Imaging features of biliary adenofibroma of the liver with malignant transformation: a case report with literature review

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Abstract
Background: Biliary adenofibroma (BAF) is a rare primary hepatic tumor with the potential risk of malignant transformation. Given the extreme rarity of the disease, the imaging features of BAF are unclear. We presented a case of malignant BAF and conducted a systematic literature review. We highlighted the key imaging features in the diagnosis and aggressiveness assessment of BAF, as well as the role of various imaging modalities in evaluating BAF.

Case presentation: We reported a 64-year-old woman with a 5-months history of pain in the right upper quadrant abdomen. US of the liver showed a hypoechoic subcapsular nodule. CT scan revealed a subcapsular solid-cystic mass in segment V of the liver. The mass showed a marked enhancement in the arterial phase followed by wash-out in the venous phase. The patient underwent partial resection of liver’s right lobe. The mass was diagnosed as BAF with malignant transformation by postoperative pathology.

Conclusions: CT and MRI are helpful in recognizing and characterizing BAF. The imaging features of BAF include a solitary, large solid-cystic mass with a well-defined margin, lobulated shape, and internal septa; subcapsular location; no intrahepatic bile duct communication; the presence of von Meyenberg complexes in background liver. The enhancement patterns may have the potential to assess the aggressiveness of BAF, and that marked enhancement in the arterial phase followed by wash-out in the venous phase is suggestive of malignant BAF.

Keywords: Biliary adenofibroma, Malignant transformation, Imaging features
Alcohol and nicotine consumption was denied. The family history was non-contributory. Notably, she had a history of hepatitis B virus infection. Hepatitis B surface antigen, e antibody, core antibody were positive. Complete blood count, chemistry, coagulation, and liver function tests were within the normal limits. The tumor markers including AFP, CA125, CA19-9, CA15-3 and CA72-4 were not elevated.

MRI scan obtained at other hospital revealed a 1.6 × 1.2 cm mass in the right liver lobe. Ultrasound (US) of the liver showed a hypoechoic subcapsular nodule of 20 × 11 mm with a well-defined margin, regular shape, and light vascularity. An abdominal plain CT scan revealed a hypodense mass measuring 1.8 × 1.3 cm underneath the liver capsule of the segment V, and the average CT value was 34 HU. An area along the left border of the mass showed even lower density, with CT values averaging 18 HU. The mass had a well-defined boundary and caused retraction of the adjacent hepatic capsule (Fig. 1a). In addition, multiple small cystic lesions with irregular margins were scattered in both lobes of the liver, especially in the subcapsular area. The largest one was 0.5 cm in diameter (Fig. 1b). After intravenous contrast medium injection, the mass showed a marked enhancement in the arterial phase followed by wash-out in the venous phase. The lower density area showed slight enhancement (Fig. 1c–e). No enhancement was seen in those small cystic lesions (Fig. 1f). Intrahepatic bile ducts looked normal. There were no enlarged lymph nodes.

The patient subsequently underwent partial resection of liver’s right lobe. Her postoperative course was uneventful and she was discharged on postoperative day 5. Gross examination of the resection specimen revealed a 1.5 × 1.5 × 1.2 cm subcapsular firm mass with irregular outline and whitish surface. Histological examination showed that the lesion was composed of tubular structures embedded in a fibrous stroma and the tubules had variable sizes and irregular shapes, with some of them dilated to cysts (Fig. 2a). Bile-like materials were observed in some lumens of the tubulocystic structures (Fig. 2b). The epithelial lining was a single layer of cuboidal to low columnar cells and apocrine-like changes were seen in some areas (Fig. 2c). A part of the lesion showed crowded tubular structures with closely packed nuclei. In these areas, the nucleoli were prominent and the nuclear membrane showed distinct contour. Mitotic figures could be easily detected. And invasive growth in the adjacent liver parenchyma could be seen focally (Fig. 2d). Immunohistochemically, the epithelial cells stained positive for CK7, CK19, CEA. Ki67 proliferation index in the benign part of the tumor was less than 10% (Fig. 2e), and that of the malignant part was 20–30% (Fig. 2f). Based on

![Fig. 1](image-url)
the histopathological result, the final diagnosis was BAF with malignant transformation (middle to well-differentiated adenocarcinoma).

Discussion and conclusion
In 1993, BAF was first described by Tsui et al. [1] as a tubulocystic hepatic tumor with abundant fibrous stroma. The WHO classification classified BAF as a benign tumor originating from bile duct [2]. However, of the 25 prior cases of BAF reported in the literature, 12 were associated with evidence of malignant transformation. In addition, abnormalities of chromosome 22 in two previously reported cases [3, 4] and another one case of adenocarcinoma with BAF features [5] indicate that BAF may originate from mesenchymal cells. Therefore, the clinical presentations, pathology and imaging manifestations of BAF remain to be explored.

We made a detailed analysis of clinical and pathological information of previous cases, and our current case was also included (Table 1). The cases consisted of 12 males and 15 females. Patients were aged from 23 to 83 years with median age of 57 years. The vast majority of symptoms were pain in the upper abdomen or asymptomatic. The physical examination and laboratory work-up of most patients were within the normal limits. Grossly, BAF is a well-circumscribed, nonencapsulated solid-cystic mass and has a white-purple surface. Histologically, BAF is comprised of tubular, microcystic and cystic structures lined by cuboidal to low columnar epithelial cells, embedded in a collagenous stroma. BAF harbors the potential for malignant transformation, but consistent criteria of its malignant histology have not been reported in the literature. We reviewed the pathologic data of all cases with malignant transformation [5–16], suggesting that malignant BAF may show the following characteristics: (1) columnar-type epithelial cells with disordered polarity; elongated, hyperchromatic, and vesicular nuclei with prominent nucleoli; eosinophilic cytoplasm with apocrine-like changes and secretory snouts; atypical mitotic figures. (2) complex papillary, cribriform-like, and back-to-back architecture. (3) stromal, perineural, lymphovascular, and liver capsule invasion. (4) cholangiocarcinoma arising in BAF. Immunohistochemically, the epithelial cells of BAF stained positive for CK7 and CK19, and the stroma cells stained positive for vimentin and SMA, negative for desmin. Ki67 proliferation index showed a significant difference between the benign and the malignant tumor components of BAF. In molecular

![Fig. 2](image-url)
| Author/Year | Sex  | Age | Symptom                      | Physical examination/ Laboratory work-up | Treatment | Immunohistochemistry/ Molecular studies | Follow-up | Malignant transformation |
|------------|------|-----|------------------------------|------------------------------------------|-----------|----------------------------------------|-----------|-------------------------|
| Tsui et al. [1]/1993 | Female | 74  | RUQ pain                     | Liver function test normal                | Wedge resection | Positive: cam5.2, AE1/3, EMA, CEA  | No recurrence after 20 years | No |
|            |      |     |                              |                                          | Partial hepatectomy             | Negative: Chromo, S100, desmin, AFP, NSE |           |                         |
| Parada et al. [3]/1997 | Female | 49  | RUQ pain                     | Liver function test normal                | Partial hepatectomy             | Monosomy 22 | No recurrence | No |
| Akin et al. [6]/2002     | Male  | 25  | Abdominal enlargement, RUQ pain | RUQ palpable mass                        | Right lobectomy                | –           | Recurrence and pulmonary metastasis after 3 years | Yes |
| Garduño-López et al. [19]/2002 | Female | 68  | RUQ pain, vomiting, diarrhea and jaundice | Liver enlargement Elevated CA19-9; hepatitis B surface Ag, ALP, total biliary, GGT, AFP normal | Left hepatectomy | Stained CA19-9 | No recurrent after 30 months | No |
| Varnholt et al. [20]/2003 | Female | 47  | RUQ pain, weight gain of 5 kg   |                                           | Incomplete resection           | Epithelial: positive for D10, p53 (50% to 75%), AE1/3, cam 5.2, CK7, CK19, CEA, EMA; negative for 1F6; Ki67 < 10%  | No metastasis or significant growth after 3 years | No |
| Gurrera et al. [31]/2010  | Male  | 79  | Vague abdominal pain          | Blood tests and AFP normal                | Partial resection              | Epithelial: positive for CK7, CK8, CK9, CK19, EMA; negative for CEA, CK5/6, P53, calretinin, HBME-1, beta-catenin  | No recurrence after 7 years | No |
| Kai et al. [7]/2012       | Male  | 40  | Upper abdominal pain          | Hematological, coagulation test, CEA, Ca19-9, AFP normal; carrier for HBV | Right hepatectomy              | Positive: CK19, Ca19-9, MUC1  | Dying of fulminant hepatitis B 8 months after surgery | Yes |
| Nguyen et al. [8]/2012    | Female | 53  | Incidentally found            | Elevated CA-125, liver function tests, clotting profile, AFP, CA 19-9, and CEA normal | Segmental resection             | Positive: CK7, CK19 | No recurrent after 12 months | Yes |
| Author/Year | Sex  | Age | Symptom                          | Physical examination/ Laboratory work-up                                      | Treatment                                      | Immunohistochemistry/ Molecular studies                                      | Follow-up | Malignant transformation |
|------------|------|-----|----------------------------------|-------------------------------------------------------------------------------|-----------------------------------------------|---------------------------------------------------------------------------------|-----------|--------------------------|
| Tsutsui et al. [9]/2014 | Female | 69  | Asymptomatic                     | General examination normal. Complete blood count, chemistry, urinalysis, tumor markers, and coagulation normal. | Partial liver resection                      | Epithelial: positive for CK7, CK19, CAM52, CKAE1/AE3, p53; negative for CEA, a-SMA; KI67:10–15% in the dysplastic epithelia; 1–2% in non-dysplastic epithelia. Stroma: positive for vimentin and SMA; negative for desmin. | No recurrent after 4 years | Yes |
| Jacobs et al. [10]/2015 | Female | 57  | Incidentally found               | Modest left costovertebral angle tenderness. Mild leukocytosis, liver enzymes, CEA, AFP normal. | Preoperative embolization and surgical resection. | –                                                                                | No recurrent after 5 years | Yes |
| Elpek et al. [32]/2016 | Male | 23  | Asymptomatic                     | Physical examination normal. Tumor markers, hematologic and coagulation normal. | Partial hepatectomy                           | Positive: CK7, CK19, CK 18 and BMA. Negative: AFP, PLAP, HCG, Hepatocyte, CK20, CD30, OCT4 and MUC2. | –         | No                       |
| Godambe et al. [11]/2016 | Female | 71  | Bilateral upper abdominal pain   | Liver function testing, serum alpha fetoprotein, CEA, and CA199 normal. | Left hepatectomy                              | Positive: CK7 and CK19, brisk Ki67 53(25% to 50%). Stroma: negative for Ki67 and p53. Negative: CD10, polyclonal CEA, Inhibin and PAX8. | –         | Yes                      |
| Thai et al. [12]/2016 | Male | 77  | Fever, lumbosacral pain disorientation, and nocturnal agitation             | Hyponatriemia, increase in inflammatory markers and anemia. | Left lobectomy                                | Positive: CK7, CK19, CA19.9, CEA and MUC1. | –         | Yes                      |
| Thompson et al. [13]/2016 | Male | 71  | Incidentally found               | AFP, CA 19–9, Liver function tests, serology for HBV and HCV normal. | Left hepatectomy                              | –                                                                                | Dying for primary lung malignancy after 9 years | Yes |
| Thompson et al. [13]/2016 | Male | 71  | Incidentally found               | AFP, CA 19–9, Liver function tests, serology for HBV and HCV normal. | Caudate lobe resection                       | Positive: CK7. Negative: CDX-2, CK20 CDKN2A mutation. | No recurrent after 4 weeks | Yes |
| Author/Year | Sex | Age | Symptom | Physical examination/Laboratory work-up | Treatment | Immunohistochemistry/ Molecular studies | Follow-up | Malignant transformation |
|------------|-----|-----|---------|----------------------------------------|-----------|------------------------------------------|-----------|-------------------------|
| Kaminsky et al. [14]/2016 | Female | 37 | Postprandial nausea, vomiting, and epigastric pain | – | Excising with wide local margins | Positive: CK7, CK19, synaptophysin, CD56; Negative: chromogranin, CK20, CDX2, heppar1, and p53 | No recurrence after 4 months | Yes |
| Arnason et al. [4]/2017 | 4 females and 2 males | 46 to 83 | Abdominal pain (4 patients); incidental findings (2 patients) | – | Surgical resection (5 patients) | Positive: CKAE1/3, CK7, CK19CA19-9; K67: less than 10% in the epithelial component, < 1% in the stromal component; Amplifications of CCND1 and ERBB2 | No recurrence in 3 patients after 3, 20, and 21 years; Local hepatic recurrences in 2 patients after 1 and 6 years | No (series of 6 including 2 cases above) |
| Chua et al. [15]/2018 | Female | 66 | Asymptomatic | AFP normal | Segmentectomy and adjuvant chemotherapy | Positive: CK7, CK20 and CDX2; K67: 2% in BAF; CC 30%; P53 positive in BAF and CC | No recurrence after 3 months | No (co-existent BAF and hepatobiliary MCN) |
| Esteban et al. [33]/2018 | Female | 26 | Jaundice and pruritus | Scleral icterus and generalized jaundice; Elevated serum total bilirubin and alkaline phosphatase; AST, ALT, hepatitis serologies normal | Left hepatectomy | – | No recurrence after 3 months | No (co-existent BAF and hepatobiliary MCN) |
| Meguro et al. [5]/2018 | Male | 63 | Found by MRI examination for liver cirrhosis | – | – | Epithelial: positive for CK7, CK19; negative for P53; Stroma: positive for vimentin, CD44, CD56, CD73, CD271; negative for P53, desmin, SMA; Osteoblasts: positive for BMP-2 | Dying for liver failure after 21 days | Yes (adenosarcoma) |
| Lee et al. [17]/2019 | Male | 63 | Asymptomatic | Liver function tests protein induced by vitamin K, AFP, antagonist II, CA 19–9, and CEA normal | Bisegmentectomy | Epithelial: positive for CK7, CK19, P53 (locally positive); K67 (< 2%); Stroma: positive for SMA | No recurrence after 41 months | No |
| Lee et al. [17]/2019 | Male | 38 | Asymptomatic | physical examination and tumor markers normal | Left lateral section | – | No recurrence after 39 months | No |
| Author/Year        | Sex   | Age | Symptom                  | Physical examination/Laboratory work-up                                      | Treatment                  | Immunohistochemistry/Molecular studies                                                                 | Follow-up            | Malignant transformation |
|-------------------|-------|-----|--------------------------|--------------------------------------------------------------------------------|----------------------------|----------------------------------------------------------------------------------------------------------|----------------------|--------------------------|
| Sturm et al. [16]/2019 | Female | 63  | unspecific abdominal complaints | The physical examination and AFP, CEA, and CA 19–9 normal                   | Left hemihepatectomy       | Epithelial: positive for CK7, Cadherin 17, CD56, Muc1, Stroma: positive for SMA, Negative: inhibin, calretinin, S100P, ERG, Muc2, Muc4, Muc5, and Muc6, MLH1, MSH2, MSH6, and PM2, nuclear expression KI67: 5–10% in biliary adenofibroma, 20–30% in the adenocarcinoma, Different polymorphisms in the encoded TP53 and KIT | No recurrence after 24 months | Yes                      |
| Present case      | Female | 64  | RUQ pain                 | Complete blood count, chemistry, coagulation, liver function test, tumor markers (AFP, CA125, CA19-9, CA15-3, and CA72-4) normal, Hepatitis B surface antigen, e antibody, core antibody positive | partial resection          | Positive: CK7, CK19, CEA, KI67: less than 10% in benign part; 20–30% in malignant part                  | No recurrence after 9 months | Yes                      |

RUQ right upper quadrant
pathology, the mutations of CDKN2A, CCND1, ERBB2, TP53 and KIT genes may contribute to tumorigenesis of BAF [4, 13, 16]. Most patients had a surgical resection. Except for 2 cases [4] that recurred for incomplete excision, all other patients with benign BAF had no recurrence or metastasis. Whereas, one case of a malignant BAF [6] had recurrence with abdominal wall invasion and multiple metastatic nodules in liver and lung at 3 years postresection. Therefore, more aggressive surgical procedures for the treatment of malignant BAF may improve the prognosis of patients compared with that of benign BAF.

Symptoms and laboratory data of BAF are nonspecific, making it difficult to differentiate BAF from other more common hepatic lesions. While pathologic diagnosis by liver biopsy is regarded as the gold standard for diagnosis, it is not without limitations. Liver biopsy is an invasive procedure with the risk of various complications, such as bleeding, seeding the tract, infection, etc. Sampling error is also an issue with liver biopsy, especially for cystic lesions which are prone to a false-negative diagnosis. These limitations emphasize the importance of developing sensitive and specific imaging techniques to diagnose BAF. However, the vast majority of case reports in the literature only focused on the clinical and pathological features of BAF, and lacked detailed professional descriptions of the imaging manifestations. Thus, we reviewed 15 reports with detailed imaging information and summarized the imaging features on US, CT and MRI of 17 patients with BAF (Table 2). To our knowledge, this is the first detailed comprehensive review of the imaging characteristics of BAF in the published literature. Lee et al. [17] simply summarized the MRI findings of 8 patients with BAF, but not the radiologic features of other imaging modalities or the enhancement patterns of lesions.

Because of wide availability, low cost and nonradiative, conventional US is the screening method of the choice. The sensitivity for US in the diagnosis of liver cystic lesions is in the range of 90% [18]. However, US characteristics of BAF were not mentioned in most literature. Only 2 patients [19] showed hypoechoic masses, and another 2 patients [9, 20] were presented as hyperechoic masses. These US manifestations are nonspecific, and two cases were misdiagnosed as hemangiomas. US can diagnose common liver lesions with confidence, but its’ ability in the evaluation of complex cystic lesions, such as rare BAF, is limited. Due to the lack of enhancement patterns, many different types of liver lesions can’t be differentiated in US. Contrast-enhanced ultrasound (CEUS) is an emerging technique in liver imaging. By using a microbubble agent as contrast, this modality can provide detailed information about tumor architectures and allow observations of enhancement patterns in real-time. The high diagnostic accuracy of CEUS for focal liver lesions has been reported in several studies [21], which may be helpful in characterizing BAF.

CT has become the most commonly used modality in the preoperative assessment and follow-up of the patients with hepatic tumors. For liver cystic lesions, CT can better demonstrate gas contents and calcification within the cyst. On CT, BAF may appear as a solitary, large hypodense solid-cystic mass with a well-defined margin, lobulated shape and internal septa. The tumor abuts the liver capsule and has a protruding liver contour. No communication is observed between the tumor and intrahepatic bile ducts. Notably, our current case is the first report of BAF with capsular retraction, which may be affected by the distribution of fiber components. And our patient showed multiple hypoattenuating lesions with sizes < 0.5 cm, irregular outlines and obscure margins in the subcapsular area of the liver, which are similar to von Meyenberg complexes [22]. In staining pattern and histology, there is a striking resemblance between BAF and biliary hamartomas. Varnholt et al. [20] suggested that BAF possibly represents transformed von Meyenburg complexes. And 2 case reports [5, 11] of BAF showed von Meyenberg complexes existed in the postoperative specimens of background liver but didn’t record their imaging findings. Thus, we considered that von Meyenberg complexes in the background liver may be a typical but rare imaging feature for BAF diagnosis.

MRI has been considered as the most useful modality for characterizing liver masses, due to its high soft-tissue contrast resolution. In MR imaging, BAF appears as a solitary, subcapsular, multisected solid-cystic mass with low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Other imaging features of BAF in MRI, such as large size, well-defined margin, lobulated shape and no intrahepatic bile duct communication, are similar to those on CT. The principal advantage of MRI over CT for liver cystic lesions is its better visualization of the mural nodule, hemorrhage and mucin within the cyst. However, histological studies showed that the cysts of BAF were non-mucinous type and intratumoral hemorrhage was uncommon [9]. And mural nodules within the tumor have never been reported. Therefore, MRI can be helpful for characterizing BAF, but it does not provide additional information compared with CT.

Benign BAF can be curative after complete surgical resection, while malignant BAF has a risk of local recurrence and distant metastasis. Therefore, the aggressiveness assessments of BAF before surgery are of great importance. On unenhanced images, the imaging findings of most BAF with malignant features resembled those of benign BAF. Yet, it was found that several
Table 2 Literature review and radiological data analysis

| Author/Year        | Malignant transformation | Location                        | Number of lesions | Size(cm) | Shape   | Margin | US                 | CT                      | MRI                         | Internal septa | EnhancementLiver contour | Bile duct communication |
|--------------------|--------------------------|---------------------------------|--------------------|----------|---------|--------|--------------------|--------------------------|--------------------------|----------------|--------------------------|------------------------|
| Akin et al. [6]/2002 | Yes                      | Subcapsular area of right lobe  | Multiple           | 14       | Lobulated | Obscure | —                  | —                        | —                        | Unilocular | Enhancement in arterial phase and early washout in portal phase | No                     |
| Garduño-López et al. [19]/2002 | No                     | Subcapsular area of left lobe  | Solitary           | 6        | Lobulated | Well-defined | hypechoic lesion | Solid-cystic mass | —                        | Multilocular | —                        | No                     |
| Varnholt et al. [20]/2003 | No                     | Subcapsular area of left lobe  | Solitary           | 16       | Lobulated | —       | cystic and solid mass with areas of increased echogenicity | Solid-cystic mass | —                        | Multilocular | —                        | No                     |
| Kai et al. [7]/2010   | Yes                      | Subcapsular area of right lobe  | Solitary           | 7        | Lobulated | Well-defined | —                  | Multicystic mass lesion | —                        | Multilocular | Gradual enhancement | No                     |
| Tsutsui et al. [9]/2014 | Yes                     | Subcapsular area of right lobe  | Solitary           | 3.5      | Lobulated | —       | hyperechoic nodule with small hypoechoic | hypodense solid-cystic mass | T1WI: low intensity; T2WI: high intensity and low intensity septa; DWI: markedly high intensity | Multilocular | One part: enhancement in arterial phase and early washout in portal phase; another part: early and prolonged enhancement | No                     |
| Jacobs et al. [10]/2015 | Yes                     | Subcapsular area of right lobe  | 2                  | 11.8     | Lobulated | —       | Heterogeneous, predominantly hypodense mass | —                        | —                        | Multilocular | —                        | No                     |
| Elpek et al. [32]/2016 | No                      | —                               | Solitary           | 6        | —       | Well-defined | —                  | Multicystic mass lesion containing solid areas | —                        | —                        | —                        | —                     |
| Godambe et al. [11]/2016 | Yes                     | Subcapsular area of left lobe  | Solitary           | 6.3      | —       | —       | —                  | —                        | —                        | Multilocular | Heterogeneous enhancement in arterial phase | —                     |
| Thai et al. [12]/2016 | Yes                      | Subcapsular area of left lobe  | Solitary           | 4        | Targetoid | —       | —                  | A targetoid lesion with a peripheral edematous halo and a necrotic central area | —                        | Unilocular | —                        | No                     |
| Author/Year | Malignant transformation | Location | Number of lesions | Size(cm) | Shape | Margin | US | CT | MRI | Internal septa | Enhancement | Liver contour | Bile duct communication |
|------------|--------------------------|----------|------------------|----------|-------|--------|----|----|-----|--------------|-------------|---------------|--------------------------|
| Thompson et al. [13]/2016 | Yes | Subcapsular area of left lobe | Solitary | 14.5 | Lobulated | Well-defined | — | — | T2WI: heterogeneously increased signal; T1WI: isoointensity to hypointensity | Multilocular enhancement in arterial phase and early washout in portal phase | Protrusion | No |
| Thompson et al. [13]/2016 | Yes | Subcapsular area of caudate lobe | Solitary | 6.6 | Lobulated | Well-defined | — | — | T2WI: heterogeneously increased signal; DWI: restricted diffusion | Multilocular enhancement on delayed imaging | Protrusion | No |
| Kaminsky et al. [14]/2016 | Yes | Subcapsular area of right lobe | Solitary | 4.9 | Lobulated | — | — | T1WI: hypointense, T2WI: heterogeneously hyperintense | Multilocular peripheral enhancement | Protrusion | No |
| Chua et al. [15]/2018 | Yes | Subcapsular area of left lobe | Solitary | — | — | — | — | DWI: restricted diffusion | — | Enhancement in arterial phase and early washout and pseudocapsule formation in portal phase | — | — |
| Lee et al. [17]/2019 | No | Subcapsular area of segments IV and VIII | Solitary | 4.7 | Lobulated | Well-defined | — | — | T1WI: low signal intensity; T2WI: bright signal intensity tumor with hypointense septa | Multilocular septal enhancement in delayed phase | Protrusion | No |
| Lee et al. [17]/2019 | No | Subcapsular area of left lobe | Solitary | 2.7 | Lobulated | Well-defined | — | low attenuation | T1WI: hypointensity; T2WI: bright signal intensity | Multilocular septal and wall enhancement in portal venous phase | Protrusion | No |
| Sturm et al. [16]/2019 | Yes | Subcapsular area of left lobe | Solitary | 6.3 | Lobulated | — | — | Solid-cystic mass | Multilocular | — | Protrusion | No |
| Present case /2021 | Yes | Subcapsular area of right lobe | Solitary | 1.8 cm | Irregular | Well-defined hypoechoic subcapsular nodule | Hypodense solid-cystic mass | — | Unilocular enhancement in arterial phase and early washout in portal phase | Retraction | No |
features showed in some malignant BAF cases, including multiple lesions, unilocular solid-cystic mass, restricted diffusion on DWI, obscure margin, peripheral edematous halo and pseudocapsule formation, have not been described in benign BAF [6, 10, 12, 15]. As for the enhanced characteristics of BAF, 10 cases offered detailed information of imaging features on contrast-enhanced CT or MR images, including 2 cases of benign BAF and 8 cases of malignant BAF. 2 patients [17] with benign BAF (100%) showed delayed enhancements, and 6 patients [6, 9, 11, 13, 15] with malignant BAF (75%) showed marked enhancements in the arterial phase and washout in the venous phase. Thus, we hypothesize that wash-in the arterial phase followed by wash-out in the venous phase is a typical imaging feature of malignant BAF. Delayed enhancement of benign BAF may be related to the high content of fibrous stroma. Malignant BAF has a complex architecture with crowded, back-to-back tubular structures, and lacks the fibrous stroma, which may be the reason leading to early enhancement. In addition, 2 of the 6 cases of malignant BAF mentioned above [9, 13] showed prolonged enhancements in some regions of the tumor, and two reports [7, 13] (25%) described malignant BAF with delayed enhancements. That may be associated with the varying degrees and ranges of malignant transformation. The various key imaging findings which may help in distinguishing benign and malignant BAF, were summarized in Table 3. Because BAF is extremely rare, the further investigations of its enhancement characteristics are required. Dual-energy computed tomography (DECT) is a promising approach in the evaluation of liver lesions. Based on CT data at two different energy spectra, DECT can yield several types of images including virtual monoenergetic imaging, effective atomic number map, iodine map and so on, which is particularly useful to improve iodine contrast visualization and quantitatively reflect the blood flow [23]. DECT increases the accuracy in the differentiation between benign and malignant hepatic lesions through iodine quantification [24]. In addition, MRI can evaluate focal liver lesions in both the dynamic and hepatocyte phases by using hepatocyte-specific contrast agents (HSCAs) [25]. Malignancy should be considered when hypervascular lesions appear hypointense in the hepatocyte phase [26]. These emerging approaches in liver imaging can provide more information about enhancement characteristics of focal liver lesions, and might be helpful in differentiating benign and malignant BAF.

The distinct imaging features can differentiate BAF from other liver cystic lesions: (1) Liver abscess [27]: abscesses usually appear as thick-walled cystic lesions with perilesion edema. The presence of internal gas is a typical imaging characteristic of the abscess. After contrast injection, the rim enhancement of lesion and hypodense perilesion edema form the so-called “ring sign”. And the patients with liver abscess often present infection symptoms such as high fever, shiver and leukocytosis. (2) Hepatic cyst [28]: hepatic cysts appear as round cystic lesions with thin walls, smooth outlines and no internal septa. No enhancement is seen after the administration of contrast material. (3) Cystic metastases [29]: metastatic tumors with obvious necrosis and cystic degeneration are regarded as cystic metastases. Cystic metastases usually appear as multiple, round, unilocular cystic lesions. Enhancing mural nodules and peripheral rim can be observed in contrast-enhanced images. In addition, the medical history of primary malignancy can help reach a correct diagnosis. (4) Cystic Hepatocellular Carcinoma [22]: cystic hepatocellular carcinoma usually occurs in the context of cirrhotic liver. The wall of cyst caused by internal necrosis has an irregular thickness. Elevated AFP also can suggest the diagnosis. (5) Intraductal papillary neoplasm of the bile duct (IPNB) [29]: IPNBs appear as soft tissue masses within the dilated bile ducts. The morphology of intraluminal mass and the degree of dilated bile ducts are various. MR cholangiography depicts the relationship of the lesion to the bile ducts well and therefore contributes to the diagnosis. (6) Mucinous cystic neoplasm (MCN) [30]: MCNs appear as uni- or multilocular cystic tumors with irregular thick walls and internal septations. Mural nodules, hemorrhage or calcification within the cyst can be observed.

| Imaging feature | Benign BAF | Malignant BAF |
|-----------------|------------|--------------|
| Number of lesions | Solitary | Multiple |
| DWI signal | — | Restricted diffusion |
| Margin | Well-defined | Obscure |
| Internal septa | Multilocular | Unilocular |
| Enhancement | Delayed enhancement | Marked enhancement in the arterial phase followed by wash-out in the venous phase |
| Additional features | — | Peripheral edematous halo, pseudocapsule formation |
MCN can present hyperintense on T1 weighted images due to its mucin production. The lesions demonstrate no or mural nodular enhancement on postcontrast enhanced images.

In conclusion, BAF is a rare hepatic tumor with the potential of malignant transformation, which requires prompt treatments and follow-ups. Although symptoms and laboratory data of BAF are nonspecific, CT and MRI may help in diagnosing BAF and evaluating its aggressiveness before surgery. The current case and literature review suggest that BAF is radiologically characterized by the following features: (1) abutting the liver capsule; (2) solitary, large solid-cystic mass with a well-defined margin, lobulated shape, internal septa; (3) no communication between the lesion and intrahepatic bile ducts; (4) von Meyenberg complexes in background liver may be a typical but rare imaging feature; (5) enhancement patterns may have the potential to assess the aggressiveness of BAF and that marked enhancement in the arterial phase followed by wash-out in the venous phase is suggestive of malignant BAF. In addition, further investigations on the role of emerging approaches, including CEUS, DECT and MRI with HSCAs, in characterizing BAF are required.

Abbreviations
AFP: Alpha-fetoprotein; CA: Carbohydrate-antigen; MRI: Magnetic resonance imaging; CT: Computed tomography; CK: Cytokeratin; CEA: Carcinoembryonic antigen; WHO: World Health Organization; SMA: Smooth muscle actin; CDKN2A: Cyclin-dependent kinase inhibitor; CCND1: CyclinD1; ERBB2: Her2/new gene.

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Authors' contributions
WH and ZH collected data during the study. WH and AL contributed to the study design. WH, YL, AL and YZ developed the first draft of the manuscript which was then reviewed and intensively revised by AL, YZ. All authors read and approved the final manuscript.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Declarations
Ethics approval and consent to participate
This study was approved by the ethics committee of the First Affiliated Hospital of Dalian Medical University. All procedures were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the patient.

Consent for publication
The patient provided written informed consent for publication of this case report and accompanying images.

Competing interests
The authors declare that they have no competing interests.

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