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Case Report

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Hepatic visceral larva migrans diagnosed clinically as cholangiolocarcinoma

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Abstract

Hepatic visceral larva migrans is diagnosed mainly on symptoms, mass appearance, laboratory data, and other visceral findings. A 36-year-old male was referred to our hospital for a liver mass suspected of being malignant. A single 30 mm low-echo mass with sharply defined vessel penetration in the middle was subsequently diagnosed clinically as cholangiolocarcinoma. However, the patient had a laparoscopic hepatic partial resection, with pathology indicating a diagnosis of hepatic visceral larva migrans. This case shows that hepatic visceral larva migrans may appear similar to hepatic malignancies and that vessel penetration through the mass is a key diagnostic factor of this disease.

Keywords: Hepatic visceral larva migrans; Cholangiolocarcinoma; Benign liver mass.

Introduction

Hepatic Visceral Larva Migrans (VLM) is a disease initially suspected mainly according to its symptoms, other systemic findings, and laboratory data especially hyper-eosinophilia and high serum levels of IgE. However, there are cases reported where the hepatic mass caused by VLM was misdiagnosed as a malignant tumor due to it being the only clinical finding. It is quite difficult to suspect hepatic VLM using images of a liver mass, and as a consequence the disease is often underdiagnosed or misdiagnosed as a malignant tumor such as a metastatic hepatic carcinoma. To date, a few cases have been reported in which hepatic VLM was diagnosed after resection. We report a rare case of a man who was diagnosed clinically as cholangiolocarcinoma (CoCC), which turned out to be a hepatic VLM, diagnosed after the patient underwent a hepatectomy followed by a pathological examination.

Case report

A 36-year-old Japanese man, who had been living in Thailand for a few years, was referred to our hospital after an asymptomatic 32 x 25 x 22 mm mass was detected on abdominal ultrasound at his health check-up in Thailand. An ultrasound one year earlier showed no abnormality and therefore a new malignant tumor was suspected. The patient had no symptoms, did not recall any sickness in the past year, nor report any loss of appetite or weight loss. His past medical history and family history were not significant, and he was negative for Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV). His body mass index was 20.3 kg/m^2, he drank no alcohol, and he was living with his wife who cooked healthy food. Laboratory examinations revealed normal liver function parameters with aspartate aminotransferase 12 IU/L, alanine aminotransferase 10 IU/L, alkaline phosphatase 46 IU/L, glutamyl transpeptidase 24 IU/L, and T-bilirubin 1.0 mg/

dL. The FIB-4 index was 0.54. Renal function and coagulation profile were also normal. The white blood count was 5100 /μL with 8.8% eosinophils and 58.5% neutrophils. The C-Reactive Protein (CRP) level was 0.01 mg/dL and tumor markers were all within the normal limits (alpha-fetoprotein (AFP) 2.1 ng/mL, Des-γ-Carboxy Prothrombin (DCP) 24 μg/mL, Carcinoembryonic Antigen (CEA) 4.4 ng/mL, and cancer antigen 19-9 (CA19-9) 21 U/mL).

Ultrasound performed at our hospital revealed a dull edged liver with a heterogenous hypoechoic 30 mm mass at S4 with a high echoed edge and blood flow in the middle. No ductal dilation was observed. Plain computed tomography showed an irregular hypoechoic mass at S4, while contrast-enhanced Computed Tomography (CT) revealed a hypoechoic mass on the arterial phase, and late enhancement on the margin in the portal to equilibrium phase. In the portal phase, the portal vein P4 was clearly seen to be penetrating through the mass (Figure 1). No other hepatic mass was identified.

Magnetic Resonance Imaging (MRI) showed a mass in S4, slightly hypointense on T1-weighed images, and hyperintense on T2-weighed and Diffusion-Weighted Images (DWI). Dynamic contrast-enhancement with gadolinium chelate established both early and late phase hypo-enhancement. The hepatobiliary phase showed uneven enhancement of the mass with some normal liver cell structures. ^{18}F – fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (PET) showed no abnormal uptake of FDG by the liver mass nor a sign of malignancy anywhere else in the body. Upper endoscopy and colonoscopy also showed no abnormality. Hepatic angiography showed a possible fibrous stroma with no artery, although one portal vein (P4) was observed to penetrate through the mass (Figure 2). Contrast-enhanced ultrasound using Sonazoid™ (hydrogenated egg phosphatidylserine stabilized perfluorobutane, GE Healthcare, Little Chalfont, UK) showed an even clearer view of a vessel penetrating through the hypoechoic mass. As shown in Figure 3, there was minor enhancement on the margin of the mass but not at the center on a Kupffer image.

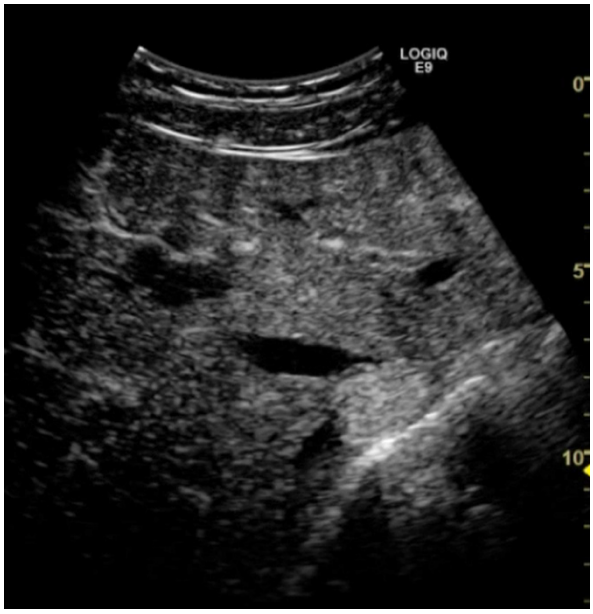

Figure 1: Contrast-enhanced CT showing P4 penetration through the mass in the portal phase. * CT: Computed Tomography.

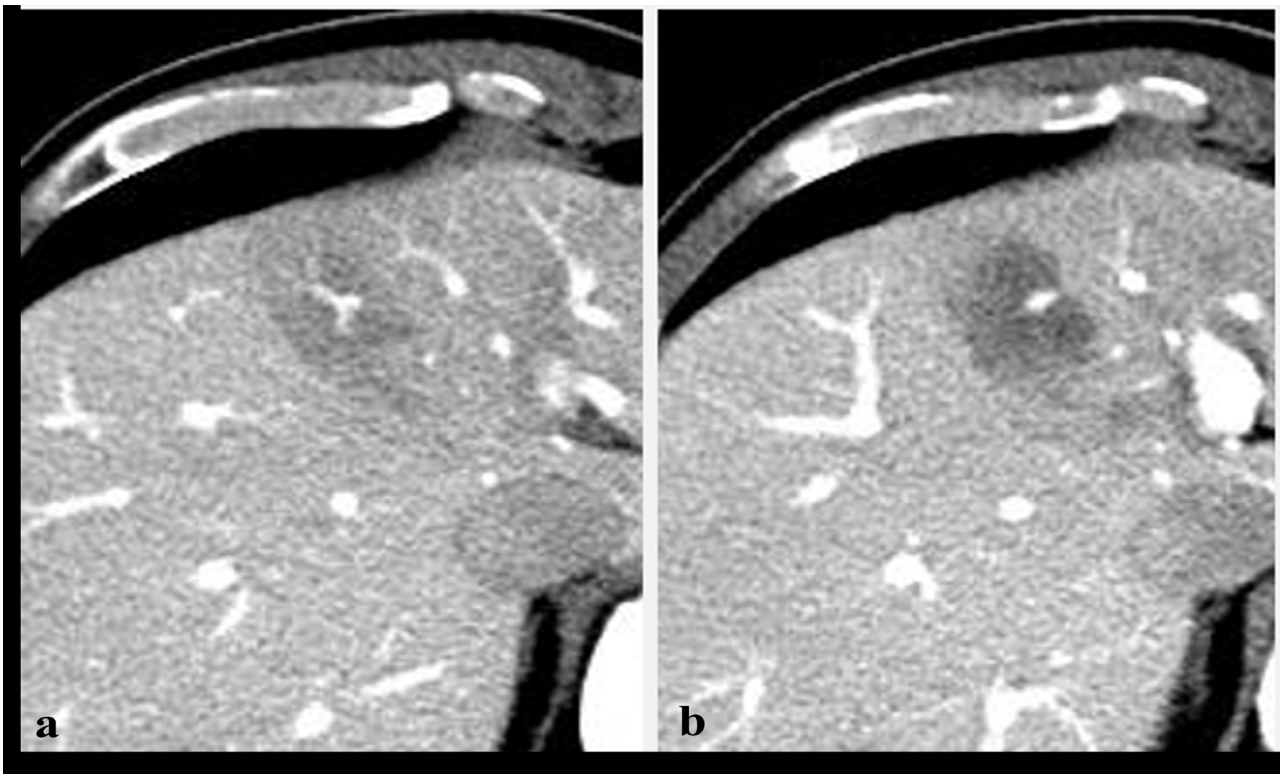

Figure 2: a) Hepatic angiography showing a possible fibrous stroma with no artery. b) Hepatic angiography showing one portal vein (P4) penetrating through the mass.

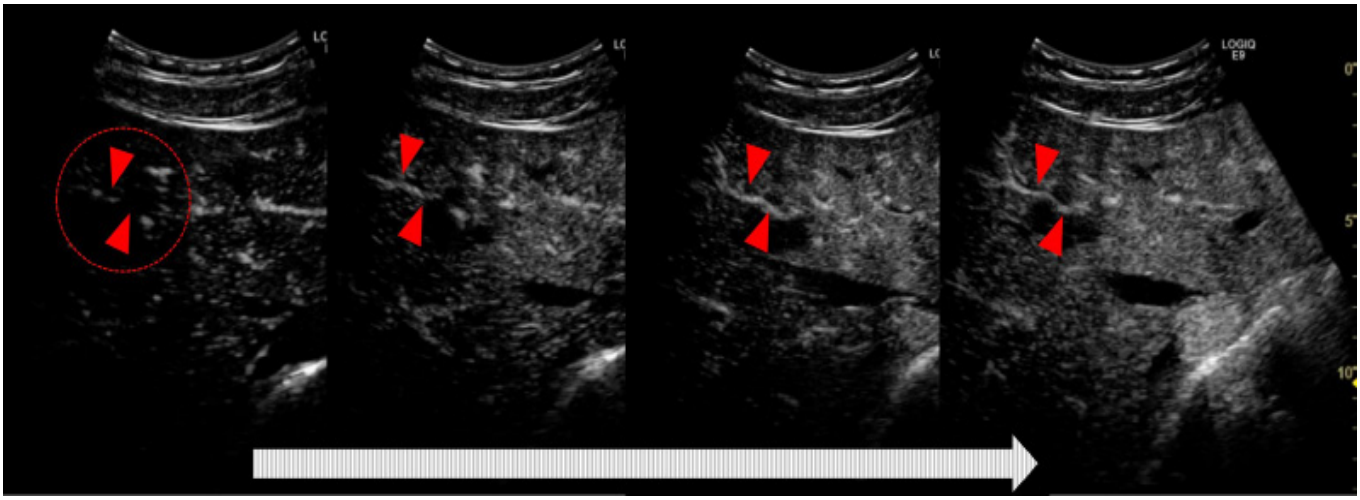

Figure 3: Contrast-enhanced Sonazoid™ ultrasound showing a clear view of vessel penetration through the mass (arrows). The mass is low echoed with minor enhancement on its margins, but not at the center.

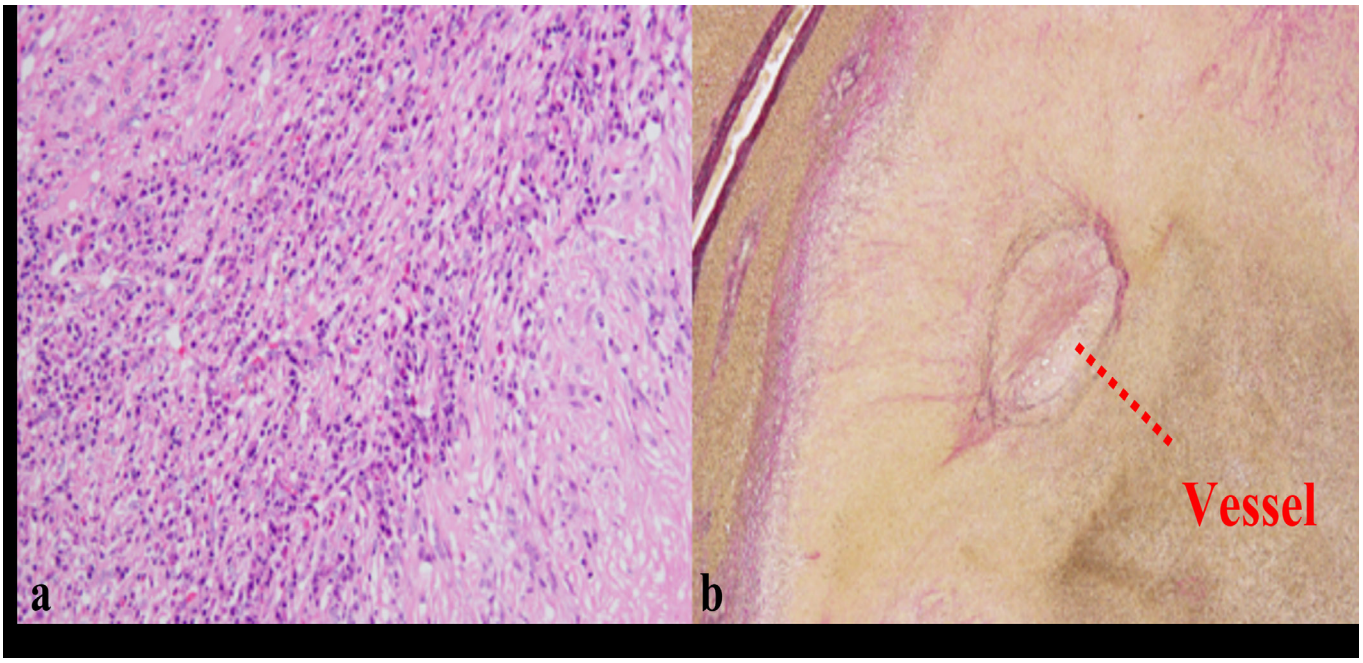

Figure 4: a) Eosinophils and neutrophils with necrotic tissue. b) A vessel-like appearance is seen in the middle of the mass.

As described, most of the image findings and morphologies were consistent with a CoCC. Therefore, the mass was diagnosed clinically as a CoCC, although tumor markers were low and the mass was PET negative. Other radiological differential diagnoses included an intrahepatic cholangial carcinoma and a metastatic hepatocellular carcinoma of unknown origin. Based on the clinical diagnosis and these differentials, a resection was the first treatment choice.

A laparoscopic hepatic S4 partial resection was performed. A mass with clear margins was clearly observable, with no major adverse events occurring during surgery. The patient recovered without any adverse events and was discharged on post-operative day eight. Follow-up laboratory data one month later showed no abnormality, with an eosinophil proportion of 8.0%.

Pathological examination showed the mass was a 29 x 19 x 16 mm yellowish-white tumor with background liver F0-1A0-1. The mass was filled with mixed inflammatory cells, necrotic degenerated tissue, and abscesses. Eosinophilic degeneration was seen with fibrotic changes and granulation tissues around the entire margin of the mass. There was a vessel-like assemblance in the middle of the mass. These findings were consistent with hepatic VLM, which was confirmed as the pathological diagnosis of the mass (Figure 4).

Discussion

We report a case initially diagnosed as a CoCC which was subsequently diagnosed as a hepatic VLM. Our initial diagnosis was considered after a thorough work-up of images. We initially, before resection, did not have sufficient information in this case to suggest hepatic VLM as one of the differential diagnoses.

VLM is a disease that involves migration of larvae through tissues of the human viscera. Parasites found in the intestines of animals, mainly dogs and cats, are the cause of the disease. Humans become infected when they consume food such as fruits and vegetables that have been in contact with infected soil mixed with feces containing eggs of the parasites. When humans consume the eggs, this may affect multiple visceral organs, with the liver known to be the most involved site followed

by the lungs and eyes. After hatching in the intestine, the larvae penetrate the intestinal wall and flow through the portal vein to reach the liver, where they form a mass mimicking a tumor. The mechanism of liver infiltration is believed to be an allergic response to the larva [1]. The mass is therefore filled mainly with mixed inflammatory cells predominantly numerous eosinophils, neutrophils, and lymphocytes with necrotic lesions. These characteristics were found in the current case.

In many cases the disease is asymptomatic, and even if the symptoms appear they are nonsignificant such as fever, general malaise, and cough. The most important serological findings are an unexplained eosinophilia and high serum IgE level. Studies have shown that the absolute eosinophil count has significant predictive value for diagnosing VLM [2].

Most hepatic VLM exist as multiple masses and are ill-defined hypodense oval shaped lesions. On enhanced CT scans, nodules of hepatic VLM are seen as faint rim-enhancing lesions in the arterial phase, seen most conspicuously in the portal venous phase appearing as low-attenuating lesions, and then becoming barely visible in the equilibrium phase [3]. The lesions tend to be located on the periphery of the liver and along the portal vein branches. In the current case, the liver mass was located at the periphery of the liver along the portal vein branches, although the mass was visible in all three phases on contrast-enhanced CT scans.

Generally, a CoCC is seen on CT as an iso-hyper enhanced tumor with peripheral enhancement and a concentric delayed filling. The presence of portal venous penetration within the tumor is a unique characteristic of this disease. The mass we examined conformed exactly with this pattern. A CT scan, angiography, Sonazoid™ ultrasound, and MRI all showed signs of penetration of the portal vein through the mass which was a unique finding.

The three findings in this patient inconsistent with a diagnosis of a CoCC were that he had no background liver disease, all the tumor markers were negative, and the mass was PET negative.

CoCC is a type of hepatocellular-cholangiocarcinoma thought to originate from cholangioles or the canals of Hering, where hepatic progenitor or stem cells are located [4]. CoCC is derived mainly from chronic liver failure including HBV and HCV after repetitive damage to liver cells. However, recent reports have shown that about 33% of CoCC are not associated with a background of liver failure, a trend more common in younger patients [5]. Although our patient did not have a background of liver disease, there was insufficient evidence to rule out a CoCC.

The sensitivity of tumor markers in all hepatocellular-cholangiocarcinomas is low. Above normal levels of CEA and CA19-9 are seen in about 18% and 69% of cases, respectively. Accordingly, we could not rule out the possibility of malignancy.

The finding of a PET negative mass was one point that we could have investigated more extensively. Micro cancers of CoCC may sometimes be PET negative [6]. However, our mass was about 30 mm in size and a malignancy of this size would likely be PET positive. Biopsy would have been an option at this point after the finding of a PET negative mass. However, even if the biopsy had revealed no sign of malignancy, this would not have stopped us from ruling out malignancy and suggesting surgery.

Hepatic VLM without other organ invasion is often diagnosed using either an enzyme-linked immune-specific assay or liver biopsy. In Japan, about 40% of all hepatic VLM cases have a liver biopsy. As mentioned earlier, liver biopsy was a procedure we could have performed before deciding the treatment. However, taking in account that the patient was living in Thailand, had returned to Japan just for the treatment of the mass, and due to the COVID-19 prevalence at the time his schedule could not be fixed smoothly and only had a few weeks of available period of stay in Japan, he was in a rush to complete treatment and waiting for the biopsy results was not ideal. In addition, a liver biopsy had the risk of spreading tumor cells to a broader area. We were assuming the mass as a CoCC and did not want to disseminate and tumor cells. Looking back, biopsy could have been the best option before deciding on the treatment in this patient as the mass had some inconsistency with malignancy; however, the patient and we decided to skip the procedure.

Because our patient did not have any symptoms or significant eosinophilia, known as the most crucial factor for suspecting VLM, the disease was not included as a differential diagnosis. It is important to note that the proportion of eosinophils was slightly elevated on admission, but did not decline after surgery, indicating that hepatic VLM was not the cause of the eosinophilia. We did not measure serum IgE levels.

Eosinophilic infiltration with necrosis and micro-abscesses in a hepatic mass are commonly caused by the larvae of parasites [7]. Studies on Focal Eosinophilic Infiltration (FEI) have reported the following findings. In MRIs, FEI is typically hypointense on T1WI, hyperintense on T2WI, and hypointense on portal phase images. 89% of CT scans show the mass on portal phase images, compared to 36% of images in the arterial phase, with most only showing up during the portal phase. 20% of all FEIs are PET positive. In addition, because the inflammatory cells spread randomly, they are mostly ill-defined. There is also evidence from one study that branches of the portal vein went through the mass in all the cases of FEI investigated [8].

There was one published paper reporting a case of hepatic VLM with portal vein penetration, with findings similar to those of the present case, except with patient having an extremely high eosinophil count and serum IgE levels [9]. Because the larvae are distributed by portal blood flow from the intestines, there is a distinct chance that occlusion at the peripheral portal vein may occur due to the larva itself. When the portal vein is occluded, inflammatory cells proliferate around the peripheral section which may look like a vessel penetrating through the mass. The mass becomes edge-shaped because it represents the focus of venous congestion due to occlusion of the portal venules by larva. This provides an important reason to consider hepatic VLM as a differential diagnosis in cases where a mass is penetrated by a vessel at the periphery of the liver.

The limitation of this report is that specific specie of the parasite could not be identified in this case. Because malignancy was our initial diagnosis, we did not spare his serum and body fluid samples taken before the mass resection. Thus, further immunological investigation could not be performed including ELISA and IgE assay. Also, remnants of parasites are only found in about 23% of all hepatic VLM cases [10]. We could not identify the species in the current case because there were no recognizable parasites in the hepatic mass. Hepatic VLM have similar pathology and are many times diagnosed by their appearance. However, this is a very valuable case as it shows the significance

Table 1: Cases which hepatic VLM was diagnosed after resection diagnosed between 2010 and 2022 [11-15].

	Year	Country	Age	Sex	Eosino.	Size	#of mass	PMH	Tumor markers	PET/CT	Other masses	Initial diagnosis	Final diagnosis
1	2011	Japan	51	M	7.20%	1cm	1	HBV			none	malignant tumor	Ascaris
2	2012	Japan	58	M	7.30%	13cm	1		w.n.l.	high	none	hepatobiliary carcinoma	Ascaris
3	2012	Turkey	47	F		obstructive jaundice	1	none	w.n.l.		none	cholangiocarcinoma	Fascioliasis
4	2017	Iran	2.5	F	4%		1	none			retroperitoneal mass	neuroblastoma	Toxocariasis
5	2019	Turkey	26	F	high (nonspecific)	6cm	1	none	w.n.l.		none	tumor (nonspecific)	Fascioliasis
6	2019	Turkey	52	F	high (nonspecific)	2.5cm	1	none	w.n.l.	w.n.l.	colon	tumor (nonspecific)	Fascioliasis
7	2022	Japan	36	M	8.80%	2.9cm	1	none	w.n.l.	w.n.l.	none	CoCC	a type of VLM

PET/CT, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography; HBV, Hepatitis B Virus positive; w.n.l., within normal limit.

of performing a tumor biopsy for a malignancy looking mass with some inconsistencies to prevent unnecessary surgeries.

Since 2010, seven cases including ours could be found on PubMed in which hepatic VLM (wide definition including toxocariasis, ascaris, and fascioliasis) was diagnosed after resection (Table 1). All these cases were diagnosed initially as malignant before surgery. The mass was found in the liver in all cases, and none had liver disease prior to the appearance of the mass. None of the seven patients had a liver biopsy beforehand.

Most cases of toxocariasis are self-limiting or are treated by mebendazole, a specific medication, and resection is not the first treatment choice. Because the lesion is often self-limiting, many of the cases are treated without ever being found. We should be aware that VLM is a differential diagnosis when image findings appear to have characteristics common to a CoCC. More studies of the images of hepatic VLM are needed in order to decrease the number of misdiagnoses of this disease, especially in the world where annual routine health checkups are easily conducted.

References

1. Sakai S, Shida Y, Takahashi N, Yabuuchi H, Soeda H, et al. Pulmonary lesions associated with visceral larva migrans due to Ascaris suum or Toxocara canis: imaging of six cases. AJR Am J Roentgenol. 2006; 186: 1697-702.
2. Laroia ST, Rastogi A, Bihari C, Bhadoria AS, Sarin SK, et al. Hepatic visceral larva migrans, a resilient entity on imaging: Experience from a tertiary liver center. Trop Parasitol. 2016; 6: 56-68.
3. Chang S, Lim JH, Choi D, Park CK, Kwon N-H, et al. Hepatic visceral larva migrans of Toxocara canis: CT and sonographic findings. AJR Am J Roentgenol. 2006; 187: W622-9.
4. Jung W, Kim BH. Cholangiolocellular carcinoma with satellite nodules showing intermediate differentiation. Clin Mol Hepatol. 2015; 21: 183-186.
5. Kitami C, Kawachi Y, Igarashi T, Makino S, Nishimura A, et al. Cholangiolocellular carcinoma arising in a normal liver. Jpn Soc Gastroenterol Surg. 2016; 49:1006–15.
6. Higashi T, Ito K, Torizuka K. Clinical Usefulness of [18F] FDG-PET for Diagnosis of Hepatocellular Carcinoma, Cholangiocarcinoma and Gall Bladder Carcinoma—An Analysis Based on Multicenter Questionnaire Survey-Radioisotopes. 2018; 57:1-11.
7. Claeys W, Delie A, Smeets P, De Scheerder M-A, Degroote H, et al. A. Focal eosinophilic infiltration of the liver, benign or malignant? Clin Case Rep. 2021;9: e04448.
8. Guo BL, Hu QG, Ouyang FS, Zhang B, Dong Y-H, et al. CT and MRI findings in focal eosinophilic infiltration of the liver. Abdom Radiol (NY). 2017; 42:2874-81.
9. Rohilla S, Jain N, Yadav R, Dhaulakhandi DB. Hepatic visceral larva migrans. BMJ Case Rep. 2013; 2013: bcr2013009288.
10. Kaplan KJ, Goodman ZD, Ishak KG. Eosinophilic granuloma of the liver: a characteristic lesion with relationship to visceral larva migrans. Am J Surg Pathol. 2001; 25: 1316-21.
11. Takasaki J, Katagiri S, Kotera Y. A Case of Hepatic Eosinophilic Granuloma Due to Visceral Larva Migrans. J Jpn Surg Assoc. 2011; 72: 2882-2888.
12. Yotsukura M, Suzuki K, Munehisa K, Osaku M. A Case Report of Visceral Larva Migrans Treated by Hepatectomy that was Difficult to Diagnose Preoperatively. J Jpn Surg Assoc. 2013; 74: 1655-60.
13. Yalav O, Yağmur Ö, Ülkü A, Akcam AT, Sönmez H. A rare cause of obstructive jaundice: Fasciola hepatica mimicking cholangiocarcinoma. Turk J Gastroenterol. 2012; 23: 604-607.
14. Ghoroobi J, Mohajerzadeh L, Khoddami M, Mirshemirani A, Sadeghian N, et al. Abdominal Mass Secondary to Human Toxocariasis. APSP J Case Rep. 2017; 8: 4.
15. Şamdanci E, Şahin N, Dağli AF, Akatli AN, Aydin NE, et al. Fascioliasis: A Rare Parasitic Infection-Mimicking Tumor in the Liver: Report of Two Cases. Turk Patoloji Derg. 2019; 35:58-60.