Polymerase Chain Reaction

The article very well written and clinically important, but why did the author not mention the option of using polymerase chain reaction (PCR) as a diagnostic tool? PCR is not a universal diagnostic miracle weapon, but when it works it does so within just a few days and is highly specific. Another advantage is that it can be performed using minimal volumes of aspirates, etc. Even if the procedure was not used in the specific case presented in the article it should have been evaluated in the discussion. The same holds true for both the disease and the test: They need to be borne in mind.

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Non-tuberculous Mycobacteria

The author reported a case of mycobacterial infection, which was diagnosed after a lengthy process. However, the case is actually not one of tuberculosis in the stricter sense: the confirmed species—Mycobacterium avium intracellulare complex—belongs to the group of non-tuberculous mycobacteria. These are often found in the environment and, in cultures, are possibly only contaminants. However, in this case the diagnosis was firmly established following the criteria of the American Thoracic Society (ATS) – the specimens came from otherwise sterile body fluids (1). Microscopy using different staining methods, as mentioned in the article, is less relevant than cultures and PCR for confirming a diagnosis, since microscopy has lower sensitivity and, in contrast to the other methods, cannot differentiate between species (2). It therefore needs to be emphasized that the diagnostic mistake in the case report consisted mainly in not doing culture and PCR.

Non-tuberculous mycobacteria—such as the described species—display sensitivities to anti-mycobacterial chemotherapy different from Mycobacterium tuberculosis complex. After resistance testing, recommended initial treatment should therefore consist of a combination of clarithromycin, ethambutol, and, if required, rifabutin. By contrast to the treatment described in the article, however, isoniazid is not the treatment of choice (3).

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Rare Pathologies

We wish to point out that in this case, no actual tuberculosis was present; rather, the patient had non-tuberculous mycobacteriosis (NTM), caused by Mycobacterium avium intracellulare. The infection was finally successfully treated over a period of 2 years with antibiotic combination therapy including clarithromycin (1, 2).

Such pathologies are rare and often affect immunocompromised persons, especially patients with HIV infection.

In the described case, PCR of the microscopically positive direct specimen would have been advantageous as this allows for rapid distinction between tuberculosis and NTM. Nowadays, an Interferon-Gamma-Release Assay (IGRA) may also facilitate this distinction, in particular since the tuberculin skin test was of limited diagnostic value in the present patient, who had previously undergone BCG vaccination (3).

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Chronic Recurrent Multifocal Osteomyelitis
Herzog’s article is of particularly topical interest, as the author has drawn renewed attention to tuberculosis (TB), which over the past 50 years seems to have disappeared and has therefore been forgotten as a differential diagnosis (1). TB—including TB of the bone—is threatening to make a comeback and be included, as a pathomorphosis, in a confusing array of differential diagnoses, such as was shown in this case report of bony tuberculosis. The range of differential diagnoses should also include the generally little known “chronic recurrent multifocal (also monofocal) osteomyelitis” (CRMO) as an important possible diagnosis. However, this diagnosis is hampered by the erroneous interpretation of results. Consequently, the rare “primary chronic osteomyelitis” might remain unrecognized as a result of such an indirectly didactic approach.

CRMO does not manifest in sterile abscesses—which by definition do not actually exist—but in larger areas of sometimes “migrating” sterile inflammation of the bone, the localization being age dependent. These inflammations develop in three stages and are primarily lymphoplasmacellular, not “purulent”—that is, never granulocytic related. Magnetic resonance tomography and biopsy specimens usually provide unequivocal findings that morphologically depend on which stage of development the pathological process has reached. Further, the localization of the focus does not correspond to any of the 6 CRMO types, where none of the foci reside in the skullcap of CRMO patients. Corticosteroids are not indicated therapeutically.

A recently discovered common radiological feature may, however, erroneously link TB and CRMO in terms of the differential diagnosis: a potential parasosseous, especially paravertebral, inflammation of the soft tissues with a tendency to ossification, which may result in vertebral CRMO being mistaken for TB.

However, this specific differential diagnosis is not likely to be common. In our SAPHO/CRMO project in Mainz, there was only one case among 183 patients.

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Lymphoblastic Neoplasia
In my opinion, the main error lies in the initial, inadequate diagnosis in the context of CT guided biopsy. Further information about the exact histological findings would have been desirable.

To base lymphatic leukemia (ALL) therapy merely on a diagnosis of suspected differentiated T-cell lymphoma seems questionable, to say the least. On the one hand, the term “differentiated T-cell lymphoma” is not a widely used medical term; on the other hand, ALL is an immature, lymphoblastic neoplasia that can be confirmed by markers such as terminal deoxynucleotide transferase. In view of the consequences of such a diagnosis, statements such as “consistent with ALL” should not have been used. I don’t see any scope for different interpretations on the basis of the patient’s history. In case of doubt, a fresh and bigger biopsy specimen should be taken, and if there is still doubt, molecular genetic testing should be used to confirm the clone (T-cell receptor rearrangement).

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Differences to Tuberculosis
The confirmed pathogen Mycobacterium avium intracellularare is in the group of non-tuberculous mycobacteria—also known as ubiquitous mycobacteria or “mycobacteria other than tuberculosis” (MOTT). In contrast to tuberculosis, the strain cannot be transmitted from person to person and the disease is not notifiable under the infection protection law. The described case is thus not one of tuberculosis of the bone—the title is erroneous and incorrect.

Where non-tuberculous mycobacteria are found, the case may be one of saprophytic colonization without clinical significance or a manifest infection that requires therapy. Mycobacterium avium complex is the most common non-tuberculous bacteria species that is associated with pathologies in humans.

The first diagnostic puncture did not provide any histological indication of tuberculosis. Because of the raised inflammatory markers and the positive Tine test, tuberculosis was then considered as a possible differential diagnosis. In the abscess specimen obtained in