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## Case Report

# Necrotizing granulomatous inflammation of the liver

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## ABSTRACT

A 73-year-old patient with necrotizing granulomatous inflammation of the liver is presented. The computed tomography demonstrated 2 hypodense tumors with progressive enhancement in the liver. They became nearly isodense to the normal hepatic parenchyma on the delayed phase.

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## Introduction

Necrotizing granulomatous inflammation (NGI) is usually caused by *Mycobacterium tuberculosis*. It usually occurs in the lung. The extrapulmonary sites commonly include lymph node, pleura, and joints, although any organ may be involved [1]. However, its causes still remained unexplained in nearly 20%-40% of cases [2,3]. We present the computed tomography (CT) findings of a case of NGI of the liver with negative results of Ziehl–Neelsen stain for acid-fast bacilli and sputum culture for *M tuberculosis*.

## Case report

A 73-year-old woman consulted the medical department with the complaint of intermittent upper abdominal pain for several weeks. She had a history of cervical squamous cell carcinoma; stage Ib, 7 years ago. She received radical hysterectomy and was regularly followed up in the gynecologic department in this 7-year period. For the present complaint, an ultrasound examination was performed and 2 mixed echogenic tumors, about 2.5-4.5 cm in size, were found in right lobe of the liver. The patient was not a hepatitis B or C carrier.

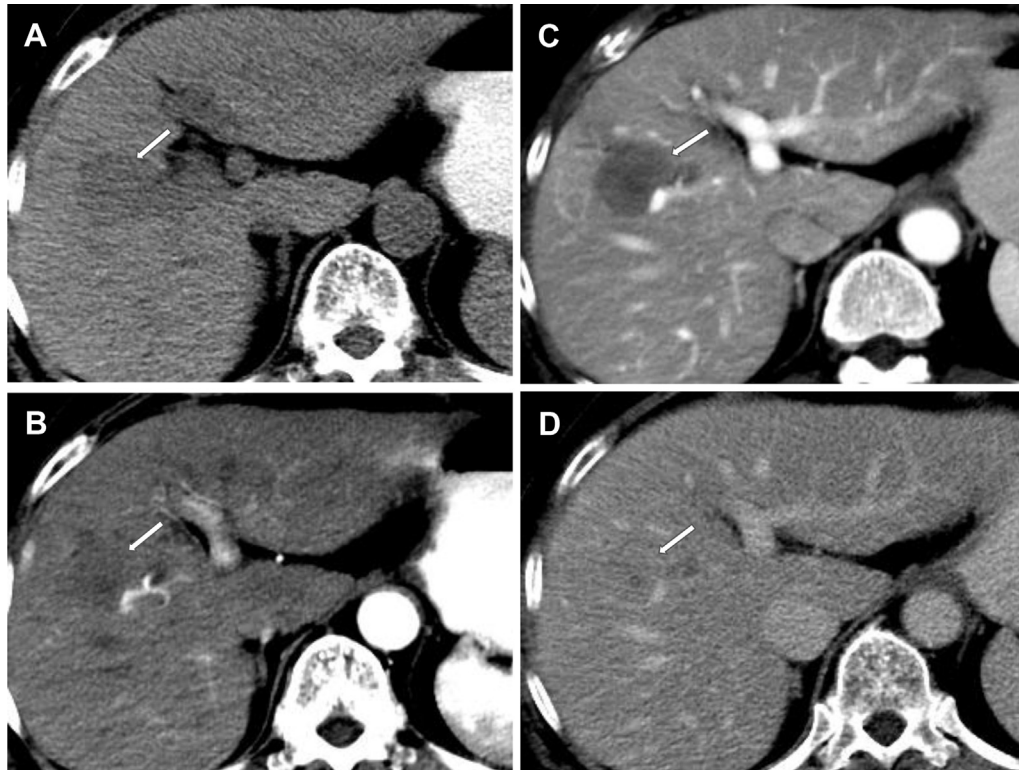
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**Fig. 1** – (A) Precontrast axial image. There is a hypodense tumor (arrow) in S8 of the liver. The density of the tumor was about 50 Hounsfield units (HUs). (B) Arterial phase of postcontrast scan. The hypodense tumor (arrow) did not show obvious enhancement. Its density was about 60 HUs. (C) Postcontrast image 30 seconds after Fig. 1B. The hypodense tumor (arrow) showed a moderate enhancement with a density of 90 HUs. (D) Postcontrast image 2 minute and 20 seconds after Fig. 1B. The whole tumor (arrow) became nearly isodense, about 100-105 HUs, to the normal liver parenchyma.

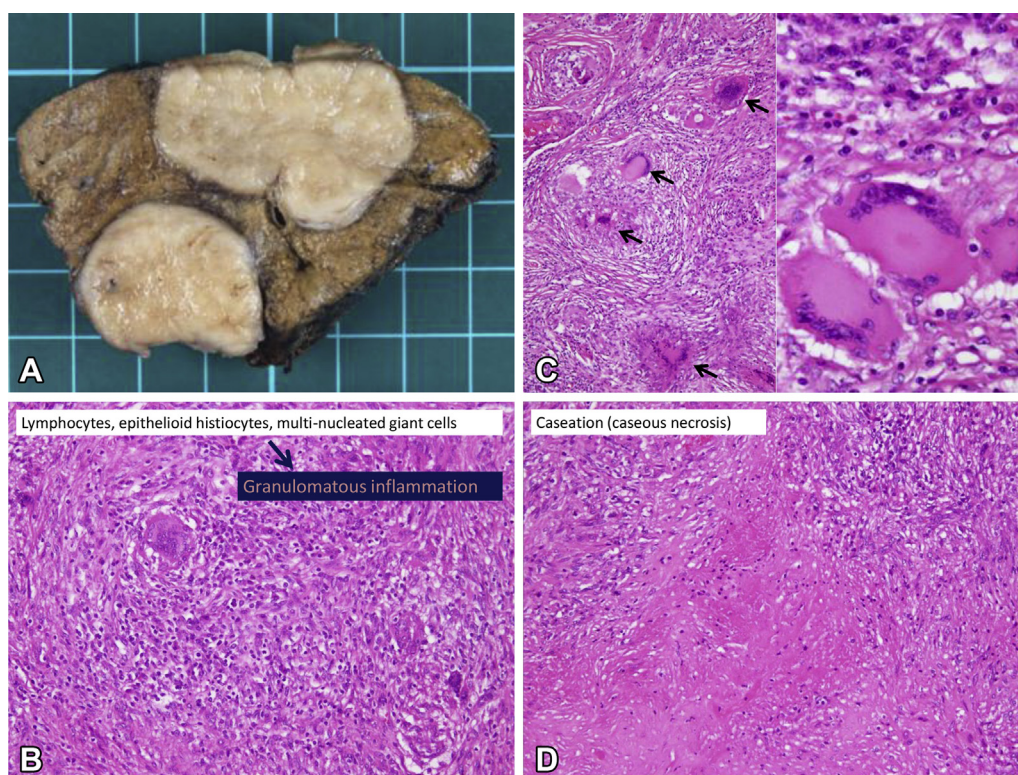
The serum carbohydrate antigen-199, carcinoembryonic antigen, and alpha-fetoprotein levels were all within normal limits. The other biochemical data were nonspecific. The chest plain film showed linear fibrotic scars and a soft-tissue nodule, about 26 × 12mm in size, in left upper lobe. A subsequent CT examination demonstrated 2 hypodense tumors, about 44 × 42 × 26 mm and 30 × 24 × 22 mm in sizes, in S4-S8 and S8 of the liver on precontrast scans. After intravenous contrast medium administration, both tumors showed a poor enhancement on the arterial phase. They were progressively enhanced and became nearly isodense to the normal parenchyma on the delayed phase, about 2 minutes and 20 seconds later to that of arterial phase (Fig. 1). The adjacent vessels were not involved. Under a presumptive CT diagnosis of cholangiocarcinoma, she was admitted to receive a partial right lobectomy of the liver. The gross specimen showed 2 white, slightly yellowish, solid tumors in S4-S8 and S8 of the liver without obvious cavitation (Fig. 2A). The microscopic examinations described epithelioid granulomas, chronic inflammatory cell infiltrations, granulation tissue, and marked fibrosis (Fig. 2B). Langhans giant cells and caseous necrosis were present (Fig. 2C and D). Neither acid-fast bacilli nor fungi could be identified in the acid-fast or periodic acid-Schiff stains. Two lymph nodes removed from the hepatoduodenal ligament also showed granulomatous inflammation without acid-fast bacilli or fungi. Because of the negative stain results, a pathologic diagnosis of NGI of the liver was made. The

patient recovered uneventfully and was discharged. A total of 7 times of sputum culture and acid-fast stains all revealed negative results of *M tuberculosis* in the after 8-month period. The later chest plain films showed no significant change of linear fibrotic scars and a soft-tissue nodule in left upper lobe. Even so, she still received anti-tuberculosis (TB) treatment and was followed up in the infectious diseases department.

## Discussion

A granuloma is a focal compact collection of inflammatory cells. It is usually the end result between the invading organisms or antigens, which are failed to be removed by the host, and the persistent active cell-mediated hypersensitivity. The local inflammation attracts monocyte macrophages. These macrophages may fuse to form multinucleated giant cells or transform to epithelioid cells [4]. Necrotizing granuloma indicates the presence of tissue necrosis in the granuloma. Its causes were found to be infectious in 71% and remained unexplained in 26% after thorough study [2]. A similar result as infectious in 42% and unexplained in 39% has also been reported [3].

Granuloma formation in the liver includes a variety of conditions, most commonly tuberculosis, sarcoidosis, and histoplasmosis [5]. They are usually discrete, sharply defined nodular infiltrates composed of epithelioid granulomas



**Fig. 2 – (A) Gross specimen showed 2 white, slightly yellowish, solid tumors without obvious cavitory lesions. (B) 200× microscopic picture showed granulomatous inflammation composed of epithelioid histiocytes, multinucleated giant cells, and lymphocytes. (C) 200× and 400× microscopic pictures showed Langhans giant cells (arrows). (D) 200× microscopic picture showed caseous necrosis.**

surround by a rim of inflammatory cells, predominantly lymphocytes. Sarcoidosis with hepatic involvement usually has no symptoms related to liver injury [6]. Hepatomegaly is most commonly seen. The granulomas may be too small, less than 2 mm, to be discernible and the liver parenchyma appears homogeneous. They may be seen as multiple hypoattenuating nodules, greater than 5 mm in size, on contrast-enhanced CT scans. These nodules may coalesce and enlarge. Hepatic involvement in histoplasmosis usually presents as hepatomegaly without focal or diffuse abnormality of the parenchymal attenuation [7]. In tuberculosis, the granuloma may have caseous necrosis, Langhans giant cells and surrounding fibrosis [4,8,9]. Tuberculosis of the liver is divided into miliary, local, and biliary forms [8,10]. The miliary form is the most common and thought to be spread via a hematogenous route. It is difficult to recognize on imaging and can only be identified by percutaneous biopsy. The local form includes parenchyma-necrotic abscess and solid tuberculoma. The biliary form involves intrahepatic or extrahepatic ducts; and external compression of the bile duct by enlarged lymph nodes [11,12].

The CT manifestations of hepatic tuberculosis are dependent on the number, size, and disease activity [13,14]. It might be solitary or multiple. If the size was small, less than 2 cm, it usually appeared as multiple hypodense nodules without obvious enhancement in both lobes. If larger than 2 cm, relatively less tumorous lesions with various degrees of enhancement and cavitations might occur. The enhancement

was related to inflammation-induced vascular hypermeability. However, they were always hypodense on the venous phase of postcontrast scans. The cavitations represented caseation-induced abscesses, from small to large in size. If persists long enough, calcification occurs in the lesion. In the current case, the 2 hepatic tumors are solid in texture. They did not show obvious enhancement on the arterial phase. Instead, they showed a rather homogeneous, progressively increased enhancement and became nearly isodense to normal parenchyma on the later images. It differs from those previously reported in that it showed delayed enhancement.

Hepatic tumors with a delayed enhancement may occur in several conditions, such as cavernous hemangioma, metastasis, abscess [15], intrahepatic cholangiocarcinoma [16], and inflammatory pseudotumor [17,18]. In hemangioma, it is due to slow blood flow in the large intravascular space which begins early in the periphery, moves centripetally and coalesces gradually in the late stage. In metastasis and abscess, the delayed enhancement is presumed to be due to extravasation of intravascular contrast material into the extravascular, interstitial space in the central zone of metastasis and peripheral zone of abscess [15]. In our case, there was no obvious enhancement of the tumors on the arterial phase, suggestive of absence of hypervascularity. The delayed enhancement most likely resulted from gradual diffusion of the contrast medium into the interstitial space of the abundant fibrous stroma. This phenomenon has been reported to occur in fibrous tissue of hepatic masses [19,20]. Considering the

differential diagnoses, cholangiocarcinoma, metastasis, and inflammatory pseudotumor tend to be inhomogeneous in texture. Hepatocellular carcinoma, adenoma, and hemangioma usually have a hyperdense enhancement, either heterogeneous or homogeneous, on the arterial phase due to their abundant vascularity.

The definitive diagnosis of *M tuberculosis* infection needs a positive culture of this organism. Although highly suggestive of TB infection, neither a microscopic demonstration of acid-fast bacilli after ZN stain nor the presence of caseous necrosis is diagnostic of *Mycobacterium tuberculosis* infection [21]. The polymerase chain reaction test is not sensitive enough to detect *Mycobacterium tuberculosis* [22]. The current case was finally diagnosed as NGI based on microscopic findings, and negative results of acid-fast bacilli smear after ZN stain and sputum culture. Because negative result of TB culture does not exclude the possibility of TB infection [1], the current case still received anti-TB treatment in the follow-up period.

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