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Diagnosis at first sight

Disseminated lymphadenopathy during chemotherapy for squamous cell lung carcinoma

Linfadenopatía generalizada durante tratamiento quimioterápico por carcinoma escamoso de pulmón

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Case report

We report the case of a 66-year-old male with diabetes on treatment with metformin, diagnosed with a 13-mm squamous cell carcinoma of the lung in the right upper lobe, with extension to a single subcarinal lymph node (T1N2M0) (Fig. 1). After administering the first cycle of chemotherapy with gemcitabine and cisplatin, the patient developed a fever of up to 39°C with no focal point, with associated mild pancytopenia. Empirical therapy was started with levofloxacin. One week later, episodes of intermittent fever persisted despite haematological recovery. At the end of the second cycle of chemotherapy, a PET scan showed progression of generalised lymphadenopathy (Fig. 2).

Progress

An excisional biopsy was performed of an enlarged left axillary lymph node that was lit up on the PET scan. The pathology diagnosis was consistent with sinus histiocytosis. Serologies against rubella, brucellosis, CMV, EBV, HIV, HHV-6, and syphilis were requested, all of which were negative for recent infection. The QuantiFERON® test (Qiagen, Hilden, Germany) for tuberculosis was negative. *Toxoplasma* IgG was positive (4642 IU/mL), as was IgM. PCR was performed on the lymph node tissue, resulting positive for *Toxoplasma* spp.

The diagnosis was made of toxoplasmosis reactivation. The patient began treatment with trimethoprim-sulfamethoxazole (800/160 mg every 8 h), showing a clear clinical improvement. The PET was repeated three weeks after treatment, showing a general decrease in the intensity of uptake in the different lymph node territories (Fig. 3). Serology performed one month after diagnosis showed an increase in IgG (11,034 IU/mL), which decreased in later tests, reflecting the natural history of reactivation. The patient subsequently started radiotherapy and completed concomitant chemotherapy with a good response, entering the periodic review programme and with no signs of reactivation of the infection to date (six months later).

Closing remarks

Infection by *Toxoplasma gondii (T. gondii)* is usually asymptomatic in immunocompetent patients. After the initial infection (even when asymptomatic), the latent infection will persist for the lifetime of the host. In patients with some type of immune deficiency (chemotherapy with alkylating agents, antimetabolites, HIV infection, haematopoietic stem cell or solid organ transplant), it can give rise to disseminated symptoms with pulmonary, cardiac and, in particular, central nervous system involvement, as these are potential risk factors for the reactivation of *T. gondii*.[1,2] In these cases, given the high prevalence of previous infection, reactivation is more common than primary infection.

The documented cases of toxoplasmosis reactivation have been linked to blood cancers.[2] To our knowledge, the association with solid tumours found in our case has not been reported previously.

The diagnosis of toxoplasmosis can be a challenge in patients such as the one described here, in whom the manifestation of new-onset lymphadenopathy suggests a progression of the cancer. In toxoplasmosis, lymph node histology is usually nonspecific, with sinus histiocytosis being common.[1,3] A definitive diagnosis can be made by serology.[3] Primary infection is characterised by the appearance of IgM antibodies, accompanied by seroconversion with low-avidity IgG. IgM can remain in serum for a long period of time, and the concentration often rises in reactivations. The typical pattern of reactivation is characterised by an increase in high-avidity IgG concentrations, regardless of the presence of IgM.[1,2]

Molecular diagnostic techniques, such as PCR for *T. gondii* in serum, cerebrospinal fluid or tissue biopsies, can be useful.[3] These techniques can be helpful when serology is inconclusive, which is common in immunosuppressed patients.[2] Diagnostic imaging can

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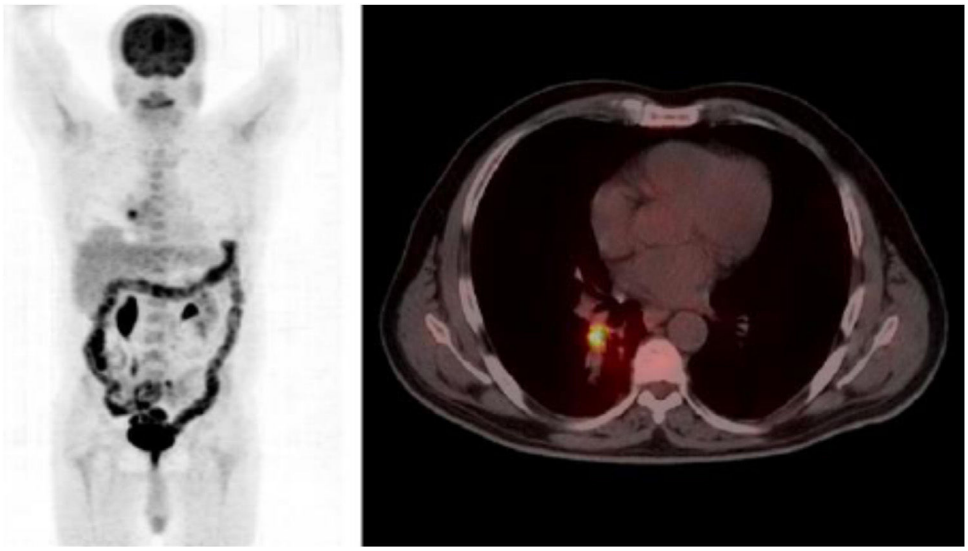

Figure 1. Baseline PET showing a hyper-uptake image in the segmental bronchus of the right lower lobe (primary tumour) and subcarinal lymphadenopathy with less uptake. Uptake by the colon is common in patients on treatment with metformin.

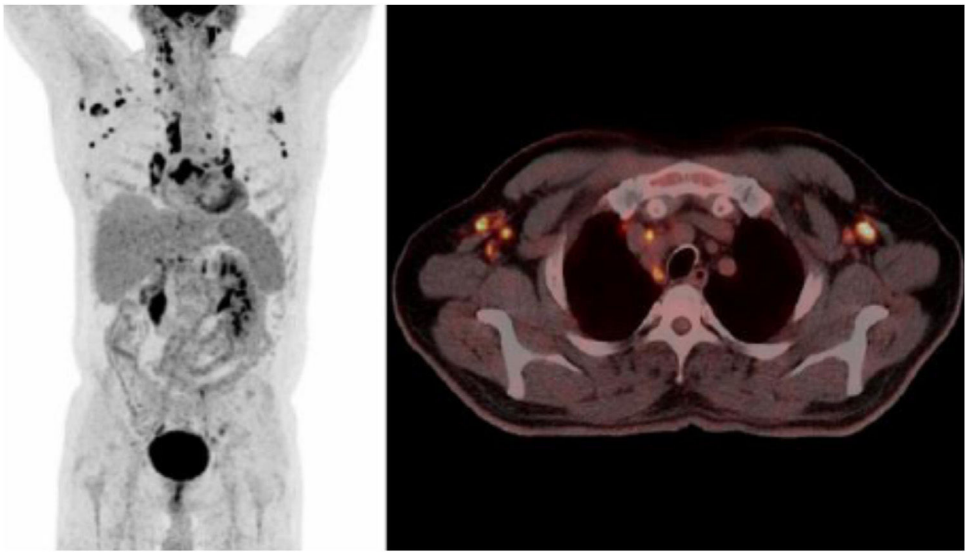

Figure 2. PET at the end of the second cycle of chemotherapy showing progression of lymphadenopathy with uptake at the mediastinum, axilla and supraclavicular and cervical areas. Uptake in the colon had decreased when the metformin treatment was replaced with insulin.

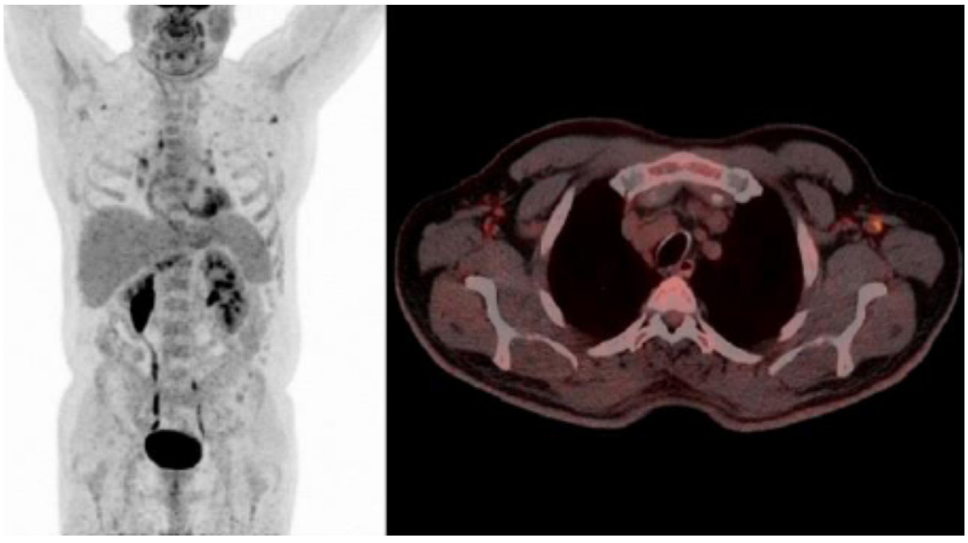

Figure 3. PET showing a general decrease in uptake at the axilla and mediastinum after antibiotic therapy.

be helpful in some cases[4], such as cerebral toxoplasmosis, where a compatible image justifies beginning empirical therapy against toxoplasma. Other conditions that needed to be included in the differential diagnosis of this case, apart from cancer progression, were Rosai-Dorfman disease, lymphoproliferative syndromes, HIV, EBV, CMV and HHV-6 infection and mycobacteriosis.[1]

In conclusion, the reactivation of toxoplasmosis should be part of the differential diagnosis when widespread lymphadenopathy is found in cancer patients, with serology and response to treatment being the main diagnostic tools. In view of the potential severity of the disseminated forms of the disease, early treatment is important and in many cases will lead to complete resolution of the condition.

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Conflicts of interest

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