PROFESSIONAL PAPER

ECTOPIC LIVER AND HEPATOCELLULAR CARCINOMA

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ABSTRACT

Received: 7 April 2021; Accepted: 23 May 2021.

The most frequent anomalies of the liver are variations of the liver lobes and accessory bile ducts, and rare anomalies are related to the abnormal position of liver tissue. In this article, we present data about case reports of ectopic liver published from 2004 to 2020, about the connection between hepatocellular carcinoma and ectopic liver, its location, and the rea- son for a visit to a medical professional.

Keywords: ectopic liver, hepatocellular carcinoma, hcc liver

INTRODUCTION

The most frequent anomalies of the liver are variations of the liver lobes and accessory bile ducts, and rare anomalies are related to the abnormal position of liver tissue¹. Abnormal locations of liver tissue, or ectopic liver, was mentioned in an article for the first time in 1922², which described ectopic liver tissue in the inferior side of the gallbladder, 17x10x4mm in size, with its own vascular and bile ducts. The literature on the subject says that these anomalies are usually not symptomatic^{1,3}.

These anomalies can be classified in four types: (1) ectopic liver, arising outside the liver and without connection to the liver; (2) microscopic ectopic liver, which is found occasionally in the wall of the gall-bladder; (3) a large accessory liver lobe attached to the liver by a stalk, (4) and a small accessory liver lobe attached to the liver⁴.

According to available data, ectopic liver is found in 0.47% patients⁵. The usual incidence of ectopic liver and accessory liver lobes is from 0.56 to 0.70%⁶.

These anomalies are hard to detect with standard imaging techniques³. Ectopic liver is usually found during abdominal surgery or autopsies⁷.

Hepatocellular carcinoma is found in 30% of ectopic liver tissue discovered⁸. It is considered that ectopic liver tissue is functionally handicapped and more susceptible to hepatocarcinogenesis because of the lack of the complete vascular and ductal structure of normal liver⁹.

Symptomatic cases can be found showing torsion, necrosis, rupture, pyloric obstruction and malignant

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transformation of this tissue¹⁰. The usual symptoms are pain, compression and bleeding^{11,12}.

Ectopic liver is usually found connected to the liver, close to the gallbladder, spleen, in the thoracic cavity and retroperitonaeal⁶.

In this article, we present data about case reports of ectopic liver published from 2004 to 2020, about the connection between hepatocellular carcinoma and ectopic liver, its location, and the reason for a visit to a medical professional, as this clinical entity can be found during laparoscopic exploration.

Materials and methods

We searched PubMed for the term "ectopic liver". Since we did not find any review articles on this topic published after 2004⁶, for this research we included articles presenting case reports of ectopic liver published from 2004 to the end of 2019.

We found 68 case reports in 64 articles, and from those we collected data about the location of ectopic liver tissue, pathology findings (hepatocellular carcinoma or other pathological findings), the diagnostic technique that revealed the tissue, if it was symptomatic, and data about the age and sex of the patients.

By statistical analysis using IBM SPSS version 21.0 for Windows, we tried to find statistically significant connections within the collected data and determine the frequency of hepatocellular carcinoma in ectopic liver, connections with location, sex, age, symptoms and whether ectopic liver is symptomatic or usually an accidental finding.

Results

All case reports, except one (1.5%), included the age of the patient at the time of finding the ectopic liver. The average age was 50.12 (±18.50) years, the youngest patient was 1, and the oldest was 91 years old (95% CI:45.61-54.63). Since we had continuous data, the Kolmorgorov-Smirnov test was performed, which showed even distribution (p=0.200), and allowed parametric statistics.

Table 1. Location of ectopic liver

| Location | Frequency | Percent | Reference |
|----------------------------------|-----------|---------|--------------------------------------------|
| Gallbladder | 15 | 22.1 | 2 5 10 13 14 15 16 17 18 19 20 21 22 23 24 |
| Spleen | 9 | 13.2 | 8 11 25 26 27 28 29 30 31 |
| Stomach | 2 | 2.9 | 32, 33 |
| Thorax | 10 | 14.7 | 4 34 35 36 37 38 39 40 41 42 |
| Liver | 6 | 8.8 | 43, 44, 28, 45, 46 |
| Right atrium, inferior vena cava | 10 | 14.7 | 47 48 49 50 51 52 53 54 55 56 |
| Pancreas | 4 | 5.9 | 57 58 59 60 |
| Peritoneum | 4 | 5.9 | 7 30 61 62 |
| Retroperitoneally | 2 | 2.9 | 63, 64 |
| Esophagus | 1 | 1.5 | 65 |
| Muscles | 1 | 1.5 | 66 |
| Small intestine | 1 | 1.5 | 67 |
| Bile duct | 2 | 2.9 | 68 ₆ 9 |
| Skull | 1 | 1.5 | 66 |
| Total | 68 | 100.0 | |

In relation to sex, ectopic liver is more frequently found in women (61.8%) than in men (38.2%).

Ectopic liver in our data was found in 14 different locations. Most frequently this was the gallbladder (22.1%), thorax (14.7%), the right atrium and inferior vena cava (14.7%) and the spleen (13.2%). It was found in other locations in less than 10% of cases. All cases classified in terms of location are shown in Table 1.

Pathological analysis of 36 cases (52.9%) found normal liver tissue, hepatocellular carcinoma was discovered in 26 cases (38.2%), inflammation in three cases (4.4%), fibrosis in one (1.5%) and hemorrhage in two cases (2.9%) .

Table 2. Pathological findings

| | Frequency | Percent |
|--------------|-----------|---------|
| Normal | 36 | 52.9 |
| HCC | 26 | 38.2 |
| Inflammation | 3 | 4.4 |
| Fibrosis | 1 | 1.5 |
| Hemorrhage | 2 | 2.9 |
| Total | 68 | 100.0 |

In 41 cases (60.3%), the patients had symptoms that indicated diagnostics which led to discovery of ectopic liver tissue, and for the rest of the cases the ectopic liver was found by accident.

In terms of location, the most frequently symptoms occurred if ectopic liver was located in the right atrium and the inferior vena cava (90%). Although the

Table 3.

| | Location | | | | | | | | | | | Total | | | | |
|--------------|-----------------------|-------------|--------|---------|--------|-------|----------------------------------|----------|------------|-------------------|-----------|---------|-----------------|-----------|--------|--------|
| | | Gallbladder | Spleen | Stomach | Thorax | Liver | Right atrium, inferior vena cava | Pancreas | Peritoneum | Retroperitoneally | Esophagus | Muscles | Small intestine | Bile duct | Skull | |
| Normal | Count | 11 | 3 | 2 | 7 | 2 | 9 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 36 |
| | % within Pathology | 30.6% | 8.3% | 5.6% | 19.4% | 5.6% | 25.0% | 0.0% | 2.8% | 0.0% | 2.8% | 0.0% | 0.0% | 0.0% | 0.0% | 100.0% |
| | % within Location | 73.3% | 33.3% | 100.0% | 70.0% | 33.3% | 90.0% | 0.0% | 25.0% | 0.0% | 100.0% | 0.0% | 0.0% | 0.0% | 0.0% | 52.9% |
| HCC | Count | 1 | 6 | 0 | 3 | 3 | 0 | 4 | 2 | 2 | 0 | 1 | 1 | 2 | 1 | 26 |
| | % within Pathology | 3.8% | 23.1% | 0.0% | 11.5% | 11.5% | 0.0% | 15.4% | 7.7% | 7.7% | 0.0% | 3.8% | 3.8% | 7.7% | 3.8% | 100.0% |
| | % within Location | 6.7% | 66.7% | 0.0% | 30.0% | 50.0% | 0.0% | 100.0% | 50.0% | 100.0% | 0.0% | 100.0% | 100.0% | 100.0% | 100.0% | 38.2% |
| Inflammation | Count | 1 | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 |
| | % within Pathology | 33.3% | 0.0% | 0.0% | 0.0% | 33.3% | 33.3% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 100.0% |
| | % within Location | 6.7% | 0.0% | 0.0% | 0.0% | 16.7% | 10.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 4.4% |
| Fibrosis | Count | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| | % within Pathology | 100.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 100.0% |
| | % within Location | 6.7% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 1.5% |

► Table 3.

| Hemorrhage | Count | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
|------------|-----------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| | % within Pathology | 50.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 50.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 100.0% |
| | % within Location | 6.7% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 25.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 2.9% |
| Total | Count | 15 | 9 | 2 | 10 | 6 | 10 | 4 | 4 | 2 | 1 | 1 | 1 | 2 | 1 | 68 |
| | % within Pathology | 22.1% | 13.2% | 2.9% | 14.7% | 8.8% | 14.7% | 5.9% | 5.9% | 2.9% | 1.5% | 1.5% | 1.5% | 2.9% | 1.5% | 100.0% |
| | % within Location | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% |

gallbladder is a frequent location for ectopic liver, in our data this location was rarest location for symptoms, occurring in 26.7% of cases.

Most cases were discovered by radiological techniques (49 or 72.1%), then during surgery (14 or 20.6%). In one case, diagnosis was set by a clinical exam, and in

Table 4.

| | | | Path_H | Path_HCC | | |
|----------|----------------------------------|-------------------|--------|----------|--------|--|
| | | | Other | HCC | Total | |
| | | Count | 14 | 1 | 15 | |
| | Gallbladder | % within Location | 93.3% | 6.7% | 100.0% | |
| | | % within Path_HCC | 33.3% | 3.8% | 22.1% | |
| | | Count | 3 | 6 | 9 | |
| | Spleen | % within Location | 33.3% | 66.7% | 100.0% | |
| | | % within Path_HCC | 7.1% | 23.1% | 13.2% | |
| | | Count | 2 | 0 | 2 | |
| | Stomach | % within Location | 100.0% | 0.0% | 100.0% | |
| | | % within Path_HCC | 4.8% | 0.0% | 2.9% | |
| | Thorax | Count | 7 | 3 | 10 | |
| Location | | % within Location | 70.0% | 30.0% | 100.0% | |
| | | % within Path_HCC | 16.7% | 11.5% | 14.7% | |
| | | Count | 3 | 3 | 6 | |
| | Liver | % within Location | 50.0% | 50.0% | 100.0% | |
| | | % within Path_HCC | 7.1% | 11.5% | 8.8% | |
| | | Count | 10 | 0 | 10 | |
| | Right atrium, inferior vena cava | % within Location | 100.0% | 0.0% | 100.0% | |
| | | % within Path_HCC | 23.8% | 0.0% | 14.7% | |
| | | Count | 0 | 4 | 4 | |
| | Pancreas | % within Location | 0.0% | 100.0% | 100.0% | |
| | | % within Path_HCC | 0.0% | 15.4% | 5.9% | |

► Table 4.

| | | Count | 2 | 2 | 4 |
|----------|-------------------|-------------------|--------|--------|--------|
| | Peritoneum | % within Location | 50.0% | 50.0% | 100.0% |
| | | % within Path_HCC | 4.8% | 7.7% | 5.9% |
| | | Count | 0 | 2 | 2 |
| | Retroperitoneally | % within Location | 0.0% | 100.0% | 100.0% |
| | | % within Path_HCC | 0.0% | 7.7% | 2.9% |
| | | Count | 1 | 0 | 1 |
| | Esophagus | % within Location | 100.0% | 0.0% | 100.0% |
| | | % within Path_HCC | 2.4% | 0.0% | 1.5% |
| Location | | Count | 0 | 1 | 1 |
| | Muscles | % within Location | 0.0% | 100.0% | 100.0% |
| | | % within Path_HCC | 0.0% | 3.8% | 1.5% |
| | Small intestine | Count | 0 | 1 | 1 |
| | | % within Location | 0.0% | 100.0% | 100.0% |
| | | % within Path_HCC | 0.0% | 3.8% | 1.5% |
| | | Count | 0 | 2 | 2 |
| | Bile duct | % within Location | 0.0% | 100.0% | 100.0% |
| | | % within Path_HCC | 0.0% | 7.7% | 2.9% |
| | | Count | 0 | 1 | 1 |
| | Skull | % within Location | 0.0% | 100.0% | 100.0% |
| | | % within Path_HCC | 0.0% | 3.8% | 1.5% |
| | | Count | 42 | 26 | 68 |
| Total | | % within Location | 61,8% | 38.2% | 100.0% |
| | | % within Path_HCC | 100,0% | 100.0% | 100.0% |

two cases by pathological analysis. 85.71% of cases discovered by surgery were asymptomatic.

In Table 3 we show the connections between pathological findings and the locations of ectopic liver.

Since all pathological findings except hepatocellular carcinoma (HCC) were benign, we performed statistical analysis of the connection between HCC and location related to all the other findings, as shown in Table 4.

We found a statistically significant difference between the location of ectopic liver and the finding of HCC (chi-squared test: x²=36,101, df=13, p=0.001). HCC was not found in the right atrium and inferior

vena cava (0/10), it was found in only 1/15 of cases in the gallbladder (6.7%), in 30.0% in the thorax, in 66.7% in the spleen, and all four cases in the pancreas (100%) had HCC (significantly frequent in the spleen and pancreas, and rare in the right atrium and inferior vena cava and gallbladder).

Of all cases of hepatocellular carcinoma, 26 of them, or 80.7%, were symptomatic, and benign cases were symptomatic at the rate of 47.6%.

Discussion

The data about ectopic liver in the literature are usually in the form of case reports as this anomaly is rare. The results of our search of case reports in PubMed

published from 2004 to 2020 showed that ectopic liver can be found in all age groups, from a newborn to old age. Ectopic liver is more frequent in women (61.8%). We found a relatively high incidence of ectopic liver in the right atrium and inferior vena cava (14.7%) that was not mentioned in earlier research⁶. Other frequently mentioned locations: the liver, gall-bladder, spleen and thorax, were also frequent in our results. Rare locations of ectopic liver are the small bowel, muscles and skull.

Although it is said that ectopic liver is usually asymptomatic^{1,3}, in our data 60.3% of patients had some complaints that led to diagnostics and the discovery of ectopic liver as the cause of their problems. It is obvious that this tissue can cause unexpected clinical issues⁹.

Contrary to the data in the literature that ectopic liver is usually found during surgery, in our sample it was mostly found by radiology (72.1%), which can be connected the greater availability and quality of radiological diagnostics in recent years.

Hepatocellular carcinoma was found in 38.2% of our cases, which is not a significant deviation from the 30% mentioned in earlier research⁸. It is significant to mention that all cases of ectopic liver in the pancreas had hepatocellular carcinoma, and that the incidence of HCC is high in the spleen and thorax. Although ectopic liver can be frequently found in the gallbladder, where it was described for the first time, occurrence of hepatocellular carcinoma at that location is rare. Other locations of ectopic liver are rare and occurrence of hepatocellular carcinoma there is also rare.

Hepatocellular carcinoma in ectopic liver causes symptoms in 80.7% of cases, which is almost double in relation to benign cases.

Ectopic liver is usually asymptomatic if it is in the gallbladder, and asymptomatic tissue is usually found during surgery.

Conclusion

Ectopic liver is a rare phenomenon which requires surgical removal and pathological analysis because of potential malignant alterations and occurrence of hepatocellular carcinoma. We must take this rare clinical entity into consideration during laparoscopic exploration when it can be removed before it becomes symptomatic or malignant.

Conflicts of interest

The authors have no conflict of interest.

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