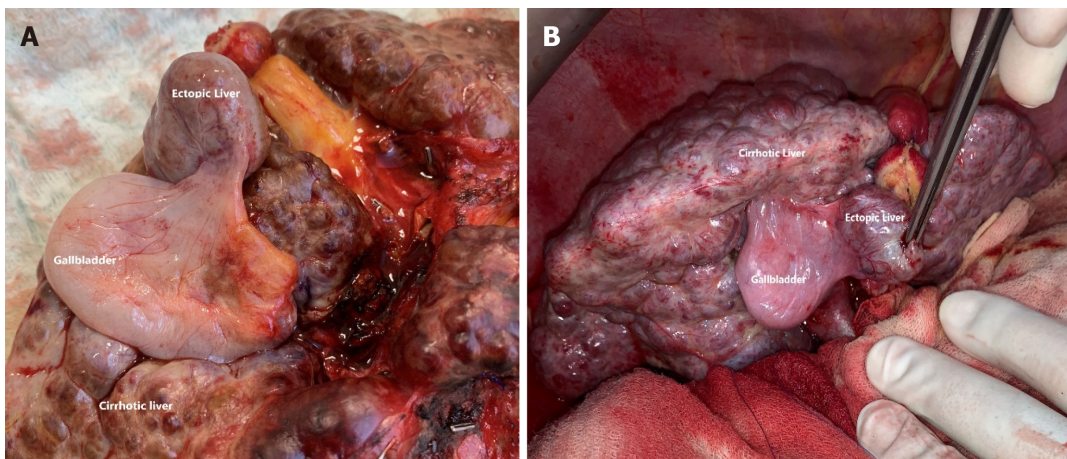


Figure 3 Intraoperative view of the ectopic liver tissue located in the gallbladder mesentery along with the main cirrhotic liver. A and B: The ectopic liver tissue was showed a cirrhotic appearance similar to the main liver tissue.

accessory lobe drains into an extrahepatic duct, it is considered Type III^[34,77].

Ectopic liver might be associated with other anomalies such as biliary atresia, agenesis of the caudate lobe, omphalocele, bile duct cyst, cardiac, and conotruncal anomalies; however, these abnormalities were not reported when the heterotopic tissue was attached to the surface of the gallbladder^[28,59].

Ectopic liver tissue and accessory liver lobes are often asymptomatic, and detection of ectopic liver tissue before surgical intervention or autopsy imaging studies is rare^[8,11,20,34]. However, ectopic livers on rare occasions have been reported to cause recurrent abdominal pain due to torsion^[78-80], intraperitoneal bleeding^[81,82], hemorrhagic necrosis^[83], compression of adjacent organs^[84], as well as obstruction of the esophagus^[85], portal vein^[86], and neonatal gastric outlet^[87].

The histological architecture of the ectopic tissue resembles normal liver, with regular lobules, central veins, and normal portal areas in most cases^[28,47,59]. Unusual architecture of hepatic tissue with absence of the classical hexagonal lobule pattern has been equally described^[34]. Ectopic liver like the main liver tissue can undergo fatty changes, hemosiderosis, cholestasis, cirrhosis, hepatitis, or malignant degeneration to hepatocellular carcinoma^[36]. Although ectopic liver tissue usually has normal histology of the liver, that is, normal portal structure, regular lobules, and central veins, ectopic liver tissue has an increased risk of hepatocellular carcinoma^[27,43,53]. The reason for this increased risk of hepatocellular carcinoma in patients with ectopic liver tissue is unclear, it has been proposed that biliary drainage is insufficient and/or blood supply is reduced in the ectopic liver tissue^[58]. Furthermore, many hepatocellular carcinoma cases are related to ectopic liver tissue, and are not associated with cirrhosis in the

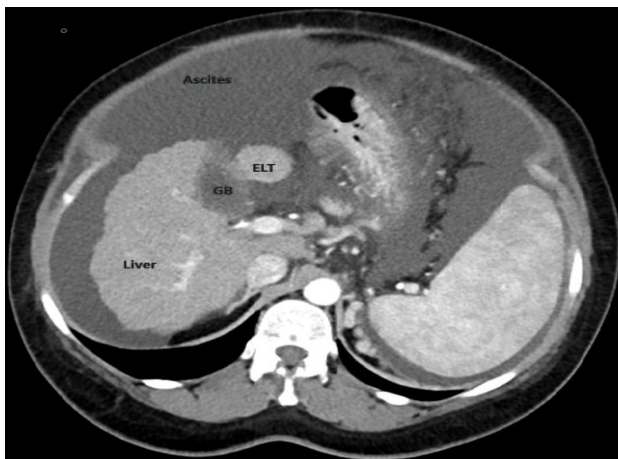


Figure 4 Axial contrast-enhanced multidetector computed tomography section shows an ectopic liver tissue-like nodular lesion associated with the gallbladder.

main liver. Arakawa and colleagues^[62] reported that in 22 hepatocellular carcinoma cases related to ectopic liver tissue, only six cases (27%) had cirrhosis in the main liver.

It has been revealed that many authors have misinterpreted the results of the article by Yamashita and colleagues^[78]. One of the most important reasons for this misinterpretation is that the article is written in Japanese. Another reason is that the authors copy each other directly without carefully reading the authors' results^[2,3,5,12,17,23,26,28,29,35,36,59,62]. In the review by Yamashita and colleagues^[78], 70 cases of ectopic liver were reported in the literature up to 1985. One (4.5%) of 22 cases with ectopic hepatic tissue attached to the gallbladder developed hepatocellular carcinoma while eight (16.7%) of 48 cases with ectopic hepatic tissue located outside the gallbladder developed hepatocellular carcinoma. As a result of the statistical analysis carried out using the Yamashita and colleagues data, no statistically significant difference was found between ectopic liver tissue located on the gallbladder surface and its location outside the gallbladder in terms of hepatocellular carcinoma risk ($P = 0.25$). Many studies have suggested that ectopic liver tissue on the gallbladder is less susceptible to hepatocellular carcinoma development than ectopic liver tissue outside the gallbladder. A possible explanation proposed for this difference is that ectopic hepatic tissue attached to the gallbladder is an anomaly occurring later during the development of the biliary bud and is; therefore, well-differentiated^[12,26,59,62]. However, the results of our analysis using the Yamashita and colleagues data^[78] revealed that there was no difference. In the 72 articles reviewed in this study, including 91 patients with ectopic liver tissue attached to the gallbladder, only one patient reported having hepatocellular carcinoma in the ectopic liver tissue (1.09%).

CONCLUSION

Ectopic liver tissue is a rare developmental anomaly usually detected incidentally during surgery or autopsy. While it is often asymptomatic, it has a risk of malignant transformation and carries the potential for other complications such as bleeding and torsion. Although most studies have suggested that ectopic liver located outside the gallbladder has a higher risk of hepatocellular carcinoma, this is not reflected in the statistical analysis results.

ARTICLE HIGHLIGHTS

Research background

Liver tissue situated outside the liver with a hepatic connection is usually called an accessory liver, and that without a connection to the mother liver, is called ectopic liver tissue. Ectopic liver tissue is a rare developmental anomaly usually detected incidentally.

Research motivation

Although a limited number of case reports on ectopic liver tissue on the gallbladder surface or gallbladder mesentery have been published to date, no systematic literature research has been conducted.

Research objectives

While the main objective of this study was to review the articles published in the medical literature on ectopic liver tissue on the gallbladder surface or gallbladder mesentery, the secondary objective of this study was to present the medical history of two patients diagnosed with ectopic liver tissue.

Research methods

A systematic literature search was conducted on PubMed, Medline, Google Scholar, and Google databases using the following keywords: Accessory liver lobe, aberrant liver tissue, ectopic liver tissue, ectopic liver nodule, heterotopic liver tissue, hepatic choristoma, heterotopic liver tissue on the gallbladder, and ectopic liver tissue on the gallbladder. The search included articles published before June 2020 with no language restriction.

Research results

A total of 72 articles were identified involving 91 patients, 62 females and 25 males; no gender data were available for the remaining four patients. The age of these 87 patients ranged from five days to 91 years; this information was unavailable for the remaining four patients. Eleven patients had a history of various liver diseases, while 12 patients had no liver disease. Forty-nine patients had surgery for chronic cholecystitis and/or cholelithiasis, while 14 patients had surgery for a presumed diagnosis of acute cholecystitis. The remaining 28 patients underwent laparotomy for unrelated reasons. Sixty-one patients underwent laparoscopic cholecystectomy and 11 underwent open cholecystectomy. The remaining 19 patients underwent cholecystectomy and various surgical procedures such as autopsy, liver transplantation, living donor hepatectomy, Whipple procedure, and liver segment V resection.

Research conclusions

Ectopic liver tissue is a rare developmental anomaly usually detected incidentally during surgery or autopsy. While it is often asymptomatic, it has a risk of malignant transformation and carries the potential of other complications such as bleeding and torsion.

Research perspectives

First, a review of the literature and our clinical experience suggest that ectopic liver tissue-like lesions around the liver should be considered in the differential diagnosis of ectopic hepatocellular carcinoma, especially in patients with chronic liver disease. Therefore, even when the macroscopic appearance is normal, all ectopic liver tissue specimens should be sent for routine histopathological examination. Second, although most studies have suggested that ectopic liver located outside the gallbladder has a higher risk of hepatocellular carcinoma, this is not reflected in the statistical analysis results.

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