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CLINICAL IMAGE

The great imitator, imitated

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Case

A 72-year-old female, born in Surinam, presented to the emergency unit of a general hospital after a month of non-productive coughing and a week of being unwell. Except for increasing chronic lower back pain, she had no other complaints and there was no fever. She had no history of tobacco use and her medical history was unremarkable other than insulin-dependent diabetes and dyslipidaemia. A chest X-ray showed uniformly distributed miliary deposits (commonly defined as: innumerable, uniformly distributed, 1-4 mm pulmonary nodules) and consolidation in the left lower lobe *(figure 1)*.

With the hypothesis of miliary tuberculosis, the patient was admitted to the pulmonology ward. A bronchoscopy showed no endobronchial abnormalities and a bronchoalveolar lavage was performed in the right upper lobe. Both the auramine-rhodamine stain and the Ziehl-Neelsen stain turned out positive, after which treatment with tuberculostatic drugs (isoniazid 300 mg/day, rifampicin 600 mg/day, ethambutol 1000 mg/day and pyrazinamide 1500 mg/day) was initiated and a PCR on *Mycobacterium tuberculosis* was ordered. The PCR later turned out to be negative. A PCR on non-tuberculous mycobacteria was not performed. The HIV test was negative.

After two days of treatment, the patient's consciousness deteriorated. A CT and MRI scan of the brain showed hydrocephalus with dilated lateral and third ventricles, a normal aqueduct and fourth ventricle and extensive leukoaraiosis. This was interpreted as impaired resorption of cerebrospinal fluid due to tuberculous meningitis.

Because of progressively deteriorating consciousness and nuchal rigidity, dexamethasone was started and the patient was transferred to our centre for placement of an external ventricular drain.

After the transfer, a previously obtained interferon-gamma release assay (IGRA, QuantiFERON) test turned out negative which, even though there are many cases of active tuberculosis with a negative IGRA, initiated doubt about the diagnosis of tuberculosis. Repeated cerebrospinal fluid samples showed no leucocytosis or low glucose and the auramine-rhodamine stains and PCR on *Mycobacterium tuberculosis* was negative.

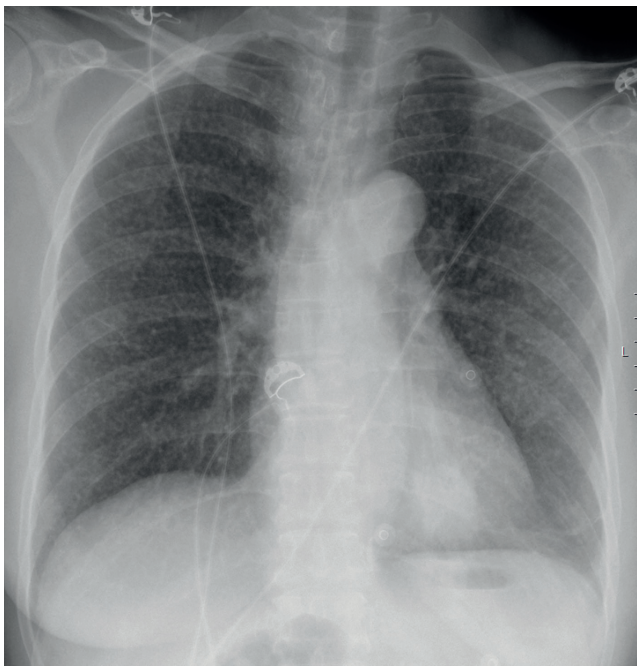

Figure 1. Chest X-ray.

False-positive results from both the auramine and Ziehl-Neelsen stains are rare. This can result from technical errors during the staining process, such as the re-use of containers or positive slides, contamination of the stain by using water containing environmental mycobacteria, use of scratched slides, inadequate decolourisation, etc. We consulted the microbiologist of the referring hospital about the discrepancies in the results and learned that the initial auramine-rhodamine

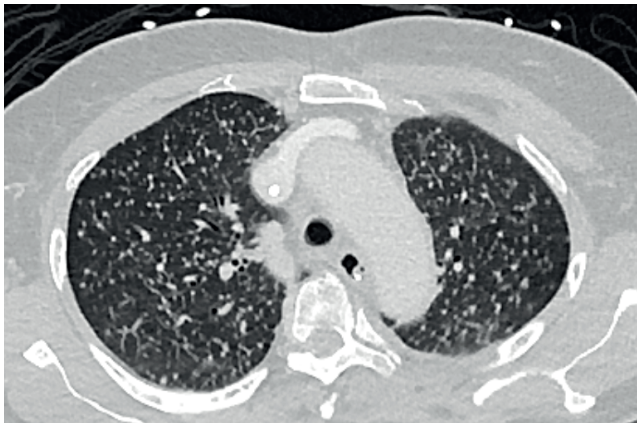

Figure 2. CT-scan showing miliary deposits.

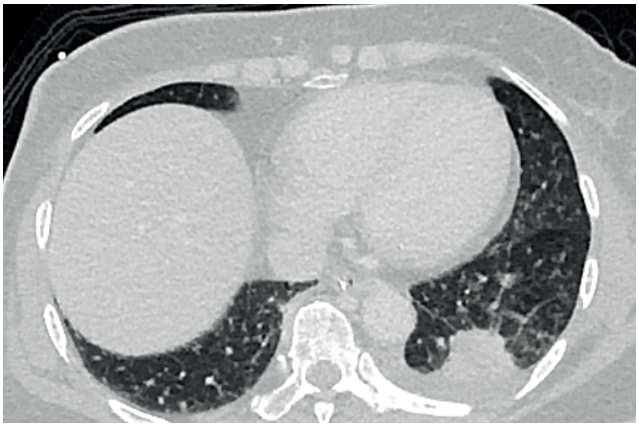

Figure 3. CT-scan showing consolidation in the left lower lobe.

and Ziehl-Neelsen stains were only doubtfully positive and that a second stain on a new glass had turned out negative.
After insertion of the external ventricular drain her consciousness improved. A CT scan of the lungs was performed, confirming the miliary deposits previously suggested on the chest X-ray *(figure 2)*, a pulmonary embolism in the left lower lobe segmental artery, consolidation in the left lower lobe being interpreted as pulmonary infarction *(figure 3)* and no significant mediastinal lymphadenopathy. A bronchoscopy was repeated to obtain transbronchial biopsies from the left lower lobe. Unfortunately, 24 hours later our patient needed to be intubated because of respiratory insufficiency. The results of the transbronchial biopsies showed an adenocarcinoma of which the immunohistochemical profile fitted a primary lung malignancy.

The cytology of the cerebrospinal fluid showed atypical cells, which in this context were most likely a metastasis of an adenocarcinoma. Together these results took us to the final diagnosis of a primary lung carcinoma with diffuse miliary pulmonary and leptomeningeal metastasis.
Neurologically the patient did not improve, she was localising to pain, but not obeying commands and was therefore maintained on mechanical ventilation. Together with the neurologist and the pulmonologist, we concluded that the prognosis was grave and life support, including mechanical ventilation, was terminated, after which our patient died. Autopsy was not performed.

All cultures from the bronchoalveolar lavage, cerebrospinal fluids and the pulmonary biopsy turned out negative for mycobacteria.

Conclusion

In conclusion, we present a patient with miliary pulmonary abnormalities suspect of tuberculosis. Tuberculosis is known as the 'great imitator' since the disease may mimic a variety of other diseases. In this case, however, the great imitator was imitated itself since the patient was diagnosed with pulmonary adenocarcinoma, with miliary pulmonary metastases and leptomeningeal metastasis. While the primary thought is often tuberculosis when confronted with miliary pulmonary abnormalities, it is important to realise that there is quite an extensive differential diagnosis. The differential diagnosis of a miliary pattern on a chest X-ray in an afebrile patient is: tuberculosis, fungal infection, viral infection (such as varicella pneumonia), sarcoidosis, silicosis, haemosiderosis, hypersensitivity pneumonitis, (eosinophilic) granulomatosis with polyangiitis ((e)GPA), eosinophilic pneumonia, pulmonary alveolar proteinosis, Langerhans cell histiocytosis and miliary metastasis of cancer (melanoma, sarcoma, carcinoma). As always, we need to keep an open mind and realise the importance of pulmonary biopsy.

Disclosures

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