



## Resolution of Bile Duct Adenoma over Follow-up Period; A Case Report

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### ABSTRACT

Bile duct adenoma (BDA) is a rare neoplasm of bile ducts with various clinical manifestations and imaging appearances. A few cases of BDA and their predisposing factors have been described. We report a 35-year-old woman with right upper quadrant pain who consumed oral contraceptive pills. Ultrasound study revealed three hypoechoic subcapsular liver masses; two of them were hypodense in computed tomography. Fine needle biopsy of the largest mass showed bile duct adenoma. Liver masses disappeared after discontinuing the pills over a 2-year follow-up. BDAs can manifest in imaging. Although previous studies have not reported tumor resolution over a follow-up period, we suggest paying more attention to predisposing factors in order to give an opportunity for tumor resolution by risk factor elimination.

### KEYWORDS

Bile duct adenoma, Liver mass, Oral contraceptives, Liver biopsy, Follow up

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### INTRODUCTION

Bile duct adenoma (BDA) is a rare benign tumor varying in size from 0.1 to 2 cm.<sup>1,2</sup> It is usually diagnosed during laparotomy or autopsy.<sup>1,3</sup> BDA consists of small acini and tubules in a background of fibrous stroma.<sup>3</sup> In the past, BDA was recognized as gland hamartoma, benign cholangioma, and/or cholangioadenoma.<sup>3</sup> Herein we report a case of BDA in a 35-year-old woman, which resolved during a 2-year follow-up.

### CASE REPORT

A 35-year-old woman was referred to our hospital with liver masses in an ultrasound study that was requested because of vague upper abdominal pain. She also mentioned mild nausea that started one month earlier. Medical history revealed three normal vaginal deliveries and she was receiving medroxyprogesterone acetate injections every 3 months for contraception.

The patient's physical examination was normal as well as her laboratory tests, which included complete blood count (CBC), liver biochemical tests, tumor markers, sedimentation rate (ESR), and C-reactive protein (CRP) (table 1). Esophagogastroduodenoscopy (EGD)

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**Table 1: Laboratory data of the patients with bile duct adenoma at initial evaluation**

Lab data	Result (UNIT)	Lab data	Result (UNIT)
White blood cells	6000 /UL	AST	18 IU/L
Neutrophil	59%	ALT	20 IU/L
Lymphocyte	37%	Alp	264 U/L
Monocyte	3%	LDH	400 U/L
Eosinophil	1%	HBsAg	negative
Hemoglobin	12.9 g/dL	Anti HBS	>10 mIU/mL
Hematocrit	38.2%	Anti HBc	negative
Platelet	273000 /UL	Anti HCV	negative
Fasting blood sugar	83 mg/dL	αFP	2.8 ng/mL
Urea	25 mg/dL	CEA	0.61 ng/mL
Creatinine	0.69 mg/dL	CA19-9	35 U/mL
Calcium	8.9 mg/dL	CA 125	21.7 U/mL
Phosphorus	3.8 mg/dL		

was done, which showed only Los Angeles grade B reflux esophagitis.

The initial ultrasound study showed three hypochoic subcapsular nodules with maximum diameters of 25 mm in the right hepatic lobe in a background of normal liver parenchyma (figure 1). Abdominal and pelvic computed tomography (CT) with intravenous/oral contrast revealed two hypodense lesions of 10 and 12 mm diameters in the anterior segment of the right hepatic lobe and one 25 mm diameter lesion with more density in the posterior segment of the right hepatic lobe. Red blood cell single photon emission computed tomography (RBC-SPECT) was performed to rule out hemangioma (figure 2). Ultrasound guided liver biopsy was done to make a definite diagnosis. Two 1×10 mm biopsy specimens were sent for histopathological study. Hematoxylin and eosin stained (H&E) sections of liver specimens showed multiple foci of proliferating bile ducts composed of bland cuboidal cells and duct formation in the fibrotic and inflamed portal spaces. Bile duct proliferation was compatible with BDA (figure 3). Immunohistochemical (IHC) staining was done for CK7 and P53, which showed positive for CK7 and negative for P53.

As no risk factors were known to have a relationship with BDA, the patient was advised to discontinue medroxyprogesterone. A proton pump

inhibitor was started to treat the esophagitis. She was then followed up for two years by routine laboratory tests and ultrasonography performed by an expert sonographer. Gradual size reduction of the lesions was reported. Liver parenchyma was normal in ultrasound after 16 months. Because magnetic resonance imaging (MRI) has more accuracy in detecting small hepatic lesions (less than 2 cm), liver MRI was performed in the 22nd month, which showed no hepatic lesion (figures 4, 5).

## DISCUSSION

BDAs are rare tumors that are usually diagnosed incidentally during surgery or autopsy. Their incidence is estimated to be 1.3%, although the true incidence is unknown. In one study, only 13 out of 2125 postmortem cases had BDA.<sup>4</sup> BDAs are subcapsular masses of 0.1-2 cm in diameter affecting individuals aged between 20-70 years. Sex does not appear to be a risk factor<sup>4</sup> and family tendency and occurrence during childhood have not been reported.<sup>3</sup>

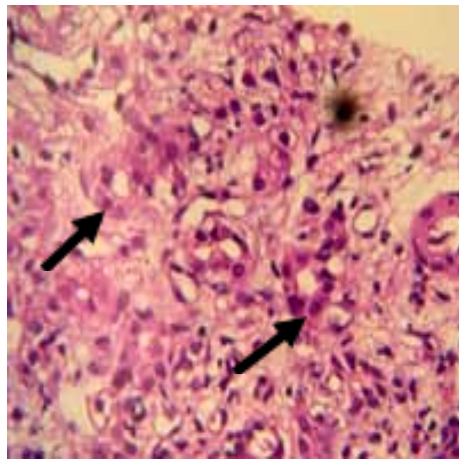
No particular sign or symptom is attributed to this lesion<sup>3</sup> and it is mainly single, although it can be multiple.<sup>4</sup> BDAs cannot be differentiated from liver metastasis during surgery.<sup>5</sup> Also, they are reported to have a benign behavior and limited growth ability.<sup>6</sup>



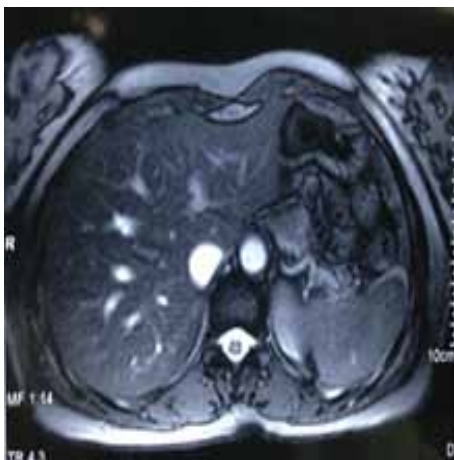
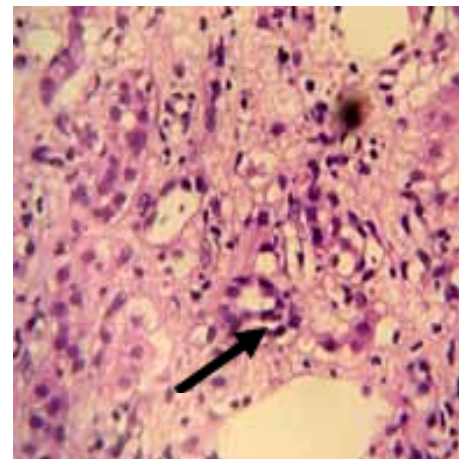
**Fig 1:** Ultrasound imaging of liver shows hypochoic nodules (red arrow).



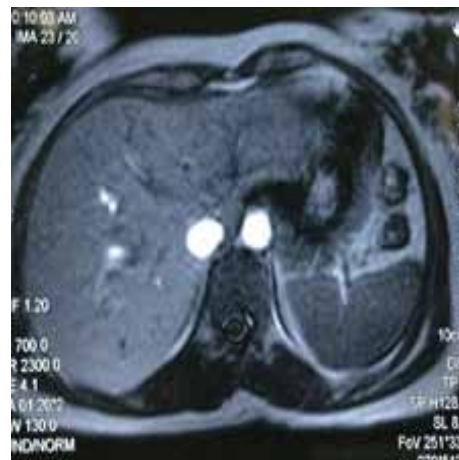
**Fig 2:** Computed tomogram of liver nodules (red arrow).



**Fig 3:** Hematoxylin and eosin stain of liver parenchyma shows multiple foci of bile duct proliferation (arrows) composed of bland cuboidal cells and duct formation in a fibrotic and inflamed portal space.



**Fig 4:** Magnetic resonance imaging at the 16th month of follow up shows normal liver parenchyma.



**Fig 5:** Magnetic resonance imaging at the 16th month of follow up shows normal liver parenchyma.

Although pathogenesis of BDA is challenging, the most acceptable one based on immunohistochemical studies is a reactive process in response to biliary ductular injury following trauma or inflammation.<sup>6</sup> Furthermore, imaging findings of BDA are not specific and are difficult to be differentiated from primary liver tumors.<sup>2</sup> In our case there were three hypoechoic lesions at ultrasound, and hypodense at CT, in which one larger mass seemed to have more density.

In the study of Lei Chen and colleagues, BDA was shown as a hypodense nodule with hazy borders in the CT.<sup>2</sup> In the study by Futa and co-workers, which is the largest study of BDA yet, lesions had heterogeneous enhancement in the CT.<sup>1</sup> In the report by Akyol and others, who presented BDA in a patient with colon cancer, a 1-cm hypodense mass in the liver was found with an appearance similar to metastasis.<sup>3</sup> Kim and colleagues reported one mass with heterogeneous enhancement and internal enhancement of the small cystic portion.<sup>6</sup>

Image reviews of case reports, especially of CTs, reveal mostly small (peripheral)<sup>7</sup> lesions that are hypodense and larger masses, which have heterogeneity, although no specific pattern is reported for BDAs at imaging. Malignant and benign lesions are both mentioned in the differential diagnosis of the disease.

In our case, histopathological examination showed foci of bile duct proliferation in an inflamed and fibrotic portal space. IHC staining was positive for CK7 and negative for P53. Histopathological test can accurately diagnose BDA and IHC is a complementary test. Reports of previous studies suggest that the lesions are usually subcapsular with a marked border, but no capsule. Proliferated bile ducts are found with few inflammatory cells. Epithelial cells of proliferated bile ducts are well differentiated with no obvious atypia. When the disease progresses, proliferated bile ducts and inflammatory cells decrease and fibrous tissue increases. Immunohistochemistry for CK7, CK19, and CD56 are positive and Ki67 and P53 are negative.<sup>2</sup> IHC staining cannot differentiate BDA from cholangiocarcinoma except for Ki67.<sup>3,8</sup> We found no signifi-

cantly increased serum tumor marker, which is similar to previous reports in which no specific serum tumor marker was reported.<sup>1,6</sup>

As far as we know this is the first reported BDA that was resolved during a 2-year follow-up. BDAs may be identified on abdominal imaging done for unrelated symptoms. Conservative treatment is recommended after the diagnosis has been established. Modification of risk factors, such as discontinuation of hormonal therapies, may result in regression of the lesions

#### CONFLICT OF INTEREST

The authors declares no conflict of interest related to this work.

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