Defining trigger related phenotypes in sarcoidosis: Does silica induced sarcoidosis exists?

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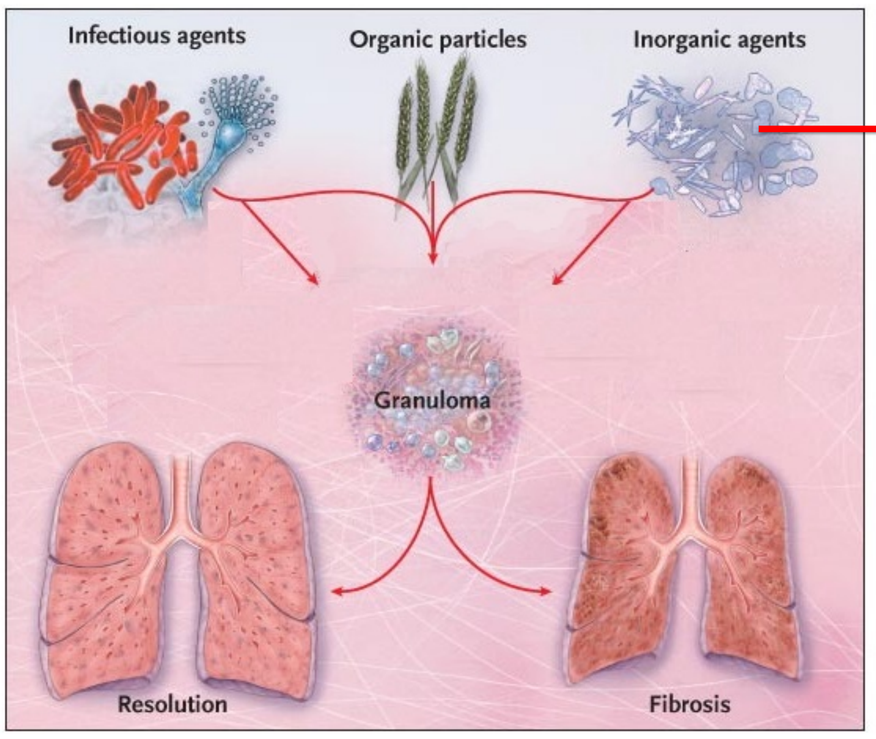
BACKGROUND

Sarcoidosis is a systemic disorder of unknown etiology, characterized by the formation of non-caseating granulomas.



For example:
- Silica
- Metals:
  - Beryllium
  - Aluminium
  - Zirconium

Fig. 1 Hypothesized Immunopathogenesis of Sarcoidosis, adapted from Michael C. Iannuzzi, M.D., Benjamin A. Rybicki, Ph.D., and Alvin S. Teirstein, M.D.N Engl J Med 2007; 357:2153-2165

Chronic beryllium disease (CBD) and sarcoidosis can present with the same clinical findings.
Diagnosis of CBD includes:
Beryllium exposure + Granulomas + Positive lymphocyte proliferation test (LPT)

Case

49 old male plasterer.
Complaints:
fatigue and dyspnea during exercise since a year.

Observations:
High-resolution computed tomography (HRCT):
lymphadenopathy with peripheral located calcifications, nodular abnormalities against the pleura and some fibrotic components. Based on those radiologic findings, a distinction between pneumoconiosis and sarcoidosis could not be made.
Video Assisted Thoracic Surgery (VATS) biopsies :
inflammatory infiltration in the pleura, non-necrotizing granulomas including multiple nucleated giant cells with hyalinization and birefringent material (fig.1).

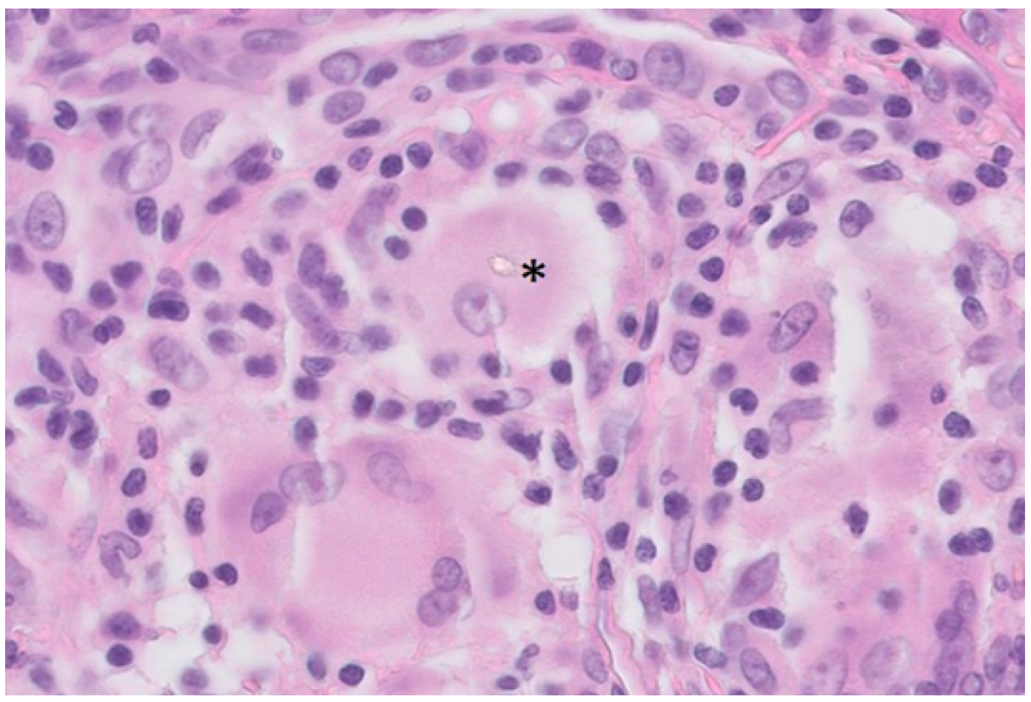


Figure 1. Lung biopsy tissue including birefringent material, as indicated with the asterisk

Analyses:
Energy-dispersive X-ray spectroscopy (EDX) :
aluminum, silicon (Si) and titanium
LPT:
Positive stimulation index of 3,2 for silica.

Diagnosis:
working diagnosis of silica induced sarcoidosis

Treatment:
- Prednisone: Induced severe weight gain
- Azathioprine: Not effective, further pulmonary deterioration occurred
- Infliximab: Seems effective, since decrease in consolidations at the HRCT-scan as decrease in activity at the PET-scan were observed (fig.2).

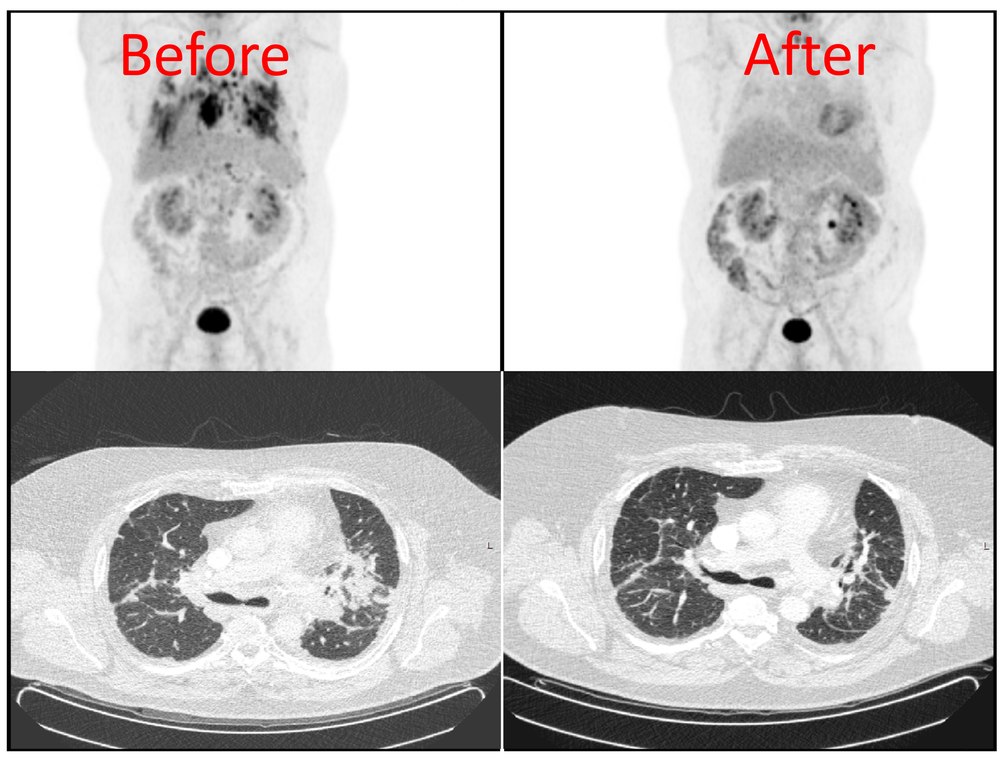


Figure 2. PET and HRCT scans before and after 7 months of infliximab therapy. Left: PET (above) and HRCT scan (below) 2 months before the start of infliximab. At this time point the patients was on azathioprine therapy for 8 months and prednisone therapy was stopped for 14 months . Right: PET (above) and HRCT scan (below) after 7 months of infliximab therapy showing decrease of consolidations.

Discussion

- Treatment of silicosis is difficult → no effective treatment exist.
- To our knowledge, this is the first case describing a patient with silicosis or, in our opinion, silica induced sarcoidosis treated with TNF-a antibodies. The effect of this treatment in silicosis patients is unknown, however refractory sarcoidosis patients have shown good responses.
- The distinction between pneumoconiosis and inorganic agent induced sarcoidosis is sometimes hard to make. The patient described here had (occupational) silica exposure, granulomatosis in lung biopsies and a positive silica LPT. Referring to the ATS guidelines on CBD, in our opinion diagnosis of silica induced sarcoidosis could be made in this patient.
- Searching for (occupational) trigger-related phenotypes in sarcoidosis could broaden therapeutic options in patients were pneumoconiosis is indistinguishable from sarcoidosis.

De lijn tussen pneumoconiose en sarcoïdose kan heel dun zijn. Chronische beryllium ziekte (CBD) is bijvoorbeeld vaak niet te onderscheiden van sarcoïdose. Zo kan CBD gezien kunnen worden als een vorm van sarcoïdose die veroorzaakt is door beryllium. De diagnose CBD wordt gesteld wanneer er naast beryllium blootstelling granuloom vorming en een positieve lymfocyten proliferatie test op beryllium aanwezig zijn. De patiënt beschreven in deze casus, voldoet aan deze criteria voor silica i.p.v. beryllium. Om deze reden zou er dus gesteld kunnen worden dat deze patiënt een vorm heeft van sarcoïdose die veroorzaakt is door silica. Behandeling met infliximab werd gestart, een behandeling normaliter gegeven bij sarcoïdose maar niet bij pneumoconiose patiënten. Deze behandeling lijkt tot zover effectief te zijn in deze patiënt.
Concluderend is het dus belangrijk om trigger gerelateerde fenotypes van sarcoïdose te onderzoeken, om zo mogelijk de behandelopties te verbreden in patiënten waar pneumoconiose en sarcoïdose niet te onderscheiden is.

Contact

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