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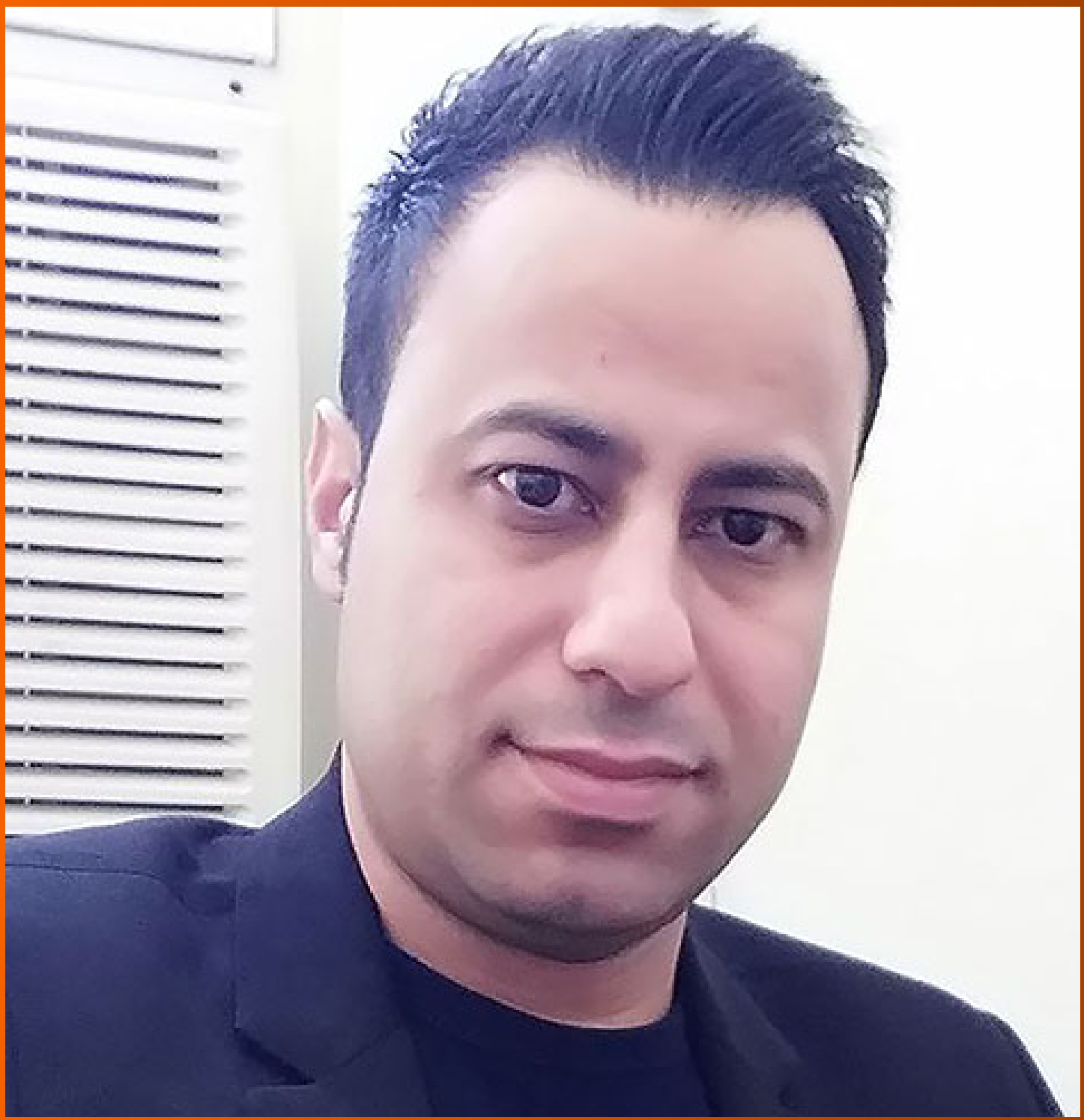

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World Journal of Clinical Cases

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ABOUT COVER

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CASE REPORT

Malignant transformation of biliary adenofibroma combined with benign lymphadenopathy mimicking advanced liver carcinoma: A case report

Shao-Cheng Wang, Yan-Yan Chen, Fei Cheng, Hai-Yong Wang, Fu-Sheng Wu, Li-Song Teng

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Abstract

BACKGROUND

Biliary adenofibromas (BAFs) are rare primary hepatic neoplasms, some of which can potentially undergo malignant transformation. Here, we describe a rare case of malignant transformation of BAF.

CASE SUMMARY

A 51-year-old female was referred to our hospital with epigastric pain. Computed tomography showed a solitary liver mass combined with the enlargement of multiple mediastinal and cervical lymph nodes, clinically mimicking a liver carcinoma with extensive lymph node metastasis. However, core needle biopsy suggested BAF with malignant transformation. Finally, the patient underwent curative resection of the neoplasm and was recurrence-free for 12 mo.

CONCLUSION

Our case serves as an example of a rare manifestation of BAF. Our report and the previously published experience, reinforce that curative resection should be considered the primary treatment for BAFs with malignant transformation, leading to a favorable prognosis.

Key Words: Biliary adenofibroma; Malignant transformation; Lymphadenopathy; Surgery; Case report

Core Tip: Biliary adenofibromas (BAFs) are rare primary hepatic neoplasms, some of which have potential of malignant transformation. Here we describe a rare case of malignant transformation of BAF presented with epigastric pain, whose imaging showed solitary liver mass combined with enlargement of multiple mediastinal and cervical lymph nodes, clinically mimicking a liver carcinoma with extensive lymph node metastasis. The patient was treated with curative resection of the neoplasm and has been recurrence-free for 12 mo. Our case is a rare manifestation of BAF and our experience supported that curative resection should be considered the primary treatment for BAFs with malignant transformation, which leads to a favorable prognosis.

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INTRODUCTION

Biliary adenofibromas (BAFs) are rare primary neoplasms of the liver first described by Tsui *et al*[1] in 1993, most of which are benign biliary cystic tumors[2,3]. Although BAFs are benign tumor with indolent biological behavior, some BAFs have the potential to undergo malignant transformation, leading to transition to invasive carcinoma. To date, few cases of BAFs with malignant features have been reported[4,5].

In the present report, we describe an extremely rare case of malignant transformation of BAF combined with benign lymphadenopathy, which clinically mimicked liver carcinoma with extensive lymph node metastasis. The patient underwent a complete surgical resection of the disease. Meanwhile, we provide a brief review of literature concerning malignant transformation of BAFs.

CASE PRESENTATION

Chief complaints

A 51-year-old female with a 2-mo history of epigastric pain.

History of present illness

The pain was barely noticeable initially and steadily worsened thereafter. On the initial evaluation, she had loss of appetite, a 5 kg weight loss, and denied nausea, vomiting, or jaundice. The patient had periodic episodes of fever ranging from 37.5°C to 38.6°C for about a week.

History of past illness

The patient had laparoscopic cholecystectomy 6 years ago. Other medical, surgical, psychosocial, and family histories were non-contributory.

Personal and family history

The patient denied any family history.

Physical examination

Physical examination revealed mild epigastric tenderness that was otherwise unremarkable.

Laboratory examinations

The patient had an elevated C-reactive protein (CRP) of 75.1 mg/L, while the white blood cell count was within the normal range. The tumor markers alpha-fetoprotein, carcinoembryonic antigen, and cancer antigen 19-9 were within normal ranges. Liver function was normal, and serology was negative for hepatitis B and hepatitis C virus infections.

Imaging examinations

The patient was referred to an oncologic surgeon. Contrast abdominal computed tomography (CT), and subsequent magnetic resonance imaging showed a 9.2 cm × 5.9 cm solitary mass in hepatic segments VII and VIII, which was unevenly enhanced during the arterial phase and washed out during the venous phase (Figure 1). Additionally, pulmonary CT showed multiple enlarged merging mediastinal and

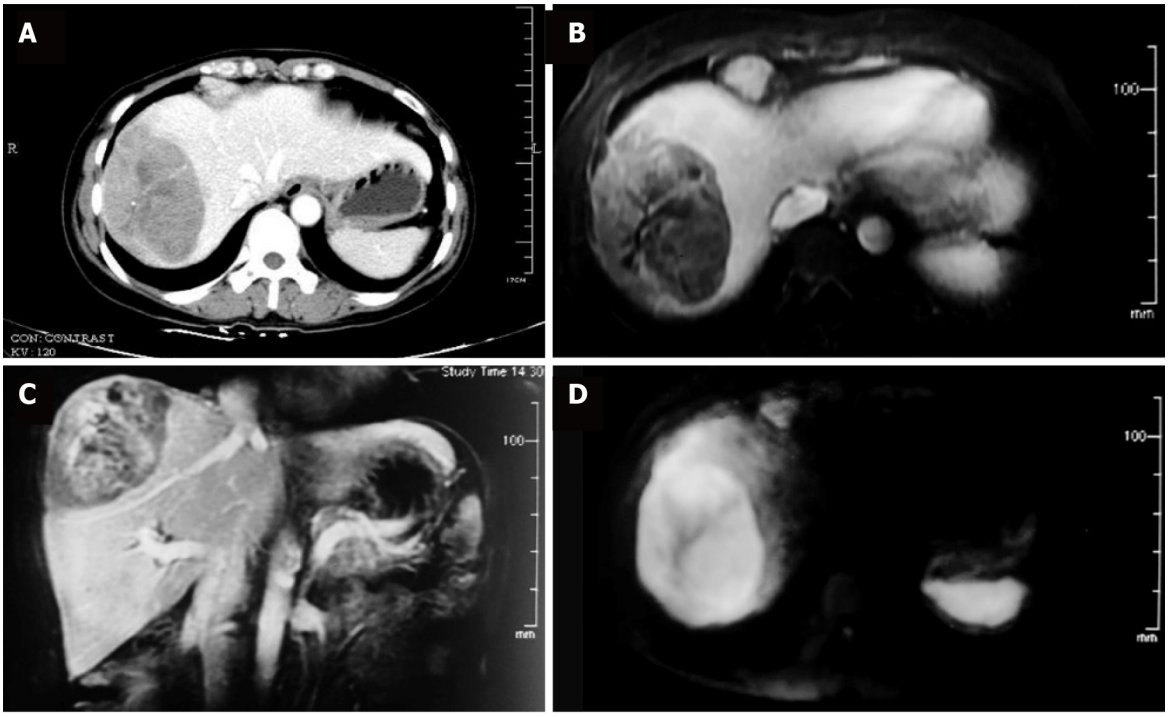

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Figure 1 Computed tomography, magnetic resonance imaging and positron emission tomography/computed tomography images of liver mass and mediastinal lymphadenopathy. A: Abdominal contrast computed tomography, venous phase; B-D: Representative images from the MRI study (B: Venous phase; C: Sagittal venous phase; D: Diffusion weighted).

cervical lymph nodes (Figure 2A). The leading diagnosis based on imaging was malignant liver carcinoma, possibly hepatocellular carcinoma or intrahepatic cholangiocarcinoma, with extensive lymph node metastasis. To exclude possible distant metastasis, positron emission tomography/computed tomography was conducted, which showed uneven fluorodeoxyglucose (FDG) uptake (maximum SUV 6.7) in the liver mass, elevated FDG uptake (maximum SUV 1.9) in multiple mediastinal and cervical lymph nodes (Figure 2B and C), and no suspicious FDG elevation in the lung, brain, or pelvic cavity.

FINAL DIAGNOSIS

A core needle biopsy was suggested to guide systemic treatment. Unexpectedly, the pathological finding for the biopsy suggested an epithelial neoplasm with a tubuloglandular structure. The epithelial cells immunohistochemically stained positive for cytokeratin (CK) 7 and CK19 but negative for glypican-3, p53, and hepatocyte-specific antigen, implying a biliary origin. The ki-67 index was approximately 5%. The morphology and molecular pathology were compatible with adenofibroma with a malignant transformation. The patient underwent a cervical lymph node excisional biopsy to exclude distant lymph node metastasis. Three swollen lymph nodes were resected, which were negative for cancerous components.

TREATMENT

Our team decided to perform surgery on this patient based on the current knowledge of biliary adenofibroma with malignant transformation. Complete local resection of the hepatic lesion and resection of multiple merged lymph nodes in the anterior-inferior mediastinum were performed (the macroscopic view is presented in Figure 3). In detail, under general anesthesia, open atypical hepatectomy was done by Cavitron Ultrasonic Surgical Aspirator to remove the tumor with a margin of at least 1cm. The mediastinum lymph nodes were dissected through the trans-esophageal hiatus approach. The surgery lasted 3.5 h and estimated blood lost was 200 mL. The patient was well-recovered and discharged 11 days after surgery (Table 1). Subsequent pathological findings of the hepatic lesion were consistent with those of needle biopsy. The resected tissue was composed of epithelial cells with irregular tubular shapes, exhibiting cytological atypia and collagenous stroma with

Table 1 Timeline of management

Time (day)	Event
1	Outpatient evaluation
4	Hospitalization
6	Found liver mass by CT
11	PET-CT
13	Core needle biopsy of the liver mass
15	Cervical lymph node biopsy
25	Surgery
36	Discharge

CT: Computed tomography; PET: Positron emission tomography.

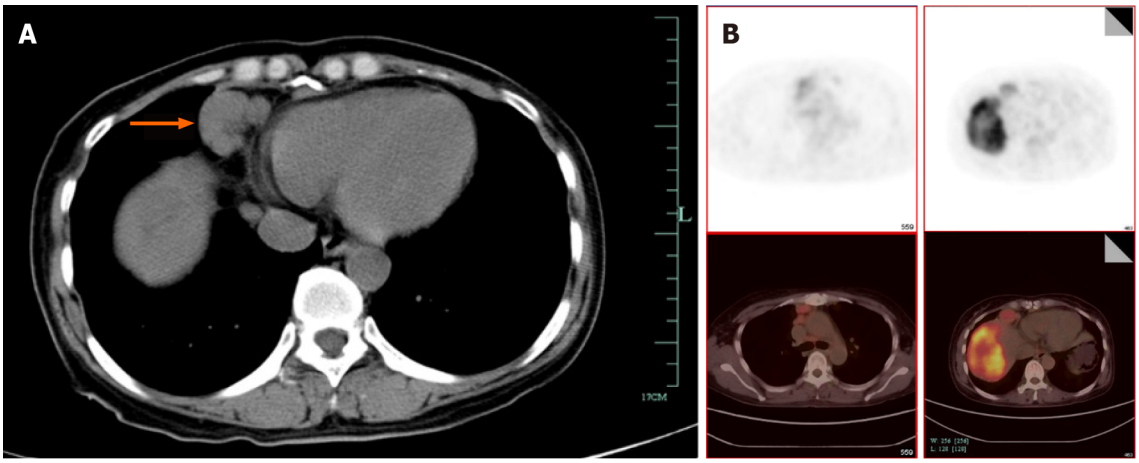

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Figure 2 computed tomography images. A: Pulmonary computed tomography, mediastinal window; B: Representative positron emission tomography/computed tomography images, left, mediastinum, right, abdominal.

plasmocytic infiltration (Figure 4A and B). All margins were negative. Again, no neoplastic composition was found in the resected lymph nodes, whereas lymphatic hyperplasia with massive plasmocytic infiltration was observed.

Immunohistochemical staining was positive for CD3, CD20, CD10, CD21, KappaK, Lambda, and IgG4 (Figure 4C) but negative for HHV8 (Figure 4D). For the differential diagnosis of immune-mediated diseases such as IgG4-related lymphadenopathy, the patient's serum IgG4, IgE, and IL-6 levels were tested, all within normal ranges.

OUTCOME AND FOLLOW-UP

The patient did not develop recurrence of the hepatic lesion during the 12 mo postoperative follow-up (assessed by local CT); no fever, epigastric pain, or other discomfort was present.

DISCUSSION

BAF is a rare primary hepatic tumor first described in 1993 by Tsui *et al*[1]. It is pathologically characterized by dilated ductular structures lined with bland cuboidal epithelial cells and an abundant fibroblastic stroma. BAFs are generally regarded as benign lesions, but they should be considered premalignant neoplasms because of their potential for malignant transformation[2,6]. The literature has limited reports of BAFs with malignant features, with only 13 cases to date (Table 2). Based on a recent review[7], the malignant transformation was found in 37% (7/19) of BAF cases that underwent

Table 2 Biliary adenofibroma with malignant transformation of the liver, review of the literature

No.	Ref.	Age	Sex	Tumor location	Size (cm)	Treatment	Ki67, %	p53	Outcome	Additional information
1	Akin *et al*[8], 2002	25	M	Right hepatic lobe	20	Right hepatectomy	NA	NA	Hepatic recurrence and pulmonary metastasis after 3 yr	
2	Kai *et al*[12], 2012	40	M	Right hepatic lobe	7	Right hepatectomy	5-10	NA	No recurrence at 8-mo follow-up	
3	Nguyen *et al* [13], 2012	53	F	Segment IVb	6.5	Resection of segments III/IV	NA	NA	No recurrence after 12 mo	
4	Tsutsui *et al* [5], 2014	69	F	Segment VI	3.5	Partial hepatectomy	10-15	Focally positive	No recurrence at 4-yr follow-up	Dysplastic changes
5	Thompson *et al* [4], 2016	71	M	Left hepatic lobe	14.5	Left hepatectomy	NA	NA	No recurrence of liver tumor for 9 yr	Moderatlely-differentiated adenocarcinoma
6	Thompson *et al* [4], 2016	71	M	Caudate lobe	6.3	Codate lobectomy	NA	NA	No recurrence at 1-mo follow-up	Well-differentiated adenocarcinoma
7	Godambe *et al* [6], 2016	71	F	Segments II, III and IVa	5.7	Left hepatectomy	50	Positive	NA	Microinvasive carcinoma
8	Thai *et al*[14], 2016	77	M	Segment II	4	Left hepatectomy	NA	NA	NA	Cholangiocarcinoma arising from BAF
9	Kaminsky *et al* [2], 2017	37	F	Segment V	4.5	Partial hepatectomy	50	Negative	No recurrence at 4-mo follow-up	Cholangiocarcinoma arising from BAF
10	Chua *et al*[7], 2018	66	F	Segment IVb	6	Wedge resection	2	Positive	No recurrence at 4-mo follow-up	Cholangiocarcinoma arising from BAF
11	Sturm *et al* [15], 2019	63	F	Segment IVa	6.3	Left hepatectomy	20-30	Focally positive	No recurrence at 24-mo follow-up	
12	Alshbib *et al* [9], 2022	63	M	Segments IVb and V	15.5	Resection of segments IVb and V	25	Weak	Hepatic recurrence 3 mo	
13	Current report	51	F	Segments VII and VIII	7.5	Partial hepatectomy	5	Negative	No recurrence at 12-mo follow-up	

BAF: Biliary adenofibroma; NA: Not available.

resection. Three cases were reported as cholangiocarcinoma arising from BAFs, 2 cases as adenocarcinomas, and 1 unspecified carcinoma, while the others contained some microscopic malignant features such as dysplastic changes and microinvasion. BAF has been reported to arise from liver cirrhosis secondary to chronic hepatitis C virus infection[7]. Immunohistochemistry (IHC) revealed that the epithelial component of the BAF was positive for CK7 and CK19. Of the 5 cases, 3 were positive for p53 on IHC staining. The Ki-67 index ranged from 2% to 50% in 6 cases with available data. Wide local resection is recommended as the primary treatment for BAFs with malignant transformation, and follow-up imaging is needed for potential recurrence[2]. Only 2 of the reported patients developed recurrence after surgery, presenting as local hepatic recurrence, and 1 with pulmonary metastasis[8,9], whereas other cases, with follow-up data from 1 mo to 9 years, had no postoperative recurrence. Therefore, despite the heterogeneity of the pathological features in these cases, BAFs with malignant transformation generally have a good prognosis after complete resection.

In the current case, the multiple enlarged lymph nodes were first misinterpreted as metastases arising from the hepatic neoplasm, leading to an initial diagnosis of advanced liver malignancy and, correspondingly, a plan for systemic treatment such as chemotherapy or targeted therapy. For advanced disease with high suspicion of hepatocellular carcinoma, pathology is not mandatory prior to systemic treatment. In this case, the imaging studies did not suggest a definite diagnosis, therefore, a core needle biopsy was conducted after prudent evaluation. Finally, the pathological diagnosis was BAF with malignant transformation, thus providing a rationale for complete resection of the neoplasm.

Lymphadenopathy showed no evidence of malignancy. It was first suspected to be IgG4-related or multicentric Castleman's disease due to its histology and positive IHC staining for IgG4[10,11]. However, the patient's serum IgG4, IgE, and IL-6 levels were within the normal range; therefore, we did not reach a definite diagnosis for her lymphadenopathy. The patient's fever was non-specific, which could be interpreted as an infection or neoplastic fever, apart from immune-mediated diseases. Notably, the fever did not recur, and CRP and erythrocyte sedimentation rates were normal after surgery.

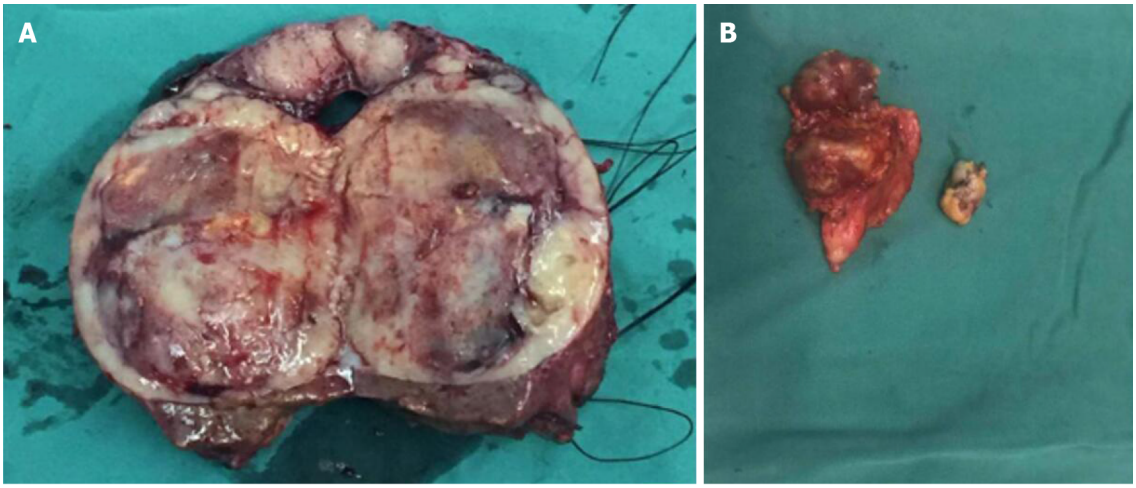

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Figure 3 Macroscopic view of surgical specimens. A: Sectional appearance of the hepatic lesion; B: Enlarged mediastinal lymph node (multiple nodes merged). Bar = 1 cm.

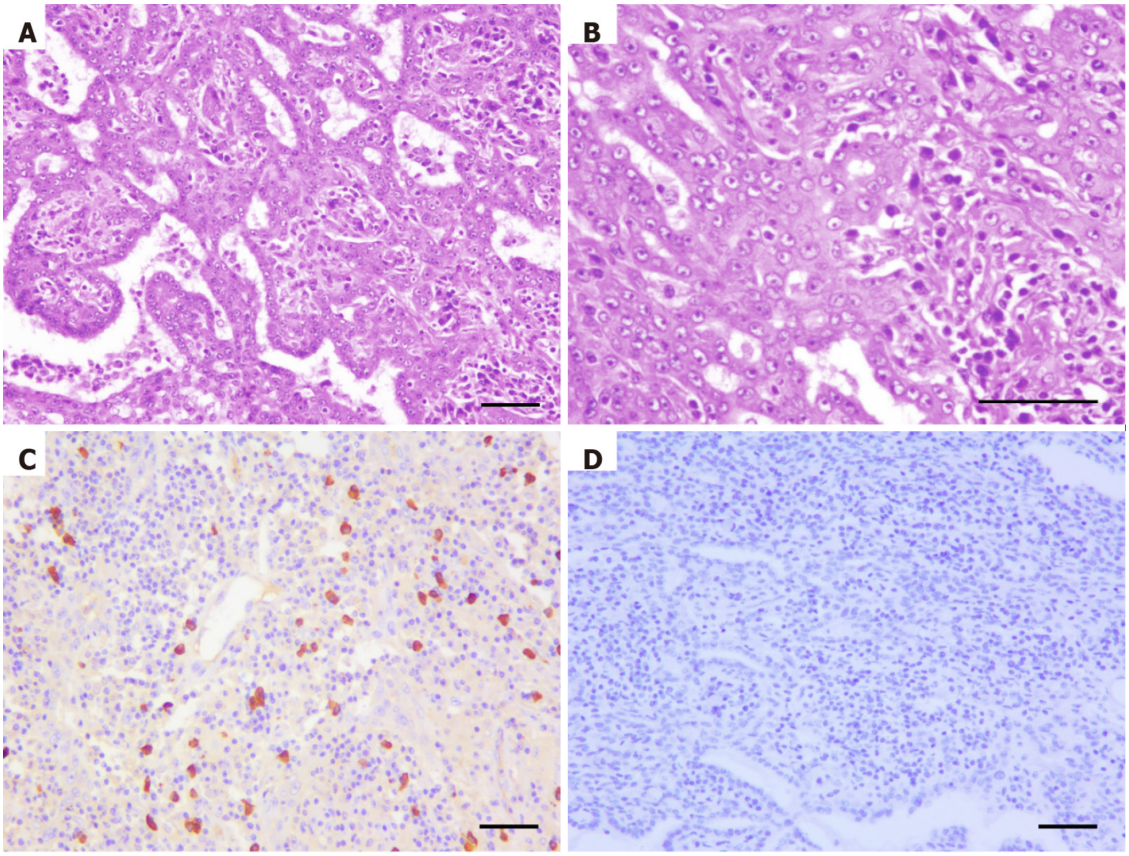

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Figure 4 Microscopic pathology of surgical specimens. A and B: H & E staining of hepatic lesion, (A) H & E × 100 (B) H & E × 200. The malignant component of a tumor consists of deformed fused glandular ducts that form a sieve, and cord-like structures. The neoplastic cells are of medium size with well-defined nucleoli, and most of the cytoplasm is pale, slightly acidophilic or vacuolated; C and D: Immunohistochemical staining of IgG4 and HHV8 in mediastinal lymph node (× 100). Bar = 100 μm.

The limitation of this case is that, despite exclusive diagnosis for IgG4-related or multicentric Castleman's disease, we eventually did not reach a diagnosis for the patient's lymphadenopathy. Besides, we did not conduct molecular analysis such as MSI state and PD-L1 expression of the BAF sample. Additional molecular analysis may assist follow-up treatment of this disease in case of recurrence.

CONCLUSION

In summary, BAFs with malignant transformation are clinically unusual and could be misinterpreted as liver carcinoma based on imaging features, especially when comorbid with other suspicious signs of malignancy, such as lymphadenopathy. Our case serves as an example of a rare manifestation of BAF, a biopsy of suspicious lesions is vital for diagnosis. According to previous reports, BAFs with malignant transformation have the potential to develop into intrahepatic cholangiocarcinoma or adenocarcinoma, curative resection should be considered an essential primary treatment, which generally leads to a favorable outcome.

FOOTNOTES

Author contributions: Wang SC and Chen YY collected, analyzed the patient data and wrote the manuscript; Cheng F conducted the pathological analysis; Teng LS, Wang SC and Wang HY performed the operation and were in charge of the patient; Teng LS and Wu FS reviewed the manuscript; all authors have read and approve the final manuscript.

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