The North American Children study[12] found a mortality rate of 30%, with 50% of patients experiencing on-going morbidity. It has become clear that some ILD entities are associated with very high mortality, whereas others have a favorable outcome.

References

1. Bush A, Cunningham S, Blic J, Barbato A, Clement A, Epaud R, et al. European protocols for the diagnosis and initial treatment of interstitial lung disease in children. Thorax. 2015;70:1078–84.
2. Kurland G, Deterding RR, Hagood JS, Young LR, Brody AS, Castile RG, et al. An official American thoracic society clinical practice guideline: classification, evaluation, and management of childhood interstitial lung disease in infancy. Am J Respir Crit Care Med. 2013;188:376–94.
3. Deutsch GH, Albright E, Chou PM, Cool CD, Coventry S, Davis MM, et al. Defining the spectrum of diffuse lung disease in infancy: a working classification of the pediatric interstitial lung disease cooperative. Mod Pathol. 2005;18:304.
4. Langston C, Dishop M. Infant lung biopsy: clarifying the pathologic spectrum. Pathol Int. 2004;54:S419–21.
5. Deutsch GH, Young LR, Deterding RR, Fan LL, Dell SD, Bean JA, et al., Pathology Cooperative Group. ChILD Research Co-operative Diffuse lung disease in young children: application of a novel classification scheme. Am J Respir Crit Care Med. 2007;176:1120–8.
6. Hines E, Walsh M, Armes J, Douglas T, Chawla J. Interstitial lung disease in infancy: a general approach. J Paediatr Child Health. 2016;52:370–6.
7. Doan ML, Guillerman RP, Dishop MK, Nogee LM, Langston C, Mallory GB, et al. Clinical, radiological and pathological features of ABCA3 mutations in children. Thorax. 2008;63:366–73.
8. Somaschini M, Nogee L, Sassi I, Danhaive O, Presi S, Boldrini R, et al. Unexplained neonatal respiratory distress due to congenital surfactant deficiency. J Pediatr. 2007;150:537–649.
9. Shulenin, Nogee LM, Annilo T, Wert SSE, Whitsett JA, Dean M. ABCA3 gene mutations in newborns with fatal surfactant deficiency. N Engl J Med. 2004;350:1296–303.
10. Bullard JE, Wert SE, Whitsett JA, Dean M, Nogee LM. ABCA3 mutations associated with pediatric intertitial lung disease. Am J Respir Crit Care Med. 2005;172:1026–31.
11. Moreno A, Maestre J, Balcells J, Marhuenda C, Cobos N, Roman A, et al. Lung transplantation in young infants with interstitial pneumonia. Transpl Proc. 2003;35:1951–3.
12. Kröner C, Wittmann T, Reu S, Teusch V, Klemme M, Rauch D, et al. Lung disease caused by ABCA3 mutations. Thorax. 2017;72:213–20.

Mª Carmen López Castillo,[a,*] Estela Pérez Ruiz,[a] Pilar Caro Aguilera,[a] María Adela Rodríguez Vives[b]

[a] *Hospital Materno Infantil de Málaga, Spain*
[b] *Facultad de Medicina de Málaga, Hospital Materno Infantil de Málaga, Spain*

* Corresponding author.
E-mail address: mcarmen.lopez123@gmail.com
(M.C. López Castillo).

Tuberculosis and Microscopic Polyangiitis. A Rare Combination☆

Tuberculosis y poliangitis microscópica. Una asociación muy poco frecuente

To the Editor:

Tuberculosis (TB) is one of the most common causes worldwide of morbidity and mortality due to infection, with a recorded incidence in Spain in 2015 of 21.5 cases/100 000 inhabitants.[1]

Vasculitis is a general term for a heterogeneous group of diseases characterized by inflammation and destruction of blood vessel walls.[2] Most cases are primary, but vasculitis can also be secondary to other diseases, including infections.[3] At times the difference between TB and vasculitis can be difficult to determine, because they share similar characteristics, and moreover, both entities can coexist in the same patient.[4] The definitions of vasculitis and its different forms are well established.[5] We report the case of a patient that who presented simultaneous TB and microscopic polyangitis (MPA).

This was a 68-year-old man with a history of TB, who attended the emergency room with a 1-month history of fever, bloody sputum, asthenia, weight loss, and dyspnea. His temperature was 38.4 °C, with no other significant findings. Blood tests were normal, and chest X-ray revealed scarring in the upper right lobe and a solid, spiculated parenchymal lesion. Chest computed tomography (CT) showed no changes in the middle and lower fields (Fig. 1A). No upper respiratory tract involvement was observed. Polymerase chain reaction was positive for *Mycobacterium tuberculosis* in bronchial aspirate and bronchoalveolar lavage. Core needle biopsy of the spiculated lesion revealed necrotizing granulomatous inflammation with multinucleated Langhans giant cells (Fig. 1B), and positive Ziehl–Neelsen staining and polymerase chain reaction for *M. tuberculosis*. The patient developed sudden onset hemoptysis with anemia (hemoglobin>6.8 g/dL, hematocrit 20.8%), acute renal failure (urea 123 mg/dL, creatinine 8.3 mg/dL), oligoanuria and elevated transaminases (values 5 times the upper limit of normal). Intubation, mechanical ventilation, and hemodialysis were required. In view of the patient's hepatic and renal insufficiency, antituberculosis treatment began with ethambutol, levofloxacin, and streptomycin. Chest CT showed diffusely increased pulmonary radiodensity, mainly ground glass opacities and areas of consolidation in the peribroncovascular region, with moderate left loculated pleural effusion, with a fissural component, that was interpreted as diffuse alveolar hemorrhage (Fig. 1C). Renal biopsy revealed vasculitis with fibrinoid necrosis of the small arteries associated with focal and segmental necrotizing glomerulonephritis with an absence of immunoglobulin, complement and light chain deposits, suggestive of MPA (Fig. 1D and E). Pleural fluid was a lymphocytic exudate; ADA 45 U/L, with no other significant changes. Anti-neutrophil cytoplasmic antibodies (ANCA) (dilution 1/320; p-ANCA pattern) with anti-myeloperoxidase antibodies>300 IU/mL were detected. Anti-glomerular basement membrane antibodies were negative. Treatment was administered with corticosteroids (3 initial boluses of methylprednisolone 500 mg/day, tapered to 15 mg/day of prednisone), plasmapheresis (7 sessions), and rituximab (700 mg/week for 4 weeks). Rifampicin and isoniazid could subsequently be reintroduced. Progress was slow but favorable, with stabilization of respiratory symptoms and radiological improvement (Fig. 1F).

The association between TB and vasculitis has been described, but generally always in association with granulomatosis with polyangitis.[4,6,7] As far as we know, this is the second case in which TB has been associated with MPA.[7] Both diagnoses appear to be confirmed: positive polymerase chain reaction in 2 different samples in the case of TB; and for MPA, granulomatous inflammation with necrosis and multinucleated giant cells in lung tissue
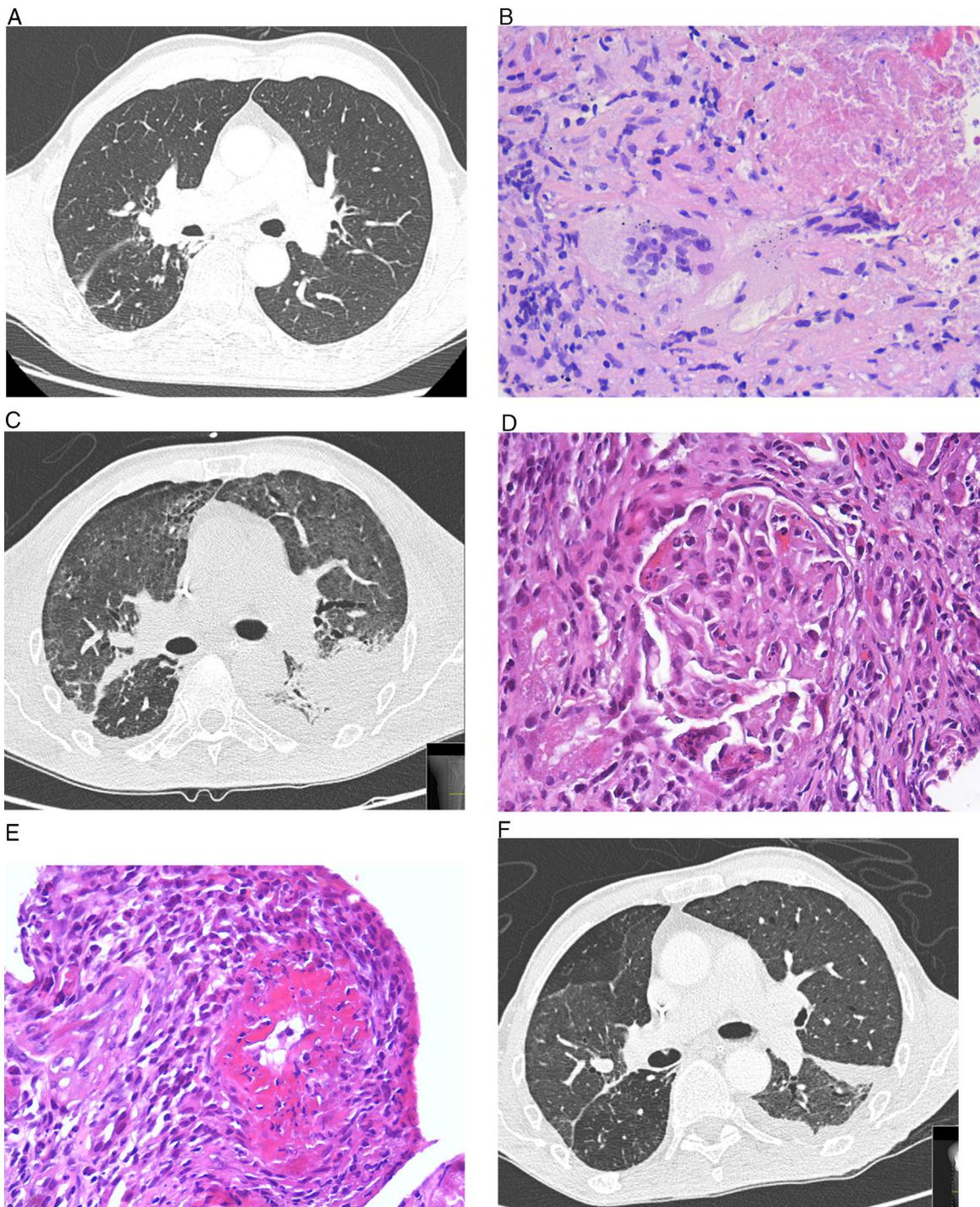
Fig. 1. (A) Chest high-resolution computed tomography (HRCT). No evidence of disease or pleural effusion observed in middle and lower fields. (B) Lung biopsy. Granulomatous inflammation with extensive areas of necrosis and multinucleated Langhans giant cells. (C) Chest HRCT. Diffuse increase of pulmonary radiodensity, mainly ground glass opacities with moderate left loculated pleural effusion, and a fissural component, interpreted as diffuse alveolar hemorrhage. (D) Renal biopsy. Renal glomerulus with area of focal necrosis and karyorrhexis. (E) Renal biopsy with fibrinoid necrosis of the small arteries affecting more than 50% of the circumference, associated with transmural inflammation. (F) Chest HRCT. Reduction of pleural effusion and slight improvement of the ground glass opacities.

with positive Ziehl–Neelsen staining, and confirmed diagnostic criteria with rapidly progressing diffuse alveolar hemorrhage and necrotizing glomerulonephritis.[5]

The question here is, is this association incidental or does one disease (TB) lead to another (MPA)? The inverse association is possible, and the administration of an immunosuppressive treatment for a diagnosis of vasculitis as a trigger for TB has been documented,[8] but this could be ruled out in our patient by the order

of events. Flores-Suárez et al. observed high odds ratios for positive p-ANCA by indirect immunofluorescence in TB patients, compared with asthma patients (odds ratio 2.96 [1.19–7.38]; $P<0.027$) and healthy subjects (odds ratio 18 [3.88–83.4]; $P<0.0001$).[9] It is difficult to establish an association between TB and MPA, although the coexistence of TB and positive ANCA may be a causative factor. Some drugs, especially isoniazid and rifampicin, can be transformed into active metabolites that develop cytotoxic prod-

ucts that destroy the neutrophils with subsequent synthesis of ANCA, a phenomenon which might explain the presence of anti-myeloperoxidase antibodies in patients receiving these drugs.[10,11] However, this is unlikely in our patient, because he had not yet received these products when the diffuse alveolar hemorrhage and necrotizing glomerulonephritis occurred. On the other hand, *M. tuberculosis* can stimulate the release of oxygen metabolites from the neutrophils. When these cells are activated in the initial stages of mycobacterial infection, lysosomal enzymes are released that could lead to the development of autoantibodies (ANCA) against the granular components of these cells.[9] These IgG antibodies that act against neutrophilic and monocytic cytoplasmic antigens (proteinase-3 and myeloperoxidase) induce neutrophil migration and degranulation in the vessel wall, and release proteases and other toxic metabolites that cause vascular damage,[12] which could give rise to this or any other vasculitis.

In summary, TB is more common in our setting than vasculitis, so diagnosis must be established promptly and treatment must be initiated in case of objective evidence. The characteristics of vasculitis and TB can overlap, and vasculitis should be considered in the differential diagnosis, particularly if azotemia is observed. Sometimes the possibility of a simultaneous presentation must be considered, and while no association between the 2 entities has been demonstrated, the mechanisms we describe may provide a physiopathological explanation. A high index of suspicion and clinical experience in the management of this presentation is necessary, since diagnostic errors and delays in treatments can lead to life-threatening situations.

References

1. Dirección Xeral de Saúde Pública. Informe da tuberculose en Galicia. Características dos casos de tuberculose de Galicia no ano 2015. Evolución do período 1996–2015 [monografía en Internet]. Santiago de Compostela: Xunta de Galicia, Consellería de Sanidade; 2016. Available from: https://www.sergas.es/Saude-publica/Documents/4154/A%20tuberculose%20en%20Galicia.%201996-2015.pdf.

2. Elefante E, Tripoli A, Ferro F, Baldini C. One year in review: systemic vasculitis. Clin Exp Rheumatol. 2016;34 Suppl. 97:S1–6.
3. Brown KK. Pulmonary vasculitis. Proc Am Thorac Soc. 2006;3:48–57.
4. Molinari L, Melamud JI, Ferrari L, Landi P, Semeniuk G, Quadrelli SA. Granulomatosis de Wegener y tuberculosis. Una mala combinación. Medicina (Buenos Aires). 2009;69:640–2.
5. Jenette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised international Chapel Hill consensus conference nomenclature of vasculitides. Arthritis Rheum. 2013;65:1–11.
6. Gordon C, Luqmani R, Fields P, Howie AJ, Emery P. Two cases of "Wegener's tuberculosis". Br J Rheumatol. 1993;32:143–9.
7. Baig ZF, Raja KM, Abbas F. Tuberculosis versus vasculitis. J Ayub Med Coll Abbottabad. 2014;26:630–2.
8. Harrison NK, Knight RK. Tuberculosis of the nasopharynx misdiagnosed as Wegener's granulomatosis. Thorax. 1986;41:219–20.
9. Flores-Suárez LF, Cabiedes J, Villa AR, van der Woude FJ, Alcocer-Varela J. Prevalence of antineutrophil cytoplasmic autoantibodies in patients with tuberculosis. Rheumatology (Oxford). 2003;42:223–9.
10. Esquivel-Valerio JA, Flores-Suárez LF, Rodríguez-Amado J, Garza-Elizondo MA, Rendón A, Salinas-Carmona MC. Antineutrophil cytoplasm autoantibodies in patients with tuberculosis are directed against bactericidal/permeability increasing protein and are detected after treatment initiation. Clin Exp Rheumatol. 2010;28 Suppl. 57:35–9.
11. Ji G, Zeng X, Sandford AJ, He JQ. Rifampicin-induced antineutrophil cytoplasmic antibody-positive vasculitis: a case report and review of the literature. Int J Clin Pharmacol Ther. 2016;54:804–7.
12. Kallenberg CG. Pathogenesis of ANCA-associated vasculitides. Ann Rheum Dis. 2011;70 Suppl. 1:i59–63.

Vanessa Riveiro,[a,*] Jorge Ricoy,[a] María E. Toubes,[a] Luis Valdés[a,b]

[a] *Servicio de Neumología, Complejo Hospitalario Universitario de Santiago, Santiago de Compostela, La Coruña, Spain*
[b] *Grupo Interdisciplinar de Investigación en Neumología, Instituto de Investigaciones Sanitarias de Santiago (IDIS), Santiago de Compostela, La Coruña, Spain*

* Corresponding author.
E-mail address: vanessa.riveiro.blanco@sergas.es (V. Riveiro).

Malignant Pleural Mesothelioma: The Last 8 Years of Experience in Our Area[☆]

Mesotelioma pleural maligno: experiencia de los últimos 8 años en nuestra área

To the Editor:

Malignant pleural mesothelioma (MPM) is a rare tumor with a poor prognosis. Treatment may include surgical resection, chemotherapy (CT), radiation therapy, or a combination of all 3. We report a descriptive retrospective study that evaluates clinical and pathological features, type of treatment, and survival in patients diagnosed with this disease in our region (Vallés Occidental, Barcelona) between 2008 and 2016.

There were 44 cases of MPM in total. Most patients were men (84%), and 56.8% were 70 years of age or older. Twenty-five patients had epithelioid type disease, 1 biphasic, 2 sarcomatoid, and 16 with no specific histology. Twenty-four (54.6%) were smokers. Nine (20.5%) had a history of asbestos exposure.

Most were in advanced stages at diagnosis, 35 (79.5%) in stages III and IV, and 9 (20.5%) in stages I and II. Twenty-three (52.3%) had performance status (PS) 0–1, and 21 (47.7%) had PS 2–3.

Surgery was indicated in 2 patients (4.5%); in 1 to limit symptoms and for disease diagnosis, and in the other due to very good response to systemic therapy and good PS in a young patient. The remaining patients were treated with talc pleurodesis. Twenty-one patients (47.7%) received first-line CT with cisplatin-pemetrexed, and 4 (9%) showed partial response or stable disease. Ten patients (47.6%) received a second line of treatment after progression, 5 (50%) with vinorelbine and 5 (50%) with gemcitabine.

Mean overall survival (OS), analyzed by the Kaplan–Meier method, was 14 months (95% CI: 11.6–16.4), with no differences between men and women (14 vs 16 months) (P=0.91). There were no significant differences in OS between patients with epithelioid tumors (15 months) and those with other histologies (14 months) (P>0.6). OS in terms of stages I/II/III/IV was 11, 15, 14 and 11 months, respectively (P>0.5). In patients treated with CT, OS was 15 months compared to 11 months in untreated patients (P>0.3).

MPM is a rare tumor that is difficult to diagnose and therapeutic options are limited. In up to 80% of cases, it is associated with occupational exposure to asbestos.[1] Symptoms include the development of pleural effusion, dyspnea or pain.[1]

Computed tomography (CT) is the radiological diagnostic procedure of choice; it reveals diffuse pleural thickening and nodular