MR features of hepatic macronodular mycobacteriosis

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Mycobacteria are a rare cause of liver parenchyma infection. Few publications, or only studies with small samples, have described the imaging features of hepatic macronodular mycobacteriosis, particularly with MRI (1-5). Here we report the MRI features of ten liver lesions found in five patients. Of all patients for whom a histological diagnosis of hepatic mycobacteria involvement was found. With the objective of describing the MRI features of this disease, our study included all patients from this first list who had also had a liver MRI examination in the month preceding or following the histological diagnosis. Each of the patients included in the study also had to have a complete medical file including clinical observation and the patient’s immune and pulmonary status.

The MRIs (Gyroscan NT-10, 1 tesla, Philips Medical Systems, Eindoven, Netherlands) comprised T2-weighted axial Turbo spin-echo sequence (TR/TE = 1800/80) with fat saturation (Spoiled Inversion Recovery), in T1-weighted in-phase and opposed-phase gradient echo sequence (TR/TE = 4/1.9) after IV injection of 0.1 mmol/kg of gadolinium contrast medium (Magnevist, Guerbet, France) and in T2-weighted sequence, and a slight rim enhancement after gadolinium-enhanced T1-weighted sequences. For two patients, we also had re-examinations in the month preceding or following the initial liver MRI.

Results
Clinical data
The mean age of the population studied was 67 years (range, 40–82 years). The entry symptoms corresponded to fever (two cases), pain in the right hypochondrium (three cases), and/or a deterioration of the general condition (three cases). For a patient treated for chronic liver disease, a focal point liver mycobacterium infection was discovered incidentally, and another patient presented with a surgical picture of acute angiocholitis with an enclosed lithiasis at the bottom of the bile duct. One patient had already been...
hospitalized 10 years before for pulmonary tuberculosis. None showed a congenital or acquired immunodeficiency. All patients improved clinically on specific antibiologic treatment within a few weeks and the lesions shown on imaging disappeared between 2 and 6 months after beginning treatment.

The biological results showed that transaminases were normal in two cases (40%) and high in three cases (eight times the normal level in one patient and 1.5 times the normal level for the two others). Gamma-glutamyl transferases were only normal for one patient and increased for the four others, between three and ten times the normal level. Alkaline phosphatases were increased in three cases, between three and four times the normal level. Total and conjugated bilirubin were only high in the acute angiocholitis case because of the bile duct obstruction. Finally, inflammation as demonstrated by the reactive protein C values was present in only two patients.

All patients had a thoracic CT, a bronchial fibroscopy examination, and several bacterial serology tests. This workup was negative in all cases. The tuberculin intradermal reaction test was positive for two patients, including the patient with a history of pulmonary tuberculosis.

MRI

The mean delay between MRI examination and histological confirmation was 29.8 days (range, 1-71 days).

Ten lesions, measuring a mean 48 mm (range, 30-70 mm), were identified. The results before biopsy are reported in Table 1 and illustrated in Figures 1-3. The lesions exhibited T2-weighted hyperintensity in seven cases and T1-weighted hypointensity in all cases. Contrast uptake was progressive, predominating in the portal time and in the periphery of the lesion in seven cases. There was no signal modification on T1-weighted opposition-phase sequences.

| Table 1 |
|------------------|------------------|------------------|------------------|------------------|
| **MR features of hepatic macronodular mycobacteriosis.** |
| Patient | Lesion no. | Size (mm) | Contours | T1 In/out phase | T2 Enhancement at portal time |
| 1 | 1 | 30 | Clear | Hypointensity | Hyperintensity | Peripheral |
| 2 | 30 | Clear |
| 3 | 40 | Clear | Hypointensity | Hyperintensity | Homogeneous |
| 4 | 50 | Clear |
| 5 | 70 | Clear | Hypointensity | Hyperintensity | Peripheral |
| 6 | 60 |
| 7 | 60 | Blurred | Hypointensity | Isointensity | Peripheral |
| 8 | 40 |
| 9 | 30 | Blurred | Hypointensity | Hyperintensity | Peripheral |
| 10 | 70 |
compared to in-phase sequences. The lesions were located in the left lobe three times and in the right lobe seven times. Patient no. 4 presented a central hepatic lesion inducing dilatation of the intrahepatic bile ducts predominating on the left.

**Histological results**

The histological analyses were done for one patient on a segmentectomy specimen and on liver biopsies for the others. For all patients, histology demonstrated giant cell granuloma lesions. In four patients, this was associated with necrosis, described as caseous for two of them. Ziehl-Nielsen staining was negative in all cases. Peliosis was noted in three patients and fibrosis in three cases. For the two patients for whom hepatic tuberculosis was suggested before biopsy, a complementary sample was sent for bacteriological analysis. The culture came back positive for *Mycobacterium fortuitum* after 90 days for one patient. The PCR method was not used to look for mycobacteria.

**Discussion**

**Physiopathology**

Hepatic tuberculosis is usually associated with active pulmonary tuberculosis or miliary tuberculosis. There is also an abdominal association in 15% of tuberculosis cases, the most often with a lymph node variant (25%-93%) (6). In a study of 92 cases of liver biopsies done in patients with pulmonary tuberculosis, Morere et al. (7) identified granulomatous lesions in 20 cases. Isolated liver involvement of a mass or tuberculoma is rare. This diagnosis is most often unrecognized and confused with primary or secondary liver tumor. The liver infection probably stems from the para-aortic or portal lymph nodes and may reach the liver through the portal system or the superior mesenteric artery (8).

**Positive diagnosis**

The clinical manifestation of tuberculosis takes several forms and can vary from the absence of symptoms to a picture of severe hepatitis with jaundice and hepatic insufficiency (6, 9). Positive diagnosis is difficult because it requires demonstrating resistant acid-fast bacilles. Ziehl-Nielsen staining is not positive in 0%-45% of cases, culture is long (90 days) and is only profitable in 10%-60% of series, so that the PCR search for mycobacteria would most often be contributive, in at least 57% of cases (8).

Nevertheless, for most authors (1-3, 8, 10-13), the diagnosis can be reached based either on the presence of hepatic granulomas associated with documented tuberculosis in another organ, particularly the lungs, or when the clinical symptoms and radiological examinations regress after starting antituberculous treatment, particularly if the initial antibiotic therapy failed (8).

In our study, only one culture was positive and demonstrated an atypical mycobacterium. Therefore, for the four other cases, the diagnosis was presumed based on a range of clinical and histological arguments.
Differential diagnosis

Tuberculoid granuloma is characterized by the presence of epithelioid cells, giant cells, or Langhans cells and lymphocytes in the peripheral rim. This is not itself specific and can be found in other diseases. A study by McCluggage (14) inventoried the hepatic granulomatous etiologies over 30 years and found a number of causes: infectious (mycobacterioses, brucellosis, mycoses, schistosomiasis), metabolic (copper overload/Wilson disease), inflammatory (sarcoidosis, primary biliary cirrhosis), and neoplastic (lymphoma). Complementary tests will therefore always be necessary to eliminate each of these hypotheses, which was done for all the patients in this retrospective study.

Imaging features

The descriptions of hepatic tuberculoma in imaging are few in number and most often are sonographic and/or CT descriptions. In ultrasound, the tuberculoma is most often hypoechoic, but hyperechoic nodules have already been described (15, 16). With CT, the nodules classically appear hypodense without enhancement or with low levels of peripheral enhancement after iodine injection (15).

To our knowledge, fewer than ten MRI observations of hepatic tuberculomas have been reported in the literature (1-5). The classically accepted feature is a lesion exhibiting hypointensity on the T1-weighted sequence and isointensity or hypointensity on the T2-weighted sequence. After injection there is a slight rim enhancement (4, 13, 15).

In our study, enhancement was absent or low in all cases after IV injection of gadolinium. When it was present, it was most often a peripheral rim enhancement at the portal time and late after injection. None of the lesions showed signs suggesting a specific hepatic lesion and the unusual aspect had encouraged pursuing investigations in the hypothesis of a malignancy. The T2-weighted signal was most often high. These data are in agreement with the preceding cases recently described in the literature. The spontaneous hypointensity on the T1-weighted sequence seemed constant (2, 3, 11). In the T2-weighted sequences, the descriptions were variable, with the intensity either lower (2, 3, 11) or higher (3, 12). Yuji et al. (1) discussed the
possible reasons for a hypointensity on the T2-weighted sequences. It could be related to the presence of fibrosis, calcifications, or free radicals (1). In this first case, the pattern could be close to the cerebral tuberculomas that classically appear in hypointensity on the T2-weighted sequences for this same reason (17). Other authors report a lesion showing hyperintensity on the T2-weighted sequences because of a cystic component (3) or liquid necrosis (11). In our case, and as suggested by Fan et al. (2), hyperintensity in T2-weighted images is most certainly related to the very presence of granulomatous tissue. The intensity of the signal may be modulated by inflammatory reorganizations, the associated fibrosis and necrosis, which may reflect the same physiopathological form at different stages of advancement (5). Moreover, the T2-weighted sequences that we obtained were systematically associated with fat saturation (18), contrary to the protocols reported by other authors (2-5). Therefore, the lesions described showing T2-weighted isointensity or hypointensity in other studies may have stemmed from hyperintensity after fat saturation, with the signal description made in relation to the adjacent healthy liver.

**Conclusion**

Isolated hepatic macronodular mycobacteriosis is rare and MRI has a low level of specificity in its positive diagnosis. The most frequent image is one showing hypointensity on the T1-weighted sequence, hyperintensity on the T2-weighted sequence, with very low rim enhancement after IV injection of gadolinium predominating in the portal and later phases.

**References**