CASE REPORT

Cat scratch disease and lymph node tuberculosis in a colon patient with cancer

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margaridamatias.onc@gmail.com**SUMMARY**

A 71-year-old man operated for a sigmoid tumour remained in the surveillance after adjuvant chemotherapy. After 3 years, a left axillary lymph node was visible on CT scan. The biopsy revealed a necrotising and abscessed granulomatous lymphadenitis, suggestive of cat scratch disease. The patient confirmed having been scratched by a cat and the serology for *Bartonella henselae* was IgM+/IgG-. Direct and culture examinations for tuberculosis were negative. The patient was treated for cat scratch disease. One year later, the CT scan showed increased left axillary lymph nodes and a left pleural effusion. Direct and cultural examinations to exclude tuberculosis were again negative. Interferon-γ release assay testing for tuberculosis was undetermined and then positive. Lymph node and pleural tuberculosis were diagnosed and treated with a good radiological response. This article provides evidence of the importance of continued search for the right diagnosis and that two diagnoses can happen in the same patient.

BACKGROUND

Persistent lymphadenopathy can have several causes, either infectious or non-infectious, and in patients with known cancer, it is of concern for eventual recurrence of the disease. Granulomatous lymphadenitis has been more often, in Portugal, due to tuberculosis (TB), but several other causes are possible, namely other granulomatous diseases (eg, sarcoidosis) and infectious diseases such as cat scratch disease (CSD) and fungal infections.

CSD is a subacute, and usually self-limited, infection of lymph nodes due to *Bartonella henselae*,¹ after contact with a cat. It causes inoculation lesion and satellite lymph node suppuration with characteristic changes in histology and bacilli on Warthin-Starry colouration. There is a serological test for diagnosis. Antibiotherapy in this entity is controversial, but a macrolide or doxycycline can be used in some situations.²

The authors present a patient with two subsequent infectious aetiologies of granulomatous lymphadenitis.

CASE PRESENTATION

A 71-year-old man was submitted to an urgent sigmoidectomy in March 2006 for a stenosing sigmoid tumour. The pathological examination revealed a grade 2 adenocarcinoma, pT3pN0cM0 and TNM stage II. Because he was operated for intestinal occlusion, he underwent adjuvant chemotherapy with 5 fluorouracil (De Gramont regimen).

The patient remained under surveillance without any evidence of local or distance recurrence.

In November 2009, the chest, abdominal and pelvic CT scan revealed a 1.8 cm left axillary adenopathy, not well-defined at palpation, but lightly tender, without erythema of the overlying skin or any other relevant alterations on the physical examination. The patient denied any symptoms such as cough, dyspnoea, night sweats or weight loss.

INVESTIGATIONS

A positron emission tomography-CT scan showed a left axillary uptake and multiple other infracentimetric adenopathies with low standardised uptake value (SUV). He underwent a breast ultrasound and mammography that revealed gynaecomastia without any other alterations.

He underwent an ultrasound-guided biopsy that revealed a lymph node with reactive pattern with few epithelioid granulomas, without cancer cells. This was followed by a surgical biopsy which revealed a necrotising and abscessed granulomatous lymphadenitis, suggesting CSD (figures 1 and 2). No bacilli were found with Ziehl-Neelsen and Warthin-Starry colourations and the direct and cultural examinations of the lymph node were also negatives for other agents.

The serology for *B. henselae* was positive for IgM (1:80) and negative for IgG.

When specifically asked, the patient confirmed not only having been strongly scratched by a street cat some months before, but also that he often gets scratched by his own cats when he plays with them. He referred that the last time he had been scratched

Figure 1 Surgical biopsy of the left axillary lymph node: granulomatous lymphadenitis with central area of necrosis and microabscess (H&E, ×200).

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Figure 2 Surgical biopsy of the left axillary lymph node: granulomatous lymphadenitis with central area of necrosis and microabscess (H&E, x400).

by one of his own cats was 1 month before the diagnosis of the adenopathy.

In order to exclude TB, blood cultures were negative, including Bactec blood cultures. Direct examinations of blood cultures including Ziehl-Neelsen colouration was negative. Sputum direct examinations and cultures were negative for mycobacterias. A tuberculin skin test (Mantoux) was carried out. The result was positive, but was considered a false positive after a clinical discussion with the infectious diseases department.

The diagnosis of CSD was admitted and the patient started treatment with clarithromycin 500 mg twice daily for 8 weeks. After completion of the treatment, he underwent a control hepatic ultrasound and repeated hepatic function tests that were all normal and a left axillary ultrasound that showed the disappearance of the left axillary adenopathies.

The control serology for *B henselae* was negative for IgG and IgM.

He remained under surveillance in oncology consultation without any evidence of recurrence of disease.

In June 2012, the chest, abdominal and pelvic CT scan as well as the chest radiograph showed an increase of size and the number of left axillary lymph nodes and a small left pleural effusion (figures 3–5). A blood chemistry panel revealed positive inflammatory markers, with erythrocyte sedimentation rate

Figure 3 Chest radiograph showing blunting of the left costophrenic angle suggestive of pleural effusion (arrow). Slight hypotransparency of the right upper lobe similar to previous examinations, suggestive of residual alterations.

Figure 4 Cervical CT scan showing left axillary lymph node (arrows; coronal plane).

65 mm and C reactive protein 1.6 mg/dL. The HIV test resulted negative.

The patient denied any respiratory or constitutional symptoms. He repeated serology for *B henselae* that was negative for IgM and positive for IgG (1:80).

His repeated blood cultures including Bactec blood cultures, as well as direct examinations of sputum and urine, with Ziehl-Neelsen colouration, were all negative examination. He underwent an interferon- γ release assay (IGRA) test for TB that was undetermined.

Three weeks later, the patient repeated the IGRA test and the result was then positive, adding evidence for active TB. The patient was addressed to the surgery consultation in order to perform a biopsy of the lymph node, but as the result of IGRA test had been positive and the patient was very reluctant in repeating the surgical procedure, the biopsy was not considered essential to the diagnosis of TB and was not performed.

On further questioning, it was possible to obtain a history of pleural TB in the remote past.

The diagnoses of lymph node and pleural TB were performed and he was orientated to the infectious diseases department and started antitubercular therapy with isoniazid, rifampin, pyrazinamide and ethambutol.

DIFFERENTIAL DIAGNOSIS

In Portugal, granulomatous lymphadenitis is more often due to TB, but several other causes are also possible, namely other granulomatous diseases (eg, sarcoidosis) and infectious diseases such as CSD and fungal infections.

OUTCOME AND FOLLOW-UP

After 2 months of treatment with tuberculostatic drugs he developed toxic hepatitis. Rifampicin and pyrazinamide were

Figures 5 Cervical CT scan showing left axillary lymph node (arrows; axial plan).

Figure 6 Cervical, chest, abdominal and pelvic CT scan (topogram) showing clear improvement of blunting of the left costophrenic angle suggestive of resolution of pleural and with slight residual pleural thickening compatible with residual lesion (arrow).

suspended and doses of isoniazid and ethambutol were also decreased.

After 5 months of TB treatment, in December 2012, he underwent a cervical, chest, abdominal and pelvic control CT scan that showed a clear improvement of axillary lymph nodes with lipomatous transformation, and resolution of pleural effusion, with only slight residual pleural thickening (figures 6 and 7). The patient repeated the chest radiograph in May 2013 and the pleural thickening was stable and compatible with residual lesion. The patient is currently on isoniazid and ethambutol and we have planned to stop antitubercular therapy after 1 year, since rifampin was not reintroduced.

Clinically the patient remained well without any evidence of colon cancer recurrence.

DISCUSSION

Lymph node is the second most common location of TB³ and the most common form of extrapulmonary disease accounting for more than a quarter of cases. It presents as a subacute or chronic painless lymphadenopathy with eventual fistulisation. In HIV-negative patients unilateral and cervical TB are frequent, but any lymph node can be involved. In this patient, taking into account the history of pleural TB, the presentation in 2012 is

Figure 7 Cervical, chest, abdominal and pelvic CT scan (axial plane) showing clear improvement of axillary lymph node with lipomatous transformation (arrow).

likely to represent a reactivation of TB secondary to the immunosuppression associated with the history of cancer and chemotherapy.

Lymphadenopathy outside the cervical area is usually accompanied by systemic dissemination. Diagnosis is classically established by biopsy with culture.^{3 4} Nevertheless, there is an emerging role of the new IGRA tests in the diagnosis of TB, and if seroconversion in IGRA test is documented, antitubercular therapy may be warranted.

In case of lymphadenopathy in patient with a history of cancer, it is important to emphasise that there may be other diagnosis besides progression of the malignant disease. So it is important to pursue for a possible intercurrent and exclude or confirm the diagnosis with serological studies and biopsies. In case of granulomatous lymphadenitis of unclear aetiology, TB should be strongly considered at least in countries with a high prevalence of TB. Some aspects of granulomatous lymphadenitis can point to CSD, in which there is a stellate granuloma with at least slight neutrophil infiltration and vascular proliferation. Warthin-Starry staining is sometimes positive. In tubercular lymphadenitis, on the other hand, there are Langhans giant cells and caseification necrosis, and the Ziehl-Neelsen stain can sometimes reveal the presence of acid-fast bacilli. Immunofluorescence assays of *Bartonella* can play a role in diagnosing CSD when the aspects of biopsy overlap with TB. IGRA test has an emerging role in the diagnosis of TB; if this test is negative, the likelihood of TB is very remote. If histopathology is compatible, and IGRA test is positive, a trial of antitubercular therapy may be warranted.⁴

We are aware of only occasional reports of coexistent CSD and tubercular lymphadenitis from the literature.⁵ In our patient, the first diagnosis of CSD confirmed serologically was treated with antibiotics. When there was progression of lymphadenitis with elevated inflammatory markers and pleural effusion, we pursued the diagnosis of TB and a trial of antitubercular therapy was ultimately successful.

Concerning the serology, the serological evolution in patients with CSD is described as very variable in several reports, with high levels of IgG and IgM, isolated IgM or low titres of both. In at least one report it is stated that there are no standard courses of CSD serological evolution.⁶ Moreover, the serological evolution may be compounded by eventual fluctuations in total IgG concentration and this case concerns an immunosuppressed patient, whose state could also contribute to the low titres.

To remember, for the diagnosis of CSD it is necessary the presence of 3 of the 4 following criteria^{7 8}:

- ▶ Cat or flea contact regardless of the presence of an inoculation site lesion;
- ▶ Negative serology for other causes of adenopathy, sterile pus aspirated from a node, a positive *Bartonella* PCR assay and/or liver or spleen lesions seen on CT scan;
- ▶ Positive serology for *B henselae* (enzyme immunoassay or indirect fluorescence assay) with a titre ratio of $\geq 1:64$;
- ▶ Biopsy showing granulomatous inflammation consistent with CSD or a positive Warthin-Starry silver stain.

In this case, the patient presented all of the criteria necessary for the diagnosis of CDS.

This case report highlights not only the rarity of the presentation of two different aetiologies of granulomatous lymphadenitis in a patient under surveillance for a colorectal cancer, but also illustrates the importance of continued search for the right diagnosis and that two different diagnoses can happen in the same patient.

Learning points

- ▶ Persistent lymphadenopathy can have several causes, either infectious or non-infectious, and in patients with known cancer, it is important to exclude recurrence of the disease.
- ▶ Granulomatous lymphadenitis can have several causes namely tuberculosis, cat scratch disease, fungal infections, sarcoidosis and others.
- ▶ Two different diagnoses can happen in the same patient.
- ▶ Continued search for the right diagnosis is very important even when the patient has another diagnosis confirmed before.

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revising the article with concern to pathological background and its importance for differential diagnosis of the patient. LR was involved in writing the article and revising the entire article.

Competing interests None.

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