surgery if lesions are inaccessible. However, cases have been described in recent years where EBUS-TBNA has become a good alternative for minimally-invasive histopathological diagnosis of those lesions that are inaccessible or in patients with high surgical risk. The results are promising, and in the future, EBUS-TBNA could even become the diagnostic technique of choice.[11–14]

References

1. Darling GE, Maziak DE, Inculet RI, Gulenchyn KY, Driedger AA, Ung YC, et al. Positron emission tomography-computed tomography compared with invasive mediastinal staging in non-small cell lung cancer: results of mediastinal staging in the early lung positron emission tomography trial. J Thorac Oncol. 2011;6:1367–72.
2. Katz SC, Shaha A. PET-associated incidental neoplasms of the thyroid. J Am Coll Surg. 2008;207:259–64.
3. Casal RF, Phan MN, Keshava K, Garcia JM, Grosu H, Lazarus DR, et al. The use of endobronchial ultrasound-guided transbronchial needle aspiration in the diagnosis of thyroid lesions. BMC Endocr Disord. 2014;14:88.
4. Barrio M, Czernin J, Yeh MW, Palma Diaz MF, Gupta P, Allen-Auerbach M, et al. The incidence of thyroid cancer in focal hypermetabolic thyroid lesions: an ^{18}F-FDG PET/CT study in more than 6000 patients. Nucl Med Commun. 2016;37:1290–6.
5. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016;26:1–133.
6. Navani N, Nankivell M, Lawrence DR, Lock S, Makker H, Baldwin DR, et al. Lung cancer diagnosis and staging with endobronchial ultrasound-guided transbronchial needle aspiration compared with conventional approaches: an open-label, pragmatic, randomised controlled trial. Lancet Respir Med. 2015;3:282–9.
7. Thiryayi SA, Rana DN, Narine N, Najib M, Bailey S. Establishment of an endobronchial ultrasound-guided transbronchial fine needle aspiration service with rapid on-site evaluation: 2 years experience of a single UK centre. Cytopathology. 2016;27:335–43.
8. Kumar A, Mohan A, Dhillon SS, Harris K. Substernal thyroid biopsy using endobronchial ultrasound-guided transbronchial needle aspiration. J Vis Exp. 2014:1–9.
9. Chow A, Oki M, Saka H, Moritani S, Usami N. Metastatic mediastinal lymph node from an unidentified primary papillary thyroid carcinoma diagnosed by endobronchial ultrasound-guided transbronchial needle aspiration. Intern Med. 2009;48:1293–6.
10. Sánchez-Font A, Peralta S, Curull V. Diagnóstico de quiste tiroideo mediante ultrasonografía endobronquial sectorial con punción-aspiración en un paciente con cáncer de pulmón. Arch Bronconeumol. 2012;49:38–9.
11. Steinfort DP, Irving LB. Endobronchial ultrasound staging of thyroid lesion in small cell lung carcinoma. Thorac Cardiovasc Surg. 2010;58:128–9.
12. Chalhoub M, Harris K. Endobronchial ultrasonography with transbronchial needle aspiration to sample a solitary substernal thyroid nodule: a new approach. Hear Lung Circ. 2012;21:761–2.
13. Li P, Zheng W, Liu H, Zhang Z, Zhao L. Endobronchial ultrasound-guided transbronchial needle aspiration for thyroid cyst therapy: a case report. Exp Ther Med. 2017;13:1944–7.
14. Filippi N, Prisciandaro E, Guarize J, Donghi SM, Sedda G, Spaggiari L. One-shot diagnosis: EBUS-TBNA as a single procedure for thyroid, pulmonary and lymph nodal lesions. Adv Respir Med. 2019;87:194–5.

Salomé Bellido-Calduch,[a] Clara Martín-Ontiyuelo,[a,b] Lara Pijuan,[c] Jaume Puig de Dou,[d] Marina Suárez-Piñera,[e] Víctor Curull,[a,b] Albert Sánchez-Font[a,b,*]

[a] *Servei de Pneumologia, Hospital del Mar-Parc de Salut Mar, UAB, CIBERES, ISCIII, Barcelona, Spain*
[b] *IMIM, Hospital del Mar Medical Research Institute, Barcelona, Spain*
[c] *Servei d'Anatomia Patològica, Hospital del Mar-Parc de Salut Mar, Barcelona, Spain*
[d] *Servei d'Endocrinologia i Nutrició, Hospital del Mar-Parc de Salut Mar, Barcelona, Spain*
[e] *Servei de Medicina Nuclear i Diagnòstic per Imatge, Hospital del Mar-Parc de Salut Mar, Barcelona, Spain*

* Corresponding author.
E-mail address: asanchezf@parcdesalutmar.cat (A. Sánchez-Font).

https://doi.org/10.1016/j.arbr.2019.11.005

Sarcoidosis Presenting With Multiple Bone Lesions and Its Regression With Infliximab

Sarcoidosis que se presenta con múltiples lesiones óseas y su regresión con infliximab

Dear Editor,

Sarcoidosis is a systemic granulomatous disorder of unknown etiology. Though pulmonary involvement is reported in the majority of sarcoidosis patients, extrapulmonary disease is seen in up to 50%. Patients may be asymptomatic, present with insidious symptoms such as malaise, fever, and dyspnea or organ-specific involvement (most commonly skin, eye, liver, heart and osteoarticular system).[1] It is a disease described in every ethnic group with a varying incidence of female preponderance. The northern European countries and black Americans have the highest incidence (50–60 and 35.5 per 100,000 people, respectively).[2]

The diagnosis is established by the combination of a suggestive clinical syndrome such as the Löfgren's syndrome (arthritis, erythema nodosum and bilateral hilar lymph nodes) and radiologic findings, supported by histologic identification of noncaseating granulomas.[3]

Bone involvement is reported in up to 13% of sarcoidosis patients, but may be underdiagnosed as specific studies are not routinely performed. Historically, it affects more frequently appendicular bones and joints of the hands and feet, but axial disease has been rarely described. Bone lesions are typically described as cystic with cortical bone involvement, although sclerotic and lytic have also been reported.[4]

In this report, the authors describe a case of systemic sarcoidosis presenting as vertebral lytic fracture and discuss clinical, diagnosis and therapeutic approaches, namely the importance of biological therapy in refractory cases.

A 59-year-old healthy female was admitted for investigation of a lumbar fracture (L2) after a low energy trauma. She presented with one year of gradually worsening generalized bone pain, fatigue, and mild dyspnea. She was a non-smoker and had no previous infections, environmental exposure or significant travel history. No significant family history was determined. Apart from lower back non-radiating pain, physical examination was unremarkable, with no skin lesions or palpable lymph nodes.

Laboratory testing showed mild hypocalcemia of 8.4 mg/dL, erythrocyte sedimentation rate of 34 mm/h and gamma monoclonal band on serum protein electrophoresis (19.8 g/dL). Computed tomography (CT) scan of the lumbar spine revealed L2 fracture and L3, S2 and S3 lytic lesions.

Etiological investigation was initiated with a CT scan that further revealed multiple lytic lesions of the skull (Fig. 1C), sternum, ribs, hip bone and cervical and thoracic vertebrae, associated with cervical, mediastinal, hilar, abdominal and pelvic lymph nodes (<2 cm) as well as nodular infiltration of the lungs and liver (<1 cm).

Neoplastic etiology was excluded after colonoscopy, endoscopy, mammogram, thyroid ultrasound and complete gynecological and dermatological evaluation. Biopsies of cervical lymph nodes,

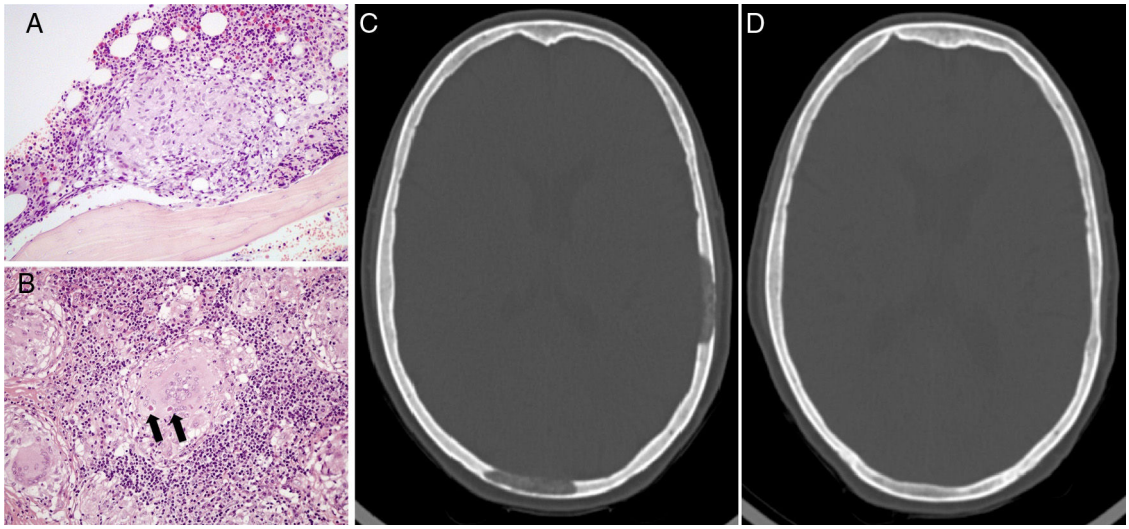

Fig. 1. (A) An epithelioid granuloma is observable next to a bone trabecula of the iliac crest, amidst the hematopoietic medullary tissue. (B) A multinucleated giant cell is shown (granuloma) in the tonsil tissue, with two dense concretions suggestive of Schaumann bodies within its cytoplasm. (C) Lytic lesions of the skull before treatment. (D) Total regression of the lytic lesions after treatment with Infliximab.

nasopharyngeal airway, tonsils and hip bone showed chronic inflammatory tissue with granulomas (Fig. 1A), some of which with caseum. There were remnants of an asteroid body and a multinucleated giant cell with two dense concretions suggestive of Schaumann bodies within its cytoplasm in the tonsil tissue (Fig. 1B).

Blood cultures, infectious and autoimmune serologies excluded other causes of systemic granulomatous disease. Bronchoalveolar lavage (BAL) revealed high lymphocytes (19%) in cellular analysis with technically indeterminable CD4/CD8 ratio. The diagnosis of tuberculosis suggested by caseating granulomas was refuted by negative Interferon Gamma Release Assay and mycobacterial and microbiological cultures of the BAL. The final diagnosis came to be sarcoidosis with important bone and lymph node involvement.

Her respiratory function tests were normal and her six-minute walk test was unremarkable, apart from the initial and final modified dyspnea Borg scale (1 very slight and 2 slight, respectively).

Treatment was started with 40 mg of prednisone and, after 5 months of treatment, there were no clinical or radiological improvements. It was then associated methotrexate 15 mg weekly and after 3 months the patient showed better physical tolerance and less generalized bone pain. In spite of clinical improvement, she was proposed to start treatment with Infliximab due to the growth of the lytic bone lesions combined with rising of angiotensin-converting enzyme value (58–92 U/L). After 11 months of biological therapy, the patient became asymptomatic and had regression of most lytic bone lesions (Fig. 1D), mediastinal lymph nodes and lung nodules. She maintains treatment with increasing radiological improvements and no adverse reactions were recorded.

Involvement of vertebrae and skull in sarcoidosis has been rarely reported and vertebral fracture after a low energy trauma was never described as the first manifestation of sarcoidosis.

The rarity of axial involvement may be explained by the fact that bone sarcoidosis is usually asymptomatic. Its diagnosis may be suggested by radiologic techniques such as magnetic resonance imaging (MRI) and positron emission tomography/computed tomography (PET/CT), which may not be easily available. Furthermore, these studies still lack specificity in distinguishing sarcoidosis from other diagnosis, mainly metastatic disease.[5] In our patient, the generalized lymph nodes and lytic bone lesions demanded, therefore, histological confirmation.

Sarcoidosis is frequently a chronic disease with multiple available treatments yet steroids are still the main treatment. In severe cases, the use of cytotoxic agents has been shown to be beneficial, such as methotrexate, azathioprine, cyclophosphamide and hydroxychloroquine.

It has been described that patients with bone sarcoidosis are frequently associated with multi-organ disease and poor prognosis, usually with decreased response to steroid treatment, as seen in our patient.[6]

In recent studies, there has been an increase in evidence of the efficacy of tumor necrosis factor (TNF)-α antagonists in the treatment of patients with pulmonary and extrapulmonary sarcoidosis, such as Infliximab and Adalimumab. They stop granulomatous inflammation, by acting against the macrophages of patients with sarcoidosis that release TNF-α, which is believed to be involved in the development of granulomas. The use of TNF-α antagonists is important by allowing the reduction of steroid effective dose, its cumulative toxicity and side-effects. They have also been proven to be effective in refractory cases, that are associated with higher levels of TNF-α in BAL.[7]

In our patient, the use of Infliximab was essential in clinical and organ involvement improvement, mainly the axial bone lesions, such as the skull and vertebrae, validating its efficacy in severe refractory cases.

Acknowledgements

We would like to express our sincere gratitude to Dr. Rita Luís for her help in the interpretation of the histological images.

References

1. Baughman RP, Teirstein AS, Judson MA, Rossman MD, Yeager H Jr, Bresnitz EA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med. 2001;164 Pt 1:1885–9.
2. Rybicki BA, Major M, Popovich J Jr, Maliank MJ, Iannuzzi MC. Racial differences in sarcoidosis incidence: a 5-year study in a health maintenance organization. Am J Epidemiol. 1997;145:234–41.
3. Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. N Engl J Med. 2007;357:2153–65.
4. Bargagli E, Prasse A. Sarcoidosis: a review for the internist. Intern Emerg Med. 2018;13:325–31.
5. Zhou Y, Lower EE, Li H, Farhey Y, Baughman RP. Clinical characteristics of patients with bone sarcoidosis. Semin Arthritis Rheum. 2017:143–8.
6. Fernández-Ruiz M, Guerra-Vales JM, Castelbón-Fernández FJ, Llenas-García J, Rodríguez-Peralto JL, López-Lancho R, et al. Sarcoidosis presenting as an osteolytic skull lesion: a case report and review of literature on skull sarcoidosis. Clin Rheumatol. 2007:1745–8.

7. Judson MA, Baughman RP, Costabel U, Flavin S, Lo KH, Kavuru MS, et al. Efficacy of infliximab in extrapulmonary sarcoidosis: results from a randomised trial. Eur Respir J. 2008:1189–96.

Andrea Lopes Machado[a,*] Nuno Jacinto[b] Dúlio Teixeira Passos[b] Leonardo Ferreira[a]

[a] *Serviço de Pneumologia – Departamento do Tórax do Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal*

[b] *Serviço de Medicina 2, Hospital de Santa Maria – Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal*

* Corresponding author.
E-mail address: astl.machado@gmail.com (A. Lopes Machado).

https://doi.org/10.1016/j.arbres.2019.11.022

Mycobacterium peregrinum: An atypical and uncommon *Mycobacterium*. A case report☆

Mycobacterium peregrinum*: micobacteria atípica e infrecuente. Reporte de un caso*

To the Editor,

Nontuberculous mycobacteria (NTM), also called atypical or environmental mycobacteria, are widely distributed in water and soil,[1] but their pathogenic potential has long been underestimated.

With the HIV/AIDS pandemic and longer survival of patients with chronic respiratory disease and other debilitating conditions such as cancer, diabetes, autoimmune diseases, transplants and immunosuppressive treatments, interest in NTM has grown, with an increasing number of cases and new species recognized.[1,2]

Mycobacterium peregrinum is a rare species of NTM, with very few cases reported worldwide, so its clinical significance and optimal treatment are not well established.[3]

In this context, case reports are of great value to increase awareness of the issue.

We report the case of a 40-year-old woman who attended the respiratory medicine clinic for a 2-month history of cough with a small amount of mucous expectoration and no other associated symptoms. She had received empirical treatment with amoxicillin and, given the persistent cough, had been prescribed salbutamol, but with no improvement.

Her history was significant for autoimmune uveitis, for which she had been receiving mycophenolate 2 g/day for 3 years prior to the visit, and she worked as a phlebotomist in our hospital laboratory.

No relevant findings were evident on physical examination.

Further tests noted: hematocrit 32%, hemoglobin 9.9 g/dL, and discrete anischromia with hypochromia. Leukocyte count 10 670/mm^3 (neutrophils 64%, lymphocytes 22%, monocytes 11%, eosinophils 2%, basophils 0.5%), and erythrocyte sedimentation rate (ESR) 54 mm/h; liver and renal function tests, blood glucose and serum protein values were within reference ranges. Tuberculin skin test: 2 mm.

Spirometry showed normal values (FVC 4.05 L [122% of predicted], FEV_1 3.27 L [119% of predicted], FEV_1/FVC 81%) with no significant bronchodilator response.

Plain chest computed tomography (CT) showed a hyperdense infiltrate with bronchiectasis in the posterior segment of the left lower lobe (Fig. 1).

Suspecting infectious disease, sputum bacilloscopy was requested. The result was positive, with development in culture of *M. peregrinum* (in 2 different sputum samples), identified using the molecular method of restriction fragment analysis of a PCR-amplified 439-bp amplicon of the *hsp65* gene. Susceptibility to clarithromycin, ciprofloxacin, amikacin and linezolid was demonstrated using the microdilution method for determining the minimum inhibitory concentration, according to CLSI standards.

After verifying normal hearing function and electrocardiogram, the patient began treatment with ciprofloxacin 500 mg/12 h and clarithromycin 500 mg/12 h. Thirty days after starting antibiotic treatment, the cough and expectoration had subsided, so new sputum samples could not be obtained for microbiological examination, and her blood count and ESR had returned to normal.

After 6 months of treatment, which was well tolerated with no significant adverse events, repeat chest CT was normal, and the patient was discharged.

NTM are classified according to their growth characteristics and the pigments they produce.[4] The slow-growing group (more than 7 days) includes *M. kansasii* and *M. avium complex,* while the rapidly-growing group includes *M. fortuitum*, *M. chelonae* and *M. abscessus.*

These species show great variability in their geographical distribution, pathological potential and presentation, even within the same region.[1,4,5] The vast majority of clinically detectable diseases are due to slow-growing mycobacteria (about 82% of cases), with reporting of rapidly-growing mycobacteria being much less frequent.

M. peregrinum falls within the category of rapidly-growing mycobacteria, in the *Mycobacterium fortuitum* group, which includes *M. fortuitum* (the most common of these, known to cause opportunistic infections), and another 8 species that share characteristics such as lack of pigmentation and susceptibility to polymyxin B, sulfonamides and the new fluoroquinolones.[3,6]

In an environmental study conducted on various water sources in Bahia Blanca, Buenos Aires, Argentina, NTM were isolated in 51.6% of reservoir and tap water samples (64/124), 11% of which corresponded to *M. peregrinum.*[7]

Despite its wide distribution, *M. peregrinum* is very rare as a pathogen for humans,[8] and is estimated to account for 1% to 2% of rapidly-growing mycobacteria infections.[3] The prevalence of respiratory infections caused by this germ is unknown.

The few reported cases are associated with diseases similar to those produced by other members of the *M. fortuitum* group, such as tonsillar abscess,[8] surgical site infection with cutaneous fistula,[9] skin infection in a patient with psoriasis,[10] endocarditis in a patient with a prosthetic aortic valve,[11] and lung infections (we found only three cases published so far).[12–14]

NTMs are generally resistant to antituberculosis agents and sensitive to traditional antibiotics such as clarithromycin, amikacin, ciprofloxacin, tigecycline and sulfonamides, but discrepancy is usually found between in vitro susceptibility tests and the clinical response.[4] The recommended treatment is with two drugs that have shown in vitro susceptibility.[5]

After studying the in vitro susceptibility of *M. peregrinum*, it was found that the new fluoroquinolones exhibit great activity against

☆ Please cite this article as: Rolan N, Limongi L, Putruele AM. *Mycobacterium peregrinum*: micobacteria atípica e infrecuente. Reporte de un caso. Arch Bronconeumol. 2020;56:331–332.