Article
Fasciola Hepatica; demographic, radiological, laboratory findings and their role in acute and chronic differentiation
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Abstract: Background: this study was to investigate demographic, radiological and laboratory features of Fasciola hepatica infection and to determine its effects on acute and chronic differentiation. Methods: Patients with Fasciola hepatica; demographic and laboratory data were obtained retrospectively. The presence of characteristic findings in radiology and / or Fasciola Hepatica IgG positivity in acute phase and endoscopic retrograde cholangiopancreatography revealed fasciola hepatica extraction as chronic phase. Results: A total of 17 patients 1 male (5.9%) and 16 female (94.1%) were included in the study. Of the cases, 10 (58.8%) were acute, 7 (41.2%) were chronic. In 10 cases (58.8%) eusinophils were higher than 5% and normal in the others. In the USG, 7 (40.9%) were normal, 7 (40.9%) were hypoechoic lesions, and 3 were defined as gallbladder Fasciola Hepatica. When compared to acute and chronic Fasciola Hepatica; there was no significant difference in laboratory data (p> 0.005) except albumin (p = 0.009) and platelet count (p = 0.004). Conclusion; female gender, history of eating watercress, the presence of eosinophilia, are finding increased susceptibility to Fasciola hepatica. Laboratory data for acute and chronic differentiation were not helpful but albumin and platelet levels were significantly lower in chronic cases.

Keywords; acute and chronic fasciola hepatica, eosinophilia, ERCP

1. Introduction

With its intermediary host being molluscs, Fasciola hepatica (FH) is observed commonly among such animals as sheep, goats, and cattle. Fasciola hepatica is a trematode from the family of flukes transmitted through the ingestion of watercress or green vegetables or of water containing metacercariae [1]. The fasciola hepatica worm sets off from the duodenum and from there, reaches firstly the peritoneal cavity and secondly the hepatic capsule. Penetrating the hepatic capsule, the worm enters the biliary tracts. Once in the biliary tracts, the helmminth develops and reaches adulthood in 3 months [2, 3]. The infection occurs in two clinical periods, namely the acute phase covering the stage of hepatic invasion and the chronic phase with the parasite involving the biliary tracts [2, 3]. The clinical symptom of acute infection depends on the damage caused by the larvae and the inflammatory response to it. General symptoms in this phase are abdominal pain, weight loss and fever. Eosinophilia and IgE elevation are frequently observed as laboratory findings. Other rare laboratory findings include pulmonary infiltrate with pleural effusion, ascites, hepatic subcapsular hemorrhage and anemia [4]. Chronic stage is characterized by adult parasite living in the hepatic and main bile ducts of the host. Patients are often asymptomatic at this stage. Eosinophilia, fever, and abdominal pain often undergo resolution in this period. In rare cases, mucosal erosion associated with biliary obstruction, ascending cholangitis, acute pancreatitis or hemobilia may occur in infected individuals [5].

The prevalence of FH was reported to be 6.7 to 47.4% (average: 24.4%) among humans in hyperendemic regions [6]. The seroprevalence was specified to be 2.78% in the eastern part of Turkey [7]. The FH infection may occur after travels to high-risk endemic regions including the Nile Delta in Egypt, Iran, Turkey, Southeast Asia, Mexico, the Caribbean, and Andean Altiplano [8].

The parasite is definitively diagnosed upon the identification of parasite eggs in stool or duodenal aspirate. However, this method offers a low chance of diagnosis due to the low number of
eggs produced by the parasite. Therefore, serological methods can be useful for the purposes of diagnosis [9].

Ultrasound imaging (USG) may indicate CBD dilatation, IHBD dilatation, bile duct wall thickening, peripheral hypoechoic nodular lesions, hyperechoic nonshadowing structures filling CBD, parenchymal heterogeneity, coarseness, flukes within the gallbladder, cystic small lesions, gallbladder wall thickening, hilar and celiac lymphadenopathies, hepatomegaly, splenomegaly, thickening of the liver capsule [10]. The most important finding for the infection in biliary phase is, on the other hand, represented by small-sized linear filling defects in the distal choledocus as evidenced by endoscopic retrograde cholangiopancreatography (ERCP) [11, 12].

If in acute phase, the infection is treated only with medication. FH-induced obstructions in the chronic phase of the infection may require ERCP and the drainage of the biliary tracts with the use of a balloon or basket catheter upon sphincterotomy [13]. ERCP stands out as the preferred method for cases in the chronic phase. ERCP allows for both the definitive diagnosis and treatment of the parasite [14, 15].

Aim: The present study aims to examine the demographic, radiological and laboratory characteristics of the Fasciola Hepatica infection and their effects on the differentiation of acute and chronic infections.

2. Results

2.1.1 A total of 17 patients were enrolled in the study including 1 (5.9%) male and 16 (94.1%) female patients (Table 1). The average age of the patients was 46.18 (min-max: 24-83) years (Table 2). The population included 10 (58.8%) acute and 7 (41.2%) chronic cases. The residential areas of the cases were divided between rural areas with 9 cases (52.9%) and urban areas with 8 cases (47.1%) (Table 1). The eosinophil count was higher than 5% in 10 (58.8%) cases and normal in others. The presenting diagnosis was FH in 13 (76.5%) cases; cholestatic enzyme elevation in 2 (11.8%) cases; pancreatitis in 1 (5.9%) case; and malignity in 1 (5.9%) case. The definitive diagnosis was secured with positivity result in serological FH IgG (58.8%) in addition to USG in 10 (59.1%) cases and with ERCP in 7 (41.2%) cases. USG determined 7 (40.9%) to be normal; 7 (40.9%) to have hypoechoic lesions; and 3 (17.5%) to present FH in the gallbladder.

A comparison between acute and chronic cases of FH indicated the average age to be median 45.5 (24-83) years to 46 (32-57) years (p=0.961). Within the context of laboratory testing, there was no significant difference in terms of AST, ALT, GGT, ALP, bilirubin count, and CRP (Table 2) (p>0.005). Albumin count was 4.6 gr/dl to 3.9 gr/dl (p=0.009) and platelet count 300 x 103/uL to 221 x 103/uL (p=0.004) for acute and chronic cases, respectively, and these results were statistically significant.

Chronic cases had been treated with ERCP + 10 mg/kg triclanendazol, while acute cases had been managed only with triclabendazol at 10 mg/kg (Table 1).

The laboratory data pertaining to the cases were as specified in Table 2.

2.2 Tables

Table 1: Demographic and laboratory data for all patients

<table>
<thead>
<tr>
<th>No.</th>
<th>age</th>
<th>sex</th>
<th>residence</th>
<th>ac(chr)</th>
<th>FH IgG</th>
<th>treatment</th>
<th>Eus (%)</th>
<th>amylase</th>
<th>alb</th>
<th>plt</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>34</td>
<td>F</td>
<td>Rural</td>
<td>chronic</td>
<td></td>
<td>ERCP+tricl</td>
<td>7.4</td>
<td>94.00</td>
<td>3.8</td>
<td>166</td>
</tr>
<tr>
<td>2</td>
<td>45</td>
<td>F</td>
<td>Urban</td>
<td>chronic</td>
<td>30</td>
<td>ERCP+tricl</td>
<td>0.4</td>
<td>17.00</td>
<td>4.3</td>
<td>250</td>
</tr>
<tr>
<td>3</td>
<td>50</td>
<td>F</td>
<td>Rural</td>
<td>chronic</td>
<td>10</td>
<td>ERCP+tricl</td>
<td>14</td>
<td>-</td>
<td>4.2</td>
<td>306</td>
</tr>
<tr>
<td>4</td>
<td>57</td>
<td>F</td>
<td>Urban</td>
<td>chronic</td>
<td></td>
<td>ERCP+tricl</td>
<td>17.6</td>
<td>2666.00</td>
<td>3.8</td>
<td>225</td>
</tr>
<tr>
<td>5</td>
<td>32</td>
<td>M</td>
<td>Rural</td>
<td>chronic</td>
<td></td>
<td>ERCP+tricl</td>
<td>4.3</td>
<td>78.00</td>
<td>3.9</td>
<td>206</td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>F</td>
<td>Urban</td>
<td>chronic</td>
<td></td>
<td>ERCP+tricl</td>
<td>0.04</td>
<td>43.00</td>
<td>3.7</td>
<td>221</td>
</tr>
<tr>
<td>7</td>
<td>46</td>
<td>F</td>
<td>Urban</td>
<td>chronic</td>
<td>15</td>
<td>ERCP+tricl</td>
<td>9.1</td>
<td>86.00</td>
<td>4.3</td>
<td>201</td>
</tr>
<tr>
<td>8</td>
<td>51</td>
<td>F</td>
<td>Rural</td>
<td></td>
<td>40</td>
<td>Tricl</td>
<td>14.3</td>
<td>75.00</td>
<td>4.23</td>
<td>279</td>
</tr>
<tr>
<td>9</td>
<td>38</td>
<td>F</td>
<td>Rural</td>
<td></td>
<td>30</td>
<td>Tricl</td>
<td>60.8</td>
<td>45.00</td>
<td>4.5</td>
<td>278</td>
</tr>
</tbody>
</table>

Table 2: Laboratory characteristics of patients.

<table>
<thead>
<tr>
<th></th>
<th>Acute (n=10)</th>
<th>Chronic (n=7)</th>
<th>Total (n=17)</th>
<th>P (&lt;0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (25-75%)</td>
<td>Median (25-75%)</td>
<td>Mean (min-max)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>45.5 (24-83)</td>
<td>46 (32-57)</td>
<td>46.18 (24-83)</td>
<td>0.961</td>
</tr>
<tr>
<td>Hb (gr/dl)</td>
<td>13.15 (12.5-13-62)</td>
<td>13 (11.7-13.3)</td>
<td>12.76 (9.9-13.9)</td>
<td>0.433</td>
</tr>
<tr>
<td>Leucocytes (x103/uL)</td>
<td>10.12 (6.4-17.35)</td>
<td>5.6 (5.2-8.82)</td>
<td>10.13 (4.9-23.29)</td>
<td>0.51</td>
</tr>
<tr>
<td>Platelet (x103/uL)</td>
<td>300 (278.75-333.75)</td>
<td>221 (201-250)</td>
<td>271 (166-349)</td>
<td>0.004</td>
</tr>
<tr>
<td>Eosinophil (x103/uL)</td>
<td>0.52 (0.14-5.2)</td>
<td>0.38 (0.03-0.51)</td>
<td>2.29 (0-16.45)</td>
<td>0.204</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>30.5 (12.75-59.25)</td>
<td>50 (20-644)</td>
<td>110.41 (12-701)</td>
<td>0.305</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>23 (14.5-38.75)</td>
<td>27 (17-137)</td>
<td>61.64 (11-5537)</td>
<td>0.526</td>
</tr>
<tr>
<td>GGT (U/L)</td>
<td>27.5 (10.5-62.25)</td>
<td>84 (14-206)</td>
<td>79.94 (7-444)</td>
<td>0.118</td>
</tr>
<tr>
<td>ALP (U/L)</td>
<td>95 (66-215)</td>
<td>107 (76-179)</td>
<td>125.58 (45-266)</td>
<td>0.591</td>
</tr>
<tr>
<td>Total bilirubin (mg/dl)</td>
<td>0.3 (0.26-0.71)</td>
<td>0.37 (0.233-3.9)</td>
<td>1.01 (0.13-6.28)</td>
<td>0.524</td>
</tr>
<tr>
<td>Sedimentation (mm/hour)</td>
<td>30 (15.5-41.5)</td>
<td>17 (11.5-38.25)</td>
<td>28.15 (11-60)</td>
<td>0.315</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>3.27 (2.92-6.5)</td>
<td>7.5 (2.57-35)</td>
<td>17.66 (0.14-149)</td>
<td>0.328</td>
</tr>
<tr>
<td>Amylase (U/L)</td>
<td>66 (69.5-91)</td>
<td>82 (51.75-2021)</td>
<td>255 (17-2666)</td>
<td>0.379</td>
</tr>
<tr>
<td>Albumin</td>
<td>4.6 (4.19-4.64)</td>
<td>3.9 (3.8-4.3)</td>
<td>4.27 (3.7-4.8)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Statistically significant items are shown in bold (P<0.05).

3. Discussion

FH infection is observed endemically among people in certain geographical regions. Its prevalence was identified to range from very low to very high [18]. In recent years, this infection has been seen to occur commonly among individuals along with climatic and global changes. In addition, the infection is considered to be increasingly significant by reason of its elevated pathogenicity in acute and advanced chronic phases in the endemic regions of developing countries [19].

FH infection may be divided in clinical and laboratory terms into two different periods, namely the acute phase involving hepatic parenchyma to a greater extent and the chronic phase affecting the biliary system [20].
The percentage of female cases was identified to be 88.2% by Akpınar MY et al. [21] and 86.3% by Kaya M et al. [22]. Similarly, 16 (94.1%) out of 17 cases in the present study were female. The main cause of parasitic transmission in our study was the ingestion of watercress. Watercress is consumed most commonly by housewives.

A history of ingesting watercress and the presence of eosinophils increase the chances of FH infection [23]. The presence of eosinophils was found at 79% by Ülger et al. [24] and 82% by Akpınar MY et al. [21]. The present study identified the percentage of eosinophils to be lower, i.e. at 58.8%. We did not determine the occurrence of eosinophils in our region at percentages as high as those reported in the literature.

A review of the residential information pertaining to the cases indicated in a study concerning 17 chronic cases of FH infection had found 10 cases to be residing in urban areas and 7 in rural locations [21]. The breakdown of the cases in the present study by residential location was 9/8 for urban/rural residence, which constituted a finding consistent with that in the relevant literature.

Imaging methods are of great significance for the diagnosis of FH infections. Transabdominal ultrasound imaging may indicate lesions in the biliary tract although not as a finding specific to FH infection [25]. Sezgin et al; normal ultrasonographic findings in 3 (42.2%) of seven cases, common bile duct dilatation in 1 (14.2%) case, dilated common bile duct filled with tissue in the same echogenic tissue as liver tissue 1 (14.2%), 1(14.2%) had echogenicity in the gallbladder and 1 (14.2%) had a polyphosphate polyp [26]. Similarly, the present study found normal USG in 7 (%41,2) cases, hypoechoic lesions in 7 (41.2%) cases and FH in the gallbladder in 3 (17.6%) cases. Ultrasound findings offer a method that may assist in the diagnosis as complementary elements for other findings rather than provide for definitive diagnosis.

FH seated in the biliary tracts in the chronic phase may be evident with the manifestation of biliary colic, jaundice or cholangitis. Certain patients had also been diagnosed upon pancreatitis [5]. Kaya M et al. identified acute pancreatitis in 3 (37.5%) out of 8 cases of FH infection [11]. The present study observed a diagnosis of acute pancreatitis (along with eosinophils) in 1 (14.2%) out of 7 cases of chronic FH infection. The differential diagnosis for cases with eosinophils coupled with acute pancreatitis should take into consideration the possibility of FH infection.

A comparison between acute and chronic cases of FH infection indicated cholestatic enzyme levels including AST, ALT, GGT, ALP, and bilirubin and CRP values, but such differences were not statistically significant (p > 0.05) (table 2).

Hypoalbuminemia can be seen as a result of the combined effects of inflammation, inadequate protein and caloric intake in patients with chronic disease. Inflammation and malnutrition reduce the concentration of albumin by reducing the rate of synthesis. Inflammation alone leads to a greater fractional catabolic rate and more albumin out of the vascular compartment when inflammation is excessive. A vicious cycle occurs in which inflammation creates anorexia, decreases the effective use of dietary protein and energy intake, and increases catabolism of important somatic protein and albumin. Inflammation is associated with vascular diseases and possibly causes damage to the vascular endothelium and may cause hypoalbuminemia [27]. In our study, albumin levels in acute and chronic cases were 4.6 g / dl and 3.9 g / dl (p = 0.009), respectively (Table 2), and were significantly lower in chronic cases. Prospective studies need to be conducted with the inclusion of a larger sample of cases to explain the relatively low albumin in chronic FH.

Platelet production can be reduced by low levels of thrombopoietin (TPO) and direct bone marrow suppression. Hepatic production of TPO plays an important role in thrombopoiesis. TPO regulates platelet production and maturation [28]. TPO is performed by both parenchymal cells and sinusoidal endothelial cells in the liver and released into the circulation at a constant rate [29]. In cases such as drugs, viruses, autoimmune diseases, cirrhosis, etc. hepatic TPO production is affected and platelet count decreases [30]. In our study, platelet count was 300 x103 / xL and 221 x103 / 300L (p = 0.004) in acute and chronic FH cases, respectively, and significantly lower in chronic cases. In chronic FH cases, we think that the lower platelet count is due to decreased hepatic TPO production. Prospective
studies need to be conducted with the inclusion of a larger sample of cases to explain the relatively low platelet counts in chronic FH.

4. Materials and Methods

In this study, ethics committee approval was obtained with Diyarbakır Gazi Yasargil Training and Research Hospital dated 12/12/2018 and numbered 456. Between January 2014 and December 2018, the demographic data including age, sex, and place of residence (urban or rural area) and clinical findings at the time of presentation for patients diagnosed with FH were queried retrospectively on the IT system operated by the hospital. Laboratory data were also queried for the cases including FH serological testing, leucocyte count, haemoglobin count, haematocrit value, platelet count, eosinophil count (rates over 5% and counts over 500 u/l were considered to be high), urea count, creatinine count, sodium count, potassium count, AST ALT, GGT, ALP, total/direct bilirubin count, amylase count, lipase count, CRP, and sedimentation testing. The IT system operated by the hospital was consulted retrospectively to identify whether the ERCP findings had resulted in the identification of FH infection on the basis of ERCP findings, to determine the relevant ultrasound findings, and to confirm whether the patients had received treatment.

With respect to the diagnosis of FH infection, the presence of characteristic findings for FH [16, 17] and/or a positive result in serological testing for FH were considered to indicate the acute phase and the extraction of live FH in ERCP to point out to the chronic phase of the infection.

For the purposes of diagnostic testing for FH, DRG Fasciola Hepatica IgG ELISA (EIA-4503, DRG Instruments, Germany) kits were employed as the test that secures early diagnosis in FH at the highest level of sensitivity (100%) and specificity (100%). The cut-off value for the kits was 11.5 DRG units (DU). Fasciola hepatica IgG > 11.5 DU was considered positive.

All patients that had undergone ERCP were made subject to sphincterotomy and hepaticolithotomy.

All patients included in the study had received triclabendazol at 10 mg/kg.

Cases without the complete set of data were excluded from the study.

5. Conclusion

The female sex, ingestion of watercress, and presence of eosinophils constitute findings that raise suspicion for infection with fasciola hepatica. Laboratory data do not appear to assist the differentiation between acute and chronic cases to a great extent, but albumin and platelet counts are lower among chronic cases. This fact points out to a need for prospective studies incorporating a larger sample of cases.

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Conflict of Interest: Declare conflicts of interest “The authors declare no conflict of interest”.

References


