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).

1579-2129/

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

☆ Please cite this article as: Benítez JC, Campayo M, Call S, Bastús R. Mesotelioma pleural maligno: experiencia de los últimos 8 años en nuestra área. Arch Bronconeumol. 2018;54:637–638.

lesions, although it lacks sensitivity in the assessment of mediastinal or contralateral involvement. The extension study can be completed with PET or a PET-CT.[2] Cytological analysis of pleural fluid helps differentiate the diagnosis from metastatic tumors.[1] Thoracoscopy is the technique of choice for obtaining guided biopsy samples. Better staging can be achieved with video-assisted thoracoscopy, and pleurectomy or decortication can be performed in selected cases.[3] In our series, diagnosis was made using CT; the study can be completed with a PET in certain patients in whom surgery is proposed by the multi-disciplinary committee. The pathology analysis is performed on biopsies obtained by thoracoscopy or fine-needle aspiration and biopsy.

Histological types vary between epithelioid, sarcomatoid, and biphasic; other rare subtypes are desmoplastic, small cell, and lymphohistiocytoid.[2]

OS is estimated to be around 1 year[4]; in our series, it was 14 months. The benefit of surgery is controversial, as it seems to have little effect on survival in most studies, whereas associated morbidity and mortality are high.[5] In 2011, Treasure et al.[6] conducted a randomized study in the United Kingdom that had a high impact on clinical practice. They found no significant differences in survival, which was lower in operated patients, while interventions were associated with high morbidity and mortality. Given these results and those of other non-randomized trials, controversy regarding the role of radical surgery is rife. Ongoing studies, such as MARS2, are analyzing the role of decortication compared to radical surgery.[7] The current evidence has prompted clinicians to reserve surgery for the local control of symptoms, pain, or pleural effusion.[5] Surgery was indicated for the control of incapacitating pleuritic pain in 1 of the patients from our series; the other operated patient, who was young with a good PS, underwent surgery after good response to CT. Surgery was performed in these 2 highly selected patients only, taking into consideration the risk and the limited potential benefit of the intervention.

Prompt initiation of treatment improves prognosis.[8] Radiation therapy can play an important role in the control of pain. OS is greater with combined cisplatin and pemetrexed[9] than with single-agent cisplatin (12 vs 8–9 months).[9,10] CT confers a limited increase in OS (15 months in our series), with improved control of symptoms. In case of progression, the second line of treatment can include pemetrexed as a single agent (if it was not used in first line), gemcitabine or vinorelbine.[11]

In addition to CT, studies with other agents have shown an improved prognosis in MPM patients. The combination of nintedanib (an anti-angiogenic tyrosine kinase inhibitor) and CT in a phase II study has shown an increase in progression-free survival, and a trend toward a longer OS compared to CT alone.[12] Finally, other options currently under development for second and third-line treatment are based on anti-PD-1 agents, such as pembrolizumab[13] or nivolumab, and its combination with ipilimumab, under study in a phase II trial in comparison with monotherapy.[2]

Despite its retrospective nature, our series provides experience in the surgical and systemic management and prognosis of a group of patients with this rare tumor. The best treatment for MPM is still to be determined. Surgery is associated with significant perioperative morbidity, and is performed only in highly selected cases in whom the risk of the procedure is understood. CT achieves a limited increase in survival, but it is associated with better control of symptoms. New systemic therapies could provide better outcomes in the prognosis of this disease.

References

1. Rodríguez Panadero F. Diagnóstico y tratamiento del mesotelioma pleural maligno. Arch Bronconeumol. 2015;51:177–84.
2. Aisner DL, Bauman J, Chirieac LRD, DeCamp TA, Miranda Hughes MMO. NCCN Guidelines Version 2.2017 Panel Members Malignant Pleural Mesothelioma NCCN Guidelines Panel Disclosures-Farber/Brigham and Women's Cancer Center; 2017.
3. Fitzgerald DB, Koegelenberg CFN, Yasufuku K, Lee YCG. Surgical and non-surgical management of malignant pleural effusions. Expert Rev Respir Med. 2018;12:15–26.
4. Muers MF, Stevens RJ, Fisher P, Darlison L, Higgs CM, Lowry E, et al. Active symptom control with or without chemotherapy in the treatment of patients with malignant pleural mesothelioma (MS01): a multicentre randomised trial. Lancet. 2008;371:1685–94.
5. Lang-Lazdunski L. Surgery for malignant pleural mesothelioma: why, when and what? Lung Cancer. 2014;84:103–9.
6. Treasure T, Lang-Lazdunski L, Waller D, Bliss JM, Tan C, Entwisle J, et al. Extra-pleural pneumonectomy versus no extra-pleural pneumonectomy for patients with malignant pleural mesothelioma: Clinical outcomes of the Mesothelioma and Radical Surgery (MARS) randomised feasibility study. Lancet Oncol. 2011;12:763–72.
7. Bertoglio P, Waller DA. The role of thoracic surgery in the management of mesothelioma: an expert opinion on the limited evidence. Expert Rev Respir Med. 2016;10:663–72.
8. Sharkey AJ, O'Byrne KJ, Nakas A, Tenconi S, Fennell DA, Waller DA. How does the timing of chemotherapy affect outcome following radical surgery for malignant pleural mesothelioma? Lung Cancer. 2016;100:5–13.
9. Van Meerbeeck JP, Gaafar R, Manegold C, Van Klaveren RJ, Van Marck EA, Vincent M, et al. Randomized phase III study of cisplatin with or without raltitrexed in patients with malignant pleural mesothelioma: an intergroup study of the European Organisation for Research and Treatment of Cancer Lung Cancer Group and National Cancer Institute of Canada. J Clin Oncol. 2005;3:6881–9.
10. Vogelzang NJ, Rusthoven JJ, Symanowski J, Denham C, Kaukel E, Ruffie P, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesotehelioma. J Clin Oncol. 2003;21:2636–44.
11. Zauderer MG, Kass SL, Woo K, Sima CS, Ginsberg MS, Krug LM, et al. Vinorelbina and gemcitabine as second—or third-line therapy for malignant pleural mesothelioma. Lung Cancer. 2014;84:271–4.
12. Grosso F, Steele N, Novello S, Nowak AK, Popat S, Greiller L, et al. Nintedanib plus pemetrexed/cisplatin in patients with malignant pleural mesothelioma: Phase II results from the randomized, placebo-controlled LUME-meso trial. J Clin Oncol. 2017;35:3591–600.
13. Alley EW, Lopez J, Santoro A, Morosky A, Saraf S, Piperdi B, et al. Clinical safety and activity of pembrolizumab in patients with malignant pleural mesothelioma (KEYNOTE-028): preliminary results from a non-randomised, open-label, phase 1b trial. Lancet Oncol. 2017;18:623–30.

José Carlos Benítez,[a] Marc Campayo,[a] Sergi Call,[b] Romà Bastús[a,*]

[a] *Servicio de Oncología Médica, Hospital Universitari Mútua de Terrassa, Universidad de Barcelona, Terrassa, Barcelona, Spain*
[b] *Servicio de Cirugía Torácica, Hospital Universitari Mútua de Terrassa, Universidad de Barcelona, Terrassa, Barcelona, Spain*

* Corresponding author.
E-mail address: rbastus@mutuaterrassa.es (R. Bastús).

1579-2129/