Disseminated tuberculosis after anti-TNF? therapy for Crohn\'s disease
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Section: Chest imaging
Area of Interest: Lung Mediastinum Spleen
Procedure: Screening
Procedure: Diagnostic procedure
Imaging Technique: CT
Imaging Technique: CAD
Special Focus: Infection Case Type: Clinical Cases
Authors: Tonolini Massimo, M.D.
Patient: 55 years, male

Clinical History:

Patient with long-standing history of Crohn's disease (CD) including partial colectomy, treated with adalimumab for four months due to steroid-refractory disease. Currently hospitalized with malaise, weight loss, mucohaemorrhagic diarrhoea, persistent high fever, abdominal pain without peritonitis and elevated C-reactive protein despite antibiotics, with presumptive clinical diagnosis of acute CD exacerbation.

Imaging Findings:

Prior to therapy start, radiographs (Fig. 1) excluded active pleuropulmonary lesions and signs of prior exposure to Mycobacterium tuberculosis (MTB), in agreement with a negative tuberculin skin test. Endoscopy and MR-enterography (not shown) diagnosed active ileo-colonic CD.

At admission, radiographs (Fig. 2) showed the appearance of a symmetric "hazy" micronodular lung pattern. CT clearly depicted miliary lung involvement using maximum-intensity projection images (Fig. 3a...d), as innumerable evenly distributed tiny nodules throughout all lobes, predominantly well-demarcated, some of them subpleural. Additional CT findings were centrally hypoattenuating lower lobe subpleural consolidation (Fig. 3e..h), necrotic lymphadenopathies with peripheral rim enhancement in the subcarinal region and right hilum (Fig. 4a...d), and some sub-centimetre hypoattenuating foci in the mildly enlarged spleen (Fig. 4e).

Haemocultures and stool cultures tested negative. Bronchoscopy and bronchoalveolar lavate disclosed acid- and alcohol-fast bacilli consistent with MTB, confirmed by positive DNA assay. Antitubercular treatment allowed prompt clinical improvement with regression of fever and normalisation of C-reactive protein.

Discussion:

Anti-tumour necrosis factor-alpha (TNF?) medications including infliximab and adalimumab represent major advancements in the treatment of chronic inflammatory and autoimmune disorders such as ankylosing spondylitis, rheumatoid arthritis and Crohn's disease (CD). However, due to its key role in immune response, TNF? blockade may result in reactivation of recent or remotely acquired viral and mycobacterial infections. The incidence of opportunistic infections reaches 9% (3.4/100 patient-years) overall and 4% (1.6/100 patient-years) for serious occurrences. Therefore, latent infections and specifically tuberculosis (TB) should be ruled out prior to treatment start: current practice guidelines recommend screening with tuberculin skin test, chest radiographs or interferon-gamma release assays [1-3].

Furthermore, de novo TB may arise after start of anti-TNF? despite negative screening [4, 5] or chemoprophylaxis...
Traditionally, primary TB occurred in childhood as a self-limiting disease manifesting with subpleural parenchymal consolidation in the middle or lower lobes (often indistinguishable from bacterial pneumonia) plus unilateral, typically right-sided paratracheal, tracheobronchial and subcarinal adenopathies with characteristic central low-density and peripheral enhancing rim; other possible manifestations of primary TB included acute bronchogenic spread, miliary TB and pleural effusion. Conversely, cavitation was the traditional hallmark of post-primary TB. Currently, primary TB is increasingly observed in previously unexposed adults. Furthermore, in immunocompromised patients such as those on TNF? inhibitors, extensive lymphatic and haematogenous spread may result in disseminated and extrapulmonary TB forms, which evolve rapidly and eventually prove fatal if unrecognized [7-11].

Encountered in the setting of both primary and reactivated TB, the miliary pattern results from the acute haematogenous dissemination of bacilli leading to the development of innumerable tuberculous granulomas in the lungs and other organs such as the liver and spleen. Particularly in immunosuppressed patients, clinical presentation varies from insidious febrile illness with malaise and anorexia, to acute respiratory distress. Sometimes initially unremarkable, plain radiographs may show either a poorly defined “haze” through both lungs or the classic appearance of diffusely scattered micronodules. As this case exemplifies, CT better demonstrates miliary disease as widespread, evenly distributed innumerable micronodular infiltrates without any topographic predominance [7-9]. In conclusion, physicians and radiologists should be aware of the increased risk of TB reactivation in people on TNF? antagonist therapies. Recognition and reporting of any suspicious abnormality suggestive of TB allows curing the disease with cessation of anti-TNF? medication and prolonged antimycobacterial antibiotic treatment [4-6, 10-12].

**Differential Diagnosis List:** Disseminated "miliary" tuberculosis during biologic (adalimumab) treatment for Crohn's disease, Other opportunistic infections e.g. fungal, atypical mycobacteriosis, Early (non-cavitated) septic emboli, Extrinsic allergic alveolitis, Sarcoidosis, Haematogenous metastases / Neoplastic lymphangitis, Drug-induced lung disorder, Cryptogenic organizing pneumonia, Eosinophilic pneumonia, Crohn’s disease related necrobiotic nodules (exceptional)

**Final Diagnosis:** Disseminated "miliary" tuberculosis during biologic (adalimumab) treatment for Crohn's disease

**References:**


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Figure 4

Description: Centrally hypoattenuating necrotic lymphadenopathies with peripheral rim enhancement were present in the subcarinal region (arrowheads) and at the right hilum (arrows). Origin: Tonolini Massimo, Department of Radiology, "Luigi Sacco" University Hospital – Milan (Italy)
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Description: Additionally, some tiny (sub-centimetre) hypoattenuating foci (thin arrow) were seen in the mildly enlarged spleen. Origin: Tonolini Massimo, Department of Radiology, “Luigi Sacco” University Hospital – Milan (Italy)