CASE REPORT

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MRI as indicator of pulmonary tuberculosis activity: from morphological to molecular level assessment – a case report

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Abstract

We present the case of an adult patient with active post-primary pulmonary tuberculosis (TB) and discuss specific morphological and textural aspects found at high-field magnetic resonance imaging (MRI) of the lung. The 42-year-old man, heavy smoker, undertook a routine employment medical examination and was admitted to a referral pulmonology and TB center due to the abnormal findings seen on his chest radiography. The patient presented nonspecific symptoms, bilateral bronchial breath at pulmonary auscultation, inflammatory syndrome on the laboratory blood tests and positive sputum smears for acid-fast bacilli, which together with the typical aspect on the chest radiography lead to a diagnosis of post-primary pulmonary TB and administration of specific medication. To exclude a possible lung cancer and to reevaluate the extent of the disease, computed tomography and magnetic resonance imaging of the lung were performed. The magnetic resonance examination showed, with an accuracy similar to that of computed tomography, the morphology of active post-primary parenchymal TB lesions, as depicted on the T2-weighted acquisition. Moreover, the T1-weighted sequence using iterative decomposition allowed the assessment of both lipid and caseous pneumonia. To the best of our knowledge, this is the first reported case to assess post-primary pulmonary TB using high field MRI equipment, with an analysis from a morphological to a molecular level. By using a fast two-sequence protocol, both morphological, through T2-weighted acquisition, and textural information such as fat content, using dedicated T1-weighted sequence, can be obtained.

Keywords: magnetic resonance imaging, morphology, pulmonary tuberculosis, texture.

Introduction

Worldwide estimations show that 9.6 million people developed tuberculosis (TB) and 1.5 million people died from the disease in 2014, TB remaining one of the world's biggest threats [1]. However, there is major improvement: TB mortality has fallen by 47% between 1990 and 2000, while effective diagnosis and treatment of TB saved an estimated 43 million lives between 2000 and 2014 [1]. To further reduce TB burden, the *World Health Organization* (WHO) makes clear recommendations: "detection and treatment gaps must be addressed, funding gaps closed and new tools developed" [1]. From 2016, the goal is to end the global TB epidemic by implementing the *End TB Strategy* [1]. By 2035, TB should no longer be a threat to people worldwide through an increased effort made both in diagnosis and treatment strategies [2]. Thus, radiological assessment plays an important part in the success of the program.

Magnetic resonance imaging (MRI) could be a new diagnostic tool, which may fill the missing gaps in the radiological diagnosis of pulmonary TB, its role being well recognized in extra-pulmonary disease assessment, such as neurological and spinal involvement [3]. MRI emerged as an alternative – radiation-free method for the evaluation of lung diseases – after chest radiography and computed tomography (CT) [4]. The recent technical advances [5] have helped MRI to overcome its main limitations (low proton density and low signal-to-noise ratio) for lung characterization [4]. Recently, a comprehensive article presented the recommended MRI standard protocols for specific lung pathology [6]. Here, only non-contrast studies are suggested for the assessment of pulmonary TB. However, to date only few publications have addressed the appearance of pulmonary TB at MRI [7–11].

We report the case of an adult patient with active post-primary pulmonary TB and discuss specific morphological and textural aspects found at high-field MRI of the lung.

Case presentation

We present the case of a 42-year-old man who undertook a routine employment medical examination and was admitted to a referral pulmonology and TB center due to the abnormal findings seen on his chest radiography.

The patient was known to be a heavy smoker, 25 pack-years, and had experienced a prolonged occupational exposure to toxic chemicals. However, his medical history

was unremarkable. Before hospitalization, the patient presented progressive symptoms such as: dyspnea during moderate effort, productive cough with scant mucoid sputum, fatigue, night sweats and 5 kg weight-loss in the past three months. The physical examination at admission showed no fever, lymphadenopathy, hepatomegaly or splenomegaly. Yet, bilateral bronchial breath was detected during pulmonary auscultation. The oxygen saturation was 96%. Other parameters were within normal limits: heart rate 80 beats/minute, blood pressure 130/80 mmHg. Laboratory blood tests revealed only an inflammatory syndrome: leukocytosis with neutrophilia, elevated ESR (erythrocytes sedimentation rate) 74/109 mm/1–2 h, and elevated CRP (C-reactive protein) 12 mg/L. The sputum smears examination was positive for acid-fast bacilli, suggestive for tuberculosis.

The initial chest radiography obtained during the employment medical examination showed bilateral multiple nodular opacities, of medium intensity, variable dimensions and patchy distribution, mainly localized in the left upper lobe. Additionally, a bilateral, perihilar reticulo-nodular interstitial pattern was presented. The aspect was suggestive for a post-primary active pulmonary TB, with typical caseous pneumonia aspect.

Antituberculosis chemotherapy was prescribed according to regimen I of treatment: seven days/week Isoniazid 300 mg, Rifampin 600 mg, Pyrazinamide 2000 mg and Ethambutol 1600 mg for the first two months, followed by four months of Isoniazid and Rifampin, three days/week.

One week after the patient started his medication, he underwent a thoracic CT, both to better reevaluate the TB lesions and to exclude a possible lung cancer. Moreover, the patient agreed to undergo an MRI examination to evaluate any further extent of the disease. A lung MRI protocol was added to the standard procedure and performed on a 3T equipment, using a surface body coil. All cross-sectional images were interpreted by the same radiologist with an experience of four years in interpreting MRI of the lung. The MRI examination showed, with an accuracy similar to that of CT, the morphology of active post-primary parenchymal TB lesions, including: areas of consolidation, cavities with small air-fluid level, "tree-in-bud" sign, further allowing for the detection of a small pleural effusion on the T2-weighted PROPELLER acquisition (Figure 1). Furthermore, on the T1-weighted gradient echo LAVA-flex IDEAL sequence the areas of consolidation showed different signal, the majority being hyperintense on water-LAVA and In-Opposed-Phase, typical for acute inflammation, other had increased signal on fat-LAVA images and became hypointense on water-LAVA and Opposed-Phase LAVA due to their fat content, suggestive for lipid pneumonia (Figure 2). The total scan time for the lung MRI protocol was 220 seconds. No mass indicating lung cancer or additional extrathoracic lesions were found.

The patient continued the antituberculosis medication and his clinical and biological response to treatment was favorable.

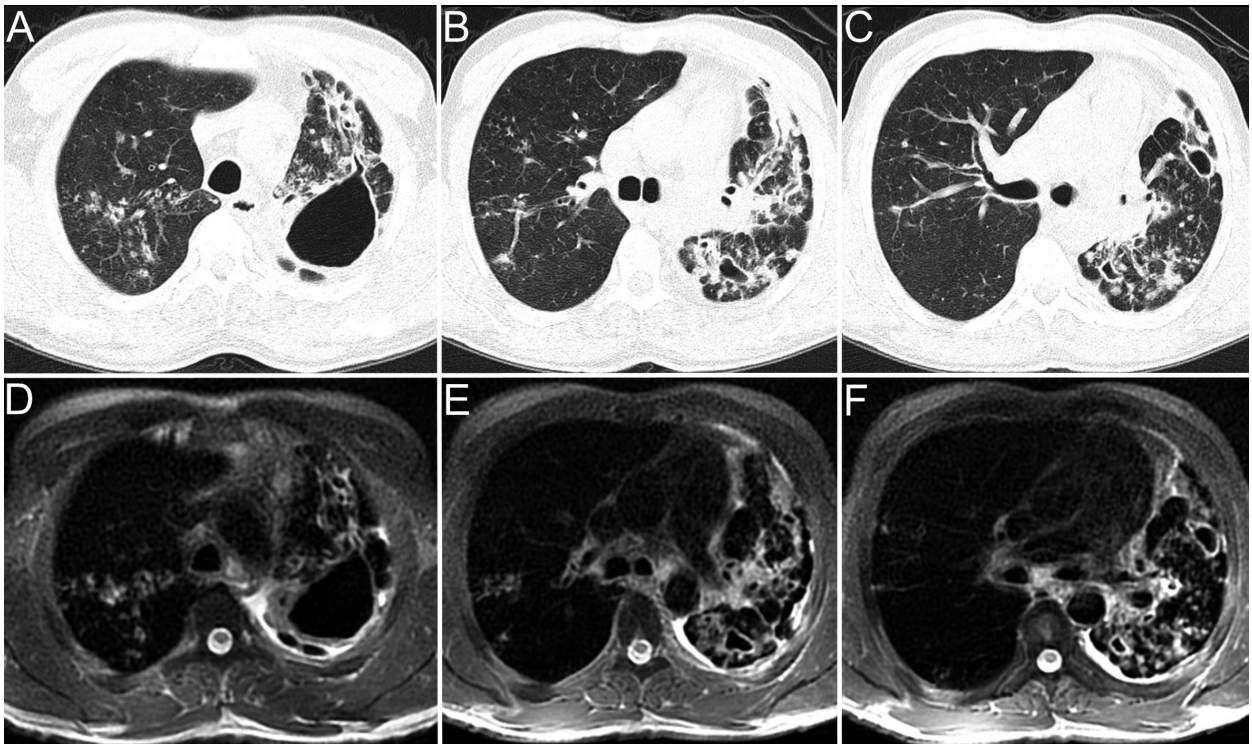

Figure 1 – ***Axial CT thorax, lung window (A–C) and axial T2-weighted fat-saturated PROPELLER sequence (D–F): slice thickness 6 mm, echo time 74.1 ms, repetition time 3750 ms. Images were acquired during breath-holds at end inspiration, with parallel imaging, no electrocardiographic or respiratory gating. Both modalities show areas of consolidation and cavities with small air-fluid level in the left upper lobe, small nodules and "tree-in-bud" pattern in the right upper lobe, small left pleural effusion more conspicuous on the T2-weighted PROPELLER acquisition, typical for post-primary pulmonary tuberculosis.***

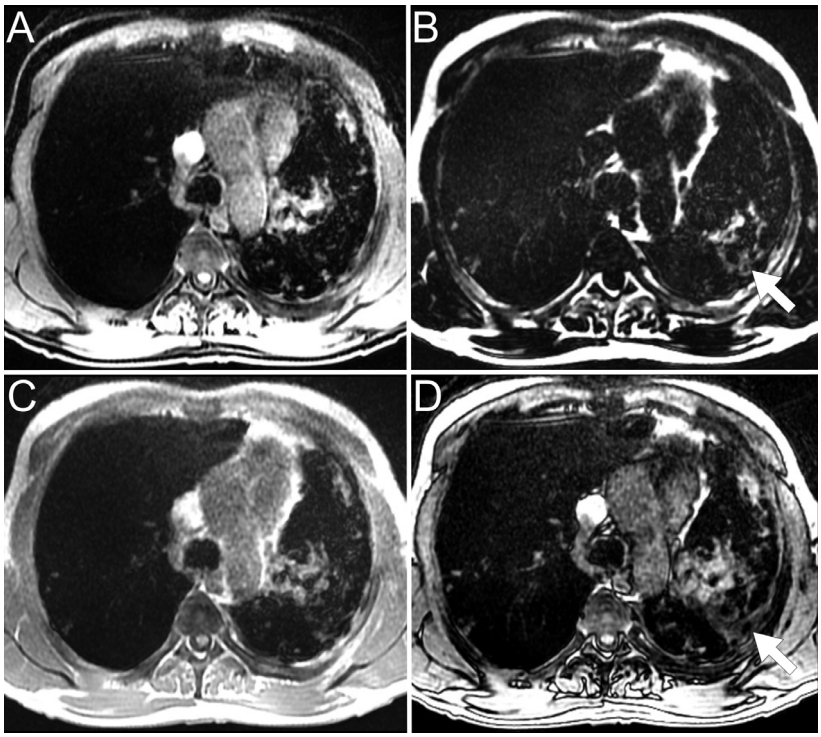

Figure 2 – ***Axial T1-weighted 3D gradient echo LAVA-flex IDEAL sequence: slice thickness 4 mm, echo time 2.7 ms, repetition time 5.4 ms, flip angle 12°. Images were acquired during breath-hold at end inspiration, with parallel imaging, no electrocardiographic or respiratory gating. The areas of consolidation show different signal: some have increased signal on water-only (A) and In-Opposed-Phase images (C and D), typical for acute inflammation, other have increased signal on fat-only (B) images and became hypointense on water-only and Opposed-Phase images, due to their high fat content, suggestive for lipid pneumonia (arrows).***

Discussion

To the best of our knowledge, this is the first reported case to assess pulmonary TB using high-field MRI equipment, with an analysis from a morphological to a molecular level. Moreover, the present case represented a national premiere for evaluating active post-primary pulmonary TB by MRI techniques.

At a morphological level, there is a broad spectrum of pulmonary parenchymal lesions, which demonstrated a good correlation between the CT and MRI appearance [12], even at high-field MRI [13]. The findings are similar regarding specific TB features including: consolidation, cavities, ground-glass opacities and "tree-in-bud" lesions, as demonstrated by Rizzi *et al.* [7]. Moreover, the authors found that MRI is superior to CT in depicting mediastinal lymph nodes, even at normal range dimensions, due to their signal alteration, and more sensitive in detecting pleural effusion (21 of the 60 examination) as compared to CT (10 of the 60 examinations). These findings are consistent with the case we present, were the small pleural effusion was visible only at MRI.

One of the reasons to perform further cross-sectional imaging in our heavy-smoker patient was to exclude the possibility of a coexistent lung cancer. There is evidence in the literature, which proves that MRI, through T2-weighted turbo spin-echo [14] allows for a better differentiation between tumor and adjacent lung atelectasis, as compared to CT. We can therefore extend the finding and suggest that MRI could be the method of choice in the diagnosis of coexistent lung cancer and pulmonary TB consolidation.

At a textural level, MRI is clearly superior to CT regarding tissue characterization [4, 5] and could allow for the differentiation between the exudative stage of pulmonary TB and the relatively acellular fibrotic phase, based on lesion signal intensity [7].

Pathologically, lipid pneumonia was described both in primary and post-primary TB. Caseation necrosis in primary TB was termed "fatty metamorphosis" by Virchow, due to its high content of lipids and foamy macrophages [15]. It was therefore not unexpected that a recent study found lung parenchymal necrosis in primary pulmonary TB in children to be of low signal intensity on T2-weighted and short-*tau* inversion recovery MRI [8]. Furthermore, another analysis in children using MR spectroscopy demonstrated high levels of lipids within the active pulmonary TB lesions [9]. In post-primary TB, the first phase is the lipid pneumonia containing only macrophages, no leukocytes or fibrin and little edema, evolving as the numbers of acid-fast bacilli declines and alveoli become filled with fibrin, cell debris, red blood cells and leukocytes, leading to necrosis and caseous exudative pneumonia phase [15]. In our TB case, the T1-weighted LAVA-flex IDEAL acquisition allowed the assessment of both lipid and caseous pneumonia. The Dixon-type pulse sequences produce four sets of images during a single acquisition: water only, fat only, in-phase, and out-of-phase based on iterative decomposition of water and fat [16], offering the potential for fat-quantification on the fat only images.

To reduce the number of invasive procedures, the method might be helpful in the differential diagnosis of atypical post-primary TB cases showing a nodular pattern from other diseases presenting multiple lung nodules, such as rheumatoid arthritis [17] or tumors. For the latter, an early study found several morphological differences between tuberculomas and malignant nodules [10]. The signal intensity ratios of tuberculomas were significantly lower than those of malignant tumors on native and contrast-enhanced T1-weighted, proton density weighted, and T2-weighted images. However, the appearance of tuberculomas ranges from hypointense to hyperintense on the T2-weighted acquisition according to its evolution [10]. Proposed explanations for the low signal intensity could be the presence of macrophage-laden oxygen free radicals with paramagnetic properties, the degree of fibrotic component and presence of microcalcifications. Furthermore,

tuberculomas showed rim-enhancement as evidence of peripheral fibrous capsules and epithelioid granulomas, and central non-enhancing caseous necrosis.

Since the key of a rentable cost-effectiveness is in the examination time, we propose a 7–8 minutes in room time protocol using two standard pulse sequences. Other sequences may be applied using fat saturated techniques, but these would lead to an increase in the examination time.

The method has the potential not only to accurately describe the morphological pulmonary findings, but also allows for a textural evaluation which may be correlated either to patient infectiousness or to predict treatment response. The concentration of infectious organisms is an important factor in the transmission of pulmonary TB, and to date a significant correlation was found between the degree of smear positivity and the radiological extent of the disease, as well as the presence of consolidation, cavitation, ground-glass opacities and nodules at CT [18]. Since the concentration and virulence of bacilli is different between lipid and caseous pneumonia phase of TB [14], MRI might be of interest to further research on this topic. Nevertheless, we found an increasing trend of severe disease in children [19]; here, MRI may find further application in differentiating bacterial pneumonia from TB consolidation, especially considering the lack of radiation dose. Additionally, to avoid unnecessary radiation exposure, the method is also recommended to pregnant women suffering from pulmonary TB, as showed in a recent case report [11]. Moreover, the method should be of particular attention in the current multicultural setting, especially in developed countries, which benefit from advanced MRI techniques. Further studies are warranted to provide stronger evidence, which may have an impact in patient's decision-making.

Conclusions

We have presented the first case to assess post-primary pulmonary TB using high field MRI equipment, with an analysis from a morphological to a molecular level. By using a fast two-sequence protocol, both morphological, through T2-weighted propeller acquisition, and textural information such as fat content, through dedicated T1-weighted sequence, can be obtained.

Conflict of interests

The authors declare that they have no conflict of interests.

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