CASE REVIEW

Multiple liver masses in a patient with breast cancer, metastasis or not? An unexpected diagnosis: hepatic fascioliasis. A case report and overview of the literature from Turkey

ÇAĞRI DAMAR, MD, ARIF EMRE EMEK, MD, HÜSEYIN UÇAR, MD, HARUN ERDAL, MD, İŞIK CONKBAYIR, MD and ÇİGDEM ÖZTUNALI, MD

1Department of Radiology, Gazi University, Ankara, Turkey
2Department of Radiology, Civil Government Hospital, Denizli, Turkey
3Department of Radiology, Afyon Kocatepe University, Afyon, Turkey
4Department of Gastroenterology, Gazi University, Ankara, Turkey
5Department of Radiology, Diskapi Yildirim Beyazit Education And Research Hospital, Ankara, Turkey

Address correspondence to: Mr Çağrı Damar
E-mail: cagridamar@hotmail.com

ABSTRACT

A patient who underwent mastectomy of the left breast owing to breast cancer was referred to our department for abdominal ultrasonography during her routine check-up. Radiological examinations demonstrated multiple masses that tended to form clusters in the liver parenchyma, and the lesions were initially thought to represent metastases from the breast cancer. Multisite biopsies and serological tests confirmed the diagnosis of Fasciola hepatica infestation. To our knowledge, this is a unique case report of a patient with a known malignant neoplasm. We also present an overview of the literature about human fascioliasis in Turkey.

SUMMARY

Owing to their long historical background, environmental and climatic features, biodiversity and proximity of the people to animals some zoonotic diseases are seen more frequently in the countries of the Mediterranean and the Middle East. Fasciola hepatica is a foodborne trematode worm (fluke) that mainly affects the liver of its final host. Its human infestation can be seen in Anatolia (the western peninsula of Asia that forms the mainland of Turkey). As its radiological findings may mimic metastases, it is important to consider F. hepatica in the differential diagnosis while evaluating imaging findings of patients with previously known malignancy. We herein present the case of a 38-year-old female patient with a history of breast cancer who had presented with multiple liver lesions that were finally proven to be consistent with fascioliasis.

CASE REPORT

A 38-year-old female who had undergone right mastectomy for breast carcinoma was referred to our department for evaluation of the multiple liver masses detected on routine follow-up examinations. Sonographic examination of the patient revealed hepatosplenomegaly and multiple heterogeneous hypoechoic masses of varying sizes that were located centrally in the right lobe of the liver and tended to form clusters. Some of the larger lesions had central necrosis and cavitation areas. We observed hypoechoic curvilinear tracts extending from the liver capsule to the parenchyma, which did not demonstrate abnormal vascularity on colour Doppler ultrasound examination. The gallbladder had normal wall thickness and endoluminal echogenicity. Contrast-enhanced CT obtained in the portal venous phase revealed multiple, clustered, hypodense nodular liver masses with irregular margins. In addition, the presence of at least three hypodense curvilinear tracts, extending from the liver capsule to the parenchyma, were confirmed. The lesions did not demonstrate any contrast enhancement. There were a number of enlarged lymph nodes in the porta hepatis.

Ultrasound-guided fine needle aspirations of the selected lesions were performed. Pathological examination of the specimens showed no evidence of malignancy but eosinophil-rich inflammatory necrotic tissue was reported. Blood
tests also revealed elevated levels of eosinophils and serological tests confirmed the presence of *F. hepatica* infestation. The patient was discharged after a course of triclabendazole treatment. A follow-up CT scan, obtained 2 years after her first admission, showed slight regression in the size of all the liver lesions (Figure 5 and Supplementary Video A) and there were no new lesions.

**DISCUSSION**

Fascioliasis is included in the group of food (or snail)-borne trematodiases and is caused by two species of parasitic flatworms: *F. hepatica* and *Fasciola gigantica*.²

**Epidemiology**

Although the natural final hosts of this parasite are sheep, goats, cattles and other herbivores, *F. hepatica* has been reported in humans with increasing frequency. Despite the belief that it has a European origin, *F. hepatica* has shown a great capacity to spread and can be seen in all the continents except Antarctica. According to the recent estimates, several million people are infected in more than 70 countries worldwide, with millions of others being at risk. The parasite can easily adapt and colonize in rural areas and wetlands, where there are plenty of freshwater *Lymnaea* snails (the intermediate hosts) and herbivorous mammals (the definitive hosts). However, human fascioliasis (HF) has a patchy geographical distribution and there are some endemic regions such as the Caribbean, northern Africa, western Europe and the Caspia. Certainly, the lifestyle and dietary habits of the people, social and economic factors, hygiene and sanitation conditions, and travel or immigration, all add to the frequency of the disease. If it is detected in some livestock animals, human cases may also exist.²–⁶

**Lifecycle of parasites**

The eggs of the parasite are excreted with the final host’s faeces. These eggs are immersed in freshwater, and the swimming, ciliated miracidia forms are released. Miracidiae use *Lymnaea* snails as their first host; once they metamorphose into motile, tailed cercaria forms, they leave the snails. Cercariae use the aquatic plants (watercress, watermint, lettuce, spinach or other salad vegetables) as another group of intermediate hosts; the cercarial...
larvae encyst and develop into the metacercarial stage. The main transmission of *F. hepatica* occurs by ingesting water or raw plants contaminated by the metacercaria forms of the parasite. The metacercariae change form during duodenal interference; they penetrate the intestinal wall and migrate through the peritoneal cavity to reach the Glisson’s capsule. After piercing the capsule of the liver, the parasites migrate through the liver parenchyma and reach the biliary system, where they grow into adults and release new eggs. The eggs reach the intestines via bile and are evacuated in the faeces, thus completing the transmission cycle of the parasites. The average size of a mature fluke is 20–40 mm in length and 8–13 mm in width.

**Human infestation, clinical features, diagnosis and treatment**

Human infestation by this trematode has two characteristic phases: an acute hepatic (parenchymal) phase and a chronic biliary (ductal) phase.6,7

The first phase is the hepatic phase. In this phase, the parasites pierce the Glisson’s capsule and migrate through the liver parenchyma towards the bile ducts in a random manner. This stage lasts for 1–3 months after metacercariae infection. The clinical features of this stage include anorexia, fatigue, nausea, vomiting, right upper quadrant pain, pruritus, fever, weight loss, respiratory symptoms, hepatomegaly, jaundice and urticaria. Laboratory findings such as elevated liver enzymes, increased erythrocyte sedimentation rate, hypergammaglobulinaemia and marked eosinophilia can be encountered in this stage as well. Mild hepatitis, severe hepatic subcapsular haemorrhage or liver necrosis may also be seen rarely in this hepatic phase. 6,7

The second stage may be asymptomatic for a long time or may be characterized by intermittent right upper quadrant pain. As a result of chronic inflammation of the bile ducts, duodenal wall thickening, common bile duct obstruction, bile duct stones or gallstones, cholestasis, cholangitis, cholecystitis or pancreatitis may occur.6,7,9 Adult flukes can live for years and the chronic phase may persist in untreated patients.8,10 *F. hepatica* can rarely settle in unusual organs and lead to ectopic disease.8,11–13

Suggested diagnostic criteria for fascioliasis in endemic regions, reported by the WHO in 2009, are:14

- history of eating raw aquatic plants
- clinical symptoms such as abdominal pain in the epigastric or right-upper quadrant region, lasting at least a week
- eosinophilia
- positive ultrasound or CT scan findings
- positive for the presence of *F. hepatica* eggs (detected by Kato–Katz thick smear or sedimentation technique)
- positive serologic tests (from the serum, stool or urine specimens).

For the treatment of the cases diagnosed with the above-mentioned criteria, the recommended drug triclabendazole (10 mg kg\(^{-1}\) of body weight) is given in a single administration. If necessary, a double dose (20 mg kg\(^{-1}\) of body weight) can be administered for the management of individual cases.14

**Radiological findings**

When the flukes follow the migration path from the liver capsule to the bile ducts, they ingest hepatocytes. Along this migration path, multiple small necrotic cavities and microabscesses arise. These abscess cavities are not large, as seen in the cases of other suppurative processes. On CT imaging, migration paths that extend from the Glisson’s capsule to deep parenchymal areas (tunnel-like tracts) can be seen. Also, serpentine, clustered, small necrotic cavities can be detected. These two findings, which were also observed in our case, are defined as the “tunnels and caves sign” in the literature10 and can help in separating other malignant lesions from these parasitic lesions. In addition, the peripheral halo sign on B-mode ultrasound examination and internal vascularity on colour Doppler mode sonography or contrast-enhanced CT imaging, which are usually seen in cases of metastatic nodules, were not present in our case.15

With the use of ultrasound imaging, adult worms can be visualized in the gallbladder and/or in the extrahepatic bile ducts.

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**Figure 5.** Post-treatment contrast-enhanced CT image in the portal phase 2 years later shows that the liver lesions had slightly regressed in size.

**Figure 6.** Ultrasound image reveals a thin, linear echogenicity, which is fixed at one end to the posterior wall of the common bile duct.
Ultrasound examination may demonstrate single or multiple, elongated filamentous structures or moving echogenic flukes. The adult forms of parasites attach to the inner wall of the bile duct through their ventral suckers. When we retrospectively re-examined our patient, we detected a thin, linear echogenicity 1.5 cm long, one end of which was fixed to the posterior wall of the common bile duct (Figure 6). Although this appearance was also consistent with the previously described sonographic appearances of the adult parasites in the literature, we did not perform any further investigations because the patient

Table 1. Publications reporting the prevalence of human fascioliasis (HF) in some regions of Turkey

| Author (year) | City/ Region | Number of selected individuals | Number of detected HF | Prevalence |
|---------------|--------------|--------------------------------|-----------------------|------------|
| Yilmaz et al (1997) | Van/Eastern Anatolia | 3,534 (14 years and above) | 1 | 0.028 |
| Yilmaz et al (1998) | Ercis (Van)/Eastern Anatolia | 206 (students, 7-15 years age group) | 5 | 2.43 |
| Yilmaz et al (1999) | Ercis (Van)/Eastern Anatolia | 293 | 2 | 0.68 |
| Yilmaz et al (2004) | Ercis (Van)/Eastern Anatolia | 500 | 9 | 1.8 |
| Yilmaz et al (2007) | Ercis (Van)/Eastern Anatolia | 867 | 1 | 0.1 |
| Tas Cengiz et al (2009) | Van/Eastern Anatolia | 2,975 | 1 | 0.03 |
| Tas Cengiz et al (2015) | Van/Eastern Anatolia | 1,600 | 89 | 5.6 |
| Tas Cengiz et al (2015) | Van/Eastern Anatolia | 5,985 | 8 | 0.1 |
| Sener et al (1998) | Ankara/Central Anatolia | 122,400 | 1 | 0.0009 |
| Kaplan et al (2002) | Elazig/Eastern Anatolia | 540 | 15 | 2.78 |
| Seker et al (2005) | Bagtepe (Adana)/Mediterranean | 291 | 30 | 10.3 |
| Turhan et al (2006) | Antalya (10 suburbs)/Mediterranean | 597 | 18 | 3 |
| Demirci et al (2003) | Isparta/Mediterranean | 756, with eosinophilia | 46 | 6.1 |
| | | | 320, others | 3 | 0.9 |
| Kaya et al (2006) | Isparta/Mediterranean | 415 | 10 | 2.4 |
| | | | A. Gokdere (Isparta)/Mediterranean | 171 | 16 | 9.3 |
| Ozturhan et al (2009) | Mersin/Mediterranean | 155, with a family history of HF | 3 | 1.93 |
| | | | 729, others | 4 | 0.55 |
| Sahin et al (2008) | Karpuzeskisi (Kayseri)/Central Anatolia | 374 | 13 | 3.48 |
| Koksal et al (2010) | Istanbul/Marmara | 27,664 | 1 | 0.003 |
| Zeren et al (2013) | Cukurova (Adana)/Mediterranean | 94, with blood samples obtained during forensic autopsies | 13 | 13.8 |
| Tas et al (2014) | Bolu/Black Sea | 2,995 | 1 | 0.039 |
| Karaman et al (2014) | Ordu/Black Sea | 7,194 | 17 | 0.23 |

*The study includes not only HF but also other parasitoses.
Table 2. The other publications on human fascioliasis from Turkey, including at least five or more cases

| Author (year) | Hospital/department of the corresponding author | City/region | Number of cases | Date range |
|---------------|-------------------------------------------------|-------------|-----------------|------------|
| Kabaalioglu et al\(^\text{a}\) (2007) | Akdeniz UMH/radiology | Antalya/Mediterranean | 87\(^\text{a}\) | 1995–2006 |
| Saba et al\(^\text{a}\) (2004) | Akdeniz UMH and other centers/infectious diseases | Antalya/Mediterranean | 53 | 1998–2003 |
| Cevikol et al\(^\text{a}\) (2003) | Akdeniz UMH/radiology | Antalya/Mediterranean | 43 | 1995–2001 |
| Cubuk et al\(^\text{a}\) (2001) | Akdeniz UMH/radiology | Antalya/Mediterranean | 52 | 1995–2000 |
| Sakru et al\(^\text{a}\) (2004) | Trakya UMH and other centers/microbiology | İzmir, Antalya/Aegean, Mediterranean | 37\(^\text{a}\) | ?–2004 |
| Taylan Ozkan et al\(^\text{a}\) (2005) | Ege UMH and other centers/parasitology | İzmir, Antalya/Aegean, Mediterranean | 14 | ?–2005 |
| Sezgi et al\(^\text{a}\) (2013) | Dicle UMH/pulmonary disease | Diyarbakir/South-Eastern Anatolia | 56 | 2010–2011 |
| Teke et al\(^\text{a}\) (2014) | Dicle UMH/radiology | Diyarbakir/South-Eastern Anatolia | 45 | 2011–2013 |
| Basarili et al\(^\text{a}\) (2011) | Dicle UMH/biochemistry | Diyarbakir/South-Eastern Anatolia | 45 | 2010–2011 |
| Kaya et al\(^\text{a}\) (2013) | Dicle UMH/gastroenterology | Diyarbakir/South-Eastern Anatolia | 42\(^\text{c}\) | 2010–2012 |
| Ulger et al\(^\text{a}\) (2014) | Dicle UMH/general surgery | Diyarbakir/South-Eastern Anatolia | 39 | 2005–2013 |
| Demirkaya et al\(^\text{a}\) (2014) | Dicle UMH/microbiology | Diyarbakir/South-Eastern Anatolia | 13 | 2011–2012 |
| Demirci et al\(^\text{a}\) (2009) | Suleyman Demirel UMH/microbiology | Isparta/Mediterranean | 50\(^\text{d}\) | ?–2009 |
| Yesildag et al\(^\text{a}\) (2009) | Suleyman Demirel UMH/radiology | Isparta/Mediterranean | 27 | 2001–2006 |
| Avcu et al\(^\text{a}\) (2009) | Van Yuzuncu Yil UMH/radiology | Van/Eastern Anatolia | 24 | 2008 |
| Karahocagil et al\(^\text{a}\) (2011) | Van Yuzuncu Yil UMH/infectious disease | Van/Eastern Anatolia | 24 | 2008 |
| Aksoy et al\(^\text{a}\) (2006) | Hacettepe UMH/internal medicine | Ankara/Central Anatolia | 10 | 1998–2005 |
| Karadag-Oncel et al\(^\text{a}\) (2012) | Hacettepe UMH/pediatric infectious disease | Ankara/Central Anatolia | 5 | 2005–2011 |
| Kayabali et al\(^\text{a}\) (1992) | Ankara UMH/general surgery | Ankara/Central Anatolia | 7 | ?–1992 |

(Continued)
had already been diagnosed with the infection and there were no signs of cholestasis that would have required further endoscopic intervention. There are also some reports that stress the importance of endoscopic retrograde cholangiopancreatography (ERCP) in the diagnosis and treatment of the chronic phase of the disease. In cases of cholestasis, adult parasites can be seen in the biliary tract and ERCP enables the removal of the parasites. In ERCP or MR cholangiography, the flukes are seen as filling defects in the bile ducts. 8,17,18 Periportal lymphadenopathies may be accompanied by other radiological findings, as in our case. 15 Other cases of hepatobiliary fascioliasis mimicking cholangiocellular or hepatocellular carcinoma or Oddi sphincter malignancy have been reported. Extrahepatic fascioliasis mimicking colon, ovarian, peritoneal carcinoma, or liver metastases of unknown origin have also been reported in the literature. 19–27 However, only one case of hepatic fascioliasis has been reported in a patient with breast carcinoma by Koc et al 28 in 2009. The patient was asymptomatic and only choledochal dilatation was found incidentally during abdominal ultrasound examination; without any other suspicious imaging findings of metastasis. To our knowledge, except for our report, there is no other report of HF mimicking liver metastases in a patient being followed up for breast carcinoma.

HF in Turkey

HF is a re-emerging disease and common in some provinces of Turkey 29 (Table 1). There are many published reports of human FH infections coming from these regions (Table 2), and also there are some case reports related to European travellers. 30–33 F. gigantica does not have the ability to spread like F. hepatica, but can be seen infrequently in Turkey. 3 There are only two case reports of biliary F. gigantica, which is distinguished from F. hepatica with its morphological features. 34,35

The disease continues to attract a large number of physicians who are studying in different departments in Turkey.

CONCLUSION

Hepatobiliary fascioliasis should be kept in mind in the differential diagnosis of multiple hepatic masses when suggestive clinical and laboratory findings are present, especially when the patients come from the endemic regions. Knowledge of the radiological imaging characteristics of HF can aid in the diagnosis, and imaging is also useful in the evaluation of the treatment response.

LEARNING POINTS

1. F. hepatica infestation must be considered in case of patients with a history of eating raw aquatic plants (watercress, etc.) in endemic regions who present with right upper quadrant pain, eosinophilia and multiple hepatic lesions.
2. Hepatobiliary fascioliasis can mimic primary or secondary hepatic malignancies.
3. “Tunnels and caves sign” is a finding of HF in radiological examinations.

CONSENT

Written informed consent was obtained from the patient for publication of this case report, including accompanying images.
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