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CASE REPORT

Inflammatory myofibroblastic tumor of the liver due to *Mycobacterium tuberculosis* in an immunocompetent girl

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Abstract The case of a 9-year-old girl with a *Mycobacterium tuberculosis* inflammatory myofibroblastic tumor (IMT) of the left lobe of the liver is reported. The tumor was surgically excised and had histological features diagnostic of IMT, a positive Ziehl-Nielsen staining for acid-fast bacilli and a positive polymerase chain reaction for *Mycobacterium tuberculosis.* Surgical excision of the tumor followed by anti-tuberculosis treatment for 9 months resulted in full recovery. The patient had no apparent immune disorder, and there was no evidence of extrahepatic tuberculosis. These findings make this case exceptional because IMTs, due mostly to atypical mycobacteria, have been described only in immunocompromised patients.

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Introduction

Mycobacterium infection, most often caused by organisms of the *Mycobacterium avium* complex, has been associated with the formation of inflammatory myofibroblastic tumor (IMT) only affecting immunocompromised patients [1, 2]. Until recently, the pathologic category and the biological behavior of IMT have been unclear. The tumor was originally classified as inflammatory pseudotumor, but a new classification defines IMT as a benign non-metastasizing proliferation of myofibroblasts with chronic inflammatory infiltrate [3]. However, rare cases of metastatic disease and malignant transformation have been reported [4]. Mycobacterial IMT predominantly involves lymph nodes [5, 6], but isolated cases of extranodal disease have also been reported [7–12]. We report a case of mycobacterial IMT, which is of particular interest, because it developed in an apparently immunocompetent child, affected the liver, and was due to *Mycobacterium tuberculosis* without any evidence of extrahepatic tuberculosis. To our knowledge, a similar lesion has not yet been described in children.

Case report

The patient, a 9-year-old girl, was admitted to Hospital with a 15-day history of fever (38.5–39°C) usually in the evening, mild anorexia, loss of 1.5 kg of body weight and intermittent epigastric pain. Her past as well as her family medical history were unremarkable. She was fully vaccinated for her age except for the BCG vaccine. She was a

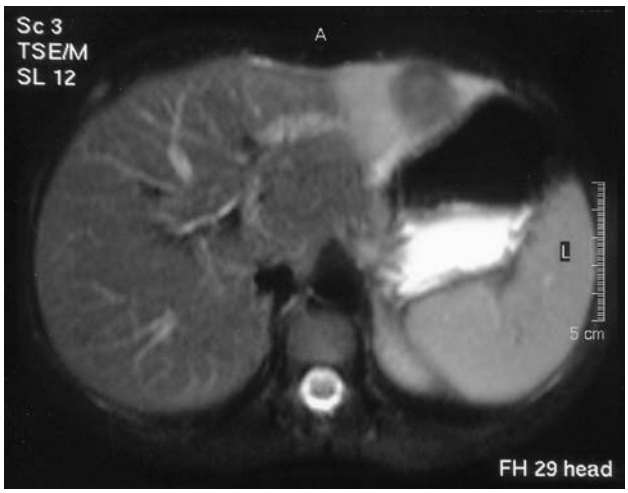

Fig. 1 Contrast-enhanced CT scan shows a mass in the segments II and III of the liver

normally developed child in good general condition without any abnormal findings on clinical examination.

Initial investigations showed: Hb 11.4 g/dl, Hct 35.3%, WBC 15,600/mm^3 (P 78%, L 15%, M 6%, E 1%), PLT 38,400/mm^3, ESR 97 mm, CRP 7.8 mg/dl. Standard biochemical and liver function tests, an infectious screen for bacterial, viral (including HIV) or other causes of prolonged fever, the autoimmune profile and a bone marrow aspiration gave either normal or negative results. The tuberculin skin test was negative and the chest X-ray normal. Liver ultrasound (US) revealed a hypoechoic lesion (3.5 × 2.5 cm) in the left lobe of the liver and one lymph node (2 × 1.5 cm) at the porta hepatitis. Computed tomographic (CT) scan (Fig. 1) confirmed a hypodense space-occupying lesion in the segments II and III of the liver, but could not support a specific diagnosis. Tumor markers (α-fetoprotein, β-human chorionic gonadotropin and carcinoembryonic antigen) were negative. The histological and immunohistochemical findings of a percutaneous US-guided biopsy of the tumor were negative for an inflammatory mass. The lesion was resected by a left lateral segmentectomy using a radiofrequency-assisted liver resection technique [13]. The excised mass and the regional lymph node were sent for histology.

Histopathology revealed a pale and firm lesion measuring 3.5 × 2.5 × 3.0 cm with whitish solid infiltrations extending to the capsule of the liver. Microscopic examination showed destruction of the lobular architecture of the liver due to proliferation of spindle-shaped cells arranged in short fascicles with an ill-defined margin. The spindle-shaped cells contained uniform oval or elongated nuclei with fine chromatin and moderate amounts of eosinophilic granular cytoplasm. They were admixed with inflammatory cells, predominantly lymphocytes, plasma cells and eosinophils (Fig. 2a). The regional lymph node showed normal architecture. Immunohistochemistry revealed positive cytoplasmic staining of spindle-shaped cells for vimentin, smooth muscle actin, CD68 and TBC, while

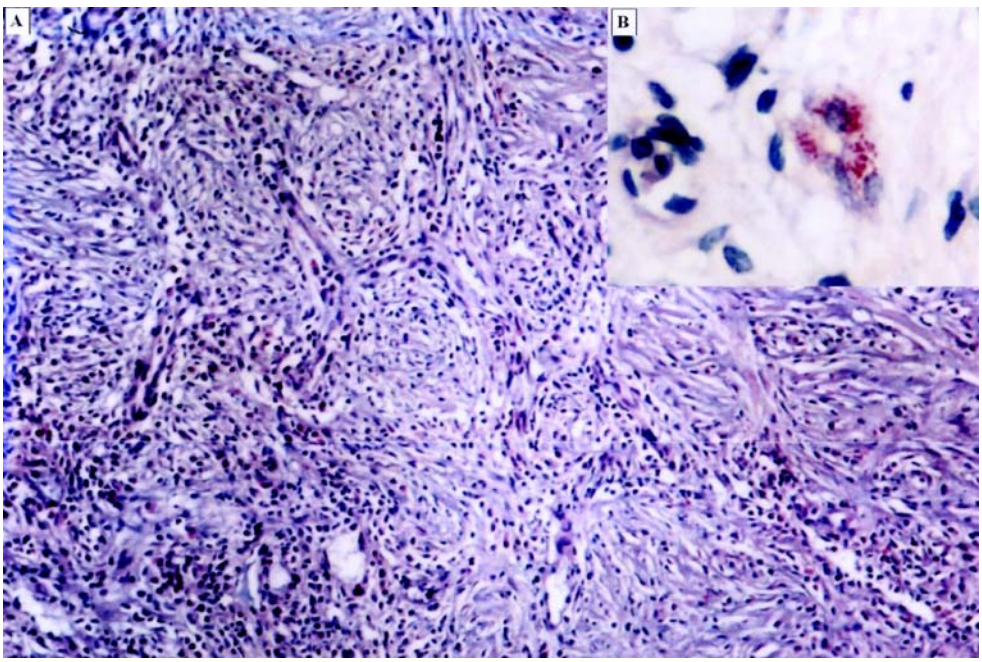

Fig. 2 **a** Liver biopsy showing fascicles of spindle cells among fibrous and fibromyxoid stroma with mixed inflammatory infiltrate forming a storiform pattern (Hematoxylin-eosin, original magnification ×200). **b** macrophages with intracytoplasmic acid-fast bacilli (Ziehl-Nielsen, original magnification ×600)

desmin, Alk-1, CEA, CD31, CD21, CD1a and S-100 were negative. The antibodies Ker AE1/AE3, Ker 16, Ker 20, and the leukocyte common antigen expressed from the residual hepatic components and lymphatic cells. Ziehl-Nielsen staining showed numerous acid-fast bacilli within the cytoplasm of the spindle-shaped cells, the inflammatory cells (Fig. 2b) and the excised lymph node. *Mycobacterium tuberculosis* DNA was detected by polymerase chain reaction (PCR—Amplicor® MTB-Roch Diagnostics, Athens, Greece). Tissue culture could not be performed due to prior exposure of the specimen to formalin.

The patient had an uneventful postoperative recovery and was started on a 9-month course of isoniazid and rifampicin in combination with pyrazinamide for the first 2 months. Over a follow-up period of 3 years, she remained asymptomatic. Repeated liver US (6, 12 and 36 months postoperatively) were normal. The diagnosis of *Mycobacterium tuberculosis* IMT prompted more extensive immunological investigations, including cytokines and lymphocyte subpopulation immunophenotype (Beckman-Coulter's facs method), which did not confirm any immunological defect.

Discussion

Including our own case, only 29 cases of mycobacterial IMT reported in the English literature [6]. The patients were particularly infected by non-tuberculous mycobacteria (NTM) (*Myobacterium avium intracellulare* and *Mycobacterium Kansasii*); only one adult patient and our patient were infected by *Mycobacterium tuberculosis.* The liver has been shown to be the least infected by *Mycobacterium tuberculosis* [14]. Although IMT of the liver has been identified in 18 children [15], only in the case presented here the tumor of the liver was caused by *Mycobacterium tuberculosis*.

Except for three cases involving infants, who developed mycobacterial IMT of the lymph nodes and our patient in whom mycobacterial IMT occurred in the liver, the others were all adult patients. One of the three infants died of complications of AIDS. The remaining two suffered from mycobacterial IMT at the age of 6 and 13 months, respectively, after receiving BCG vaccination. Among the 25 adult patients, 21 patients showed positive anti-serum antibodies for HIV or AIDS and only four had non-HIV related immunodeficiency [1, 7, 10, 16]. Immunodeficiency seems to predispose to atypical manifestations of mycobacterial infection. The individual genetic immunological profile, among other factors, may affect this response, but a complex host-micro-organism interaction may also be responsible for the formation of the mycobacterial IMT. Our patient, an apparent immunocompetent girl, could have specific defects in natural immune system mechanisms that could favor predisposition to this infection.

Clinical presentation, radiological appearance and macroscopic pattern of mycobacterial IMTs make them extremely indistinguishable from malignant tumors [2]. In our case, there was a history of non-specific symptoms and inflammatory responses, while examination findings were unremarkable. The lesion in the left lobe of the liver closely resembled a tumor on imaging studies. Percutaneous hepatic biopsy did not provide certainty in confirming the mass since it could not exclude malignancy. A mycobacterial IMT may also be histologically misdiagnosed as a primary or secondary malignancy. Conditions that may enter the morphologic differential diagnosis of this lesion in children include primary malignant mesenchymal liver tumors, especially sarcomas; embryonal sarcoma, rhabdomyosarcoma, leiomyosarcoma and angiosarcoma [17]. Segmental liver resection has helped in defining the non-malignant nature of the tumor, with resultant symptomatic relief and cure.

The case we described here combines some distinct characteristics: (1) This is a *Mycobacterium tuberculosis*. IMT of the liver without extrahepatic mycobacterial disease or exposure of the child to a tuberculous family or environment. (2) Most cases of mycobacterial IMT have been associated with NTM and not with *Mycobacterium tuberculosis*. (3) In all other reported cases, mycobacterial IMT was localized in other sites but not in the liver. (4) Mycobacterial IMT has been described only in immunocompromised patients. Our patient was HIV negative and apparently immunocompetent, as no particular immunological defect was confirmed by immunological investigations, and there was no history suggestive of some type of immunodeficiency.

In conclusion, *Mycobacterium tuberculosis* IMT of the liver in a child with no apparent immune disorder is an extremely rare entity. The primary therapeutic approach is complete resection of the tumor to confirm the histological diagnosis, to allow differentiation from other liver tumors, and to result in a favorable outcome.

Conflict of interest statement The authors declare that they have no conflict of interest.

References

1. Wood C, Nickoloff BJ, Todes-Taylor NR (1985) Pseudotumor resulting from atypical mycobacterial infection: a "histoid" variety of Mycobacterium avium-intracellulare complex infection. Am J Clin Pathol 83:524–527
2. Coffin CM, Dehner LP, Meis-Kindblom JM (1998) Inflammatory myofibroblastic tumor, inflammatory fibrosarcoma, and related lesions: an historical review with differential diagnostic considerations. Semin Diagn Pathol 15:102–110

3. Coffin CM, Watterson J, Priest JR et al (1995) Extrapulmonary inflammatory myofibroblastic tumor (Inflammatory pseudotumor). Am J Surg Pathol 19:859–872. doi:10.1097/00000478-199508000-00001
4. Kovach SJ, Fissher AC, Katzman PJ et al (2006) Inflammatory myofibroblastic tumors. J Surg Oncol 94:385–391. doi:10.1002/jso.20516
5. Logani S, Lucas DR, Cheng JD et al (1999) Spindle cell tumors associated with mycobacteria in lymph nodes of HIV-positive patients. Am J Surg Pathol 23:656–661. doi:10.1097/00000478-199906000-00004
6. Yin HL, Zhou XJ, Wu JP et al (2004) Mycobacterial spindle cell pseudotumor of lymph nodes after receiving Bacille Calmette-Guerin (BCG) vaccination. Chin Med J 117:308–310
7. Sekosan M, Cleto M, Senseng C et al (1994) Spindle cell pseudotumors in the lungs due to *Mycobacterium tuberculosis* in a transplant patient. Am J Surg Pathol 18:1065–1068. doi:10.1097/00000478-199410000-00010
8. Suster S, Moran CA, Blanco M (1994) Mycobacterial spindle cell pseudotumor of the spleen. Am J Clin Pathol 101:539–542
9. Basilio-de-Oliveira CA, Eyer-Silva WA et al (2001) Mycobacterial spindle cell pseudotumor of the appendix vermiformis in a patient with AIDS. Braz J Infect Dis 5:98–100
10. Morrison A, Gyure KA, Stone J et al (1999) Mycobacterial spindle cell pseudotumor of the brain: a case report and review of the literature. Am J Surg Pathol 23:1294–1299. doi:10.1097/00000478-199910000-00017
11. Shiomi T, Yamamoto T, Manabe T (2007) Mycobacterial spindle cell pseudotumor of skin. J Cutan Pathol 34:246–251. doi:10.1111/j.1600-0560.2006.00611.x
12. Umlas J, Federman M, Crawford C et al (1991) Spindle cell pseudotumor due to Mycobacterium avium intracellulare in patients with acquired immunodeficiency syndrome (AIDS). Positive staining of mycobacteria for cytoskeleton filaments. Am J Surg Pathol 15:1181–1187. doi:10.1097/00000478-199112000-00009
13. Jiao Ir, Navarra G, Weber JC et al (2005) Radiofrequency assisted liver resection—a novel technique. Hepatogastroenterology 52:1685–1687
14. Seiler P, Schwendener RA, Bandermann S et al (2001) Limited mycobacterial infection of the liver as a consequence of its microanatomical structure causing restriction of mycobacterial growth to professional phagocytes. Infect Immun 69:7922–7926. doi:10.1128/IAI.69.12.7922-7926.2001
15. Lee SL, DuBois JJ (2001) Hepatic inflammatory pseudotumor: case report, review of the literature, and a proposal for morphologic classification. Pediatr Surg Int 17:555–559. doi:10.1007/s003830000518
16. Apel R (1993) Lymph node pseudotumor. Am J Surg Pathol 17:91–92. doi:10.1097/00000478-199301000-00012
17. Koea JB, Broadhurst GW, Rodgers MS et al (2003) Inflammatory pseudotumor of the liver: demographics, diagnosis, and the case for nonoperative management. J Am Coll Surg 196:226–235. doi:10.1016/S1072-7515(02)01495-3