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An 8-Year Survival of a Probable Pleural Mesothelium: A Case Report

F. Z. Ballouk[1*], A. Sabiq[1], N. Kadri[1], I. Zaytoune[1], B. Mahrouch[1], M. Bennani[1], A. A. Agouzzal[1], S. Kandri Rody[1], M. Darfaoui[1], A. El Omrani[1], M. Khouchani[1]

[1]Radiation Oncology Department, Hematology and Oncology Hospital, Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco

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***Corresponding author:** F. Z. Ballouk
Radiation Oncology Department, Hematology and Oncology hospital, Faculty of Medicine and Pharmacy, Cadi Ayyad University, Marrakech, Morocco

Abstract **Case Report**

Malignant mesothelioma is a very aggressive cancer that develops from the mesothelium, the protective membrane lining the inside of the body's serous cavities. It is an aggressive tumor, which, although rare, remains a real societal problem. We report a case of 71-year-old patient former mine worker with a history of chronic smoking estimated at 45 packs/year, who presented a Malignant pleural mesothelioma revealed by an exertional dyspnoea. He was evaluated with a chest scan, a CT-guided biopsy was performed with the pathological examination revealed a malignant tumoral proliferation whose morphological appearance may be consistent with an epithelial-type mesothelium. The patient received 6 cures of chemotherapy. Pathological and radiological evaluation, treatement of this neoplasm are discussed.

Keywords: Malignant mesothelioma, serous cavities, chronic smoking, exertional dyspnoea.

INTRODUCTION

Malignant mesothelioma is a very aggressive cancer that develops from the mesothelium, the protective membrane lining the inside of the body's serous cavities. There are three serous cavities in the body: the pleura (enveloping the lungs), the pericardium (enveloping the heart) and the peritoneum (which lines the abdominal cavity). Mesothelioma most often develops at the expense of the pleura (90%) which gives malignant pleural mesothelioma, and more rarely affects the peritoneum and pericardium (10%).

Malignant pleural mesothelioma (MPM) is an aggressive tumor, which, although rare, remains a real societal problem.

CASE REPORT

A 71-year-old patient former mine worker with a history of chronic smoking estimated at 45 packs/year, a brother who died of cancer and a cousin followed for malignant mesothelium, who presented a malignant mesothelium revealed by an exertional dyspnoea without coughing or hemoptysis or chest pain, all evolving in a context of apyrexia and impairment of general condition.

The patient consulted a pulmonologist and a chest scan was done which objectified a diffuse nodular pleural thickening of the right lung with an ipsilateral pleural effusion compatible with a pleural mesothelium.

A CT-guided biopsy was performed with the pathological study: pleural and pulmonary tissue infiltrated by poorly differentiated malignant tumoral proliferation whose morphological appearance may be consistent with an epithelial-type mesothelium.

Immunostaining: immunohistochemical aspect of a poorly differentiated adenocarcinoma pointing to a pulmonary origin.

An abdominopelvic CT scan and a bone scintigraphy were done and did not show any secondary location the case was discussed in thoracic surgery and no surgical indication was retained the patient received 6 cures of chemotherapy (paclitaxel-carboplatin), with TAP CT for evaluation: stable aspect of right pleural thickening, emphysematous lung, absence of suspicious bone lesions, calcified circumferential atheroma plaque of the abdominal aorta under the kidney the patient was put under surveillance with control CT every 4 months

then every 6 months and which all showed a stable aspect of the right apical pleural nodular thickening of 21x9mm without bone lesion opposite, emphysematous lung and no remote suspicious lesion.

DISCUSSION

Malignant mesothelioma is a primary cancer developed from a serosa, most often the pleura Due to the post-war increase in industrial exposure to asbestos, the peak increase is expected around 2020 [1, 2].

The occurrence of pleural mesothelioma is in fact closely linked to exposure to asbestos, found in 70% of cases, mainly in humans in the form of occupational exposure (90% of cases), more rarely in women (< 50% of cases), but this exposure can also be domestic and/or environmental.

The relationship between mesothelioma and exposure to asbestos has been demonstrated since 1960 [3].

Genetic factors are emerging in particular with the loss of expression of BAP1, or protein associated with BRCA1, which is a deubiquitination enzyme [4]. BAP1 is considered a suppressor geneof tumour. The presence of germline mutations promotes the occurrence of pleural mesothelioma (if it is associated with exposure to asbestos) and other types of tumors (uveal melanoma, cell kidney cancer clear) [5]. If several members of the same family have mesothelioma or uveal melanoma, an oncogenetics consultation may be offered. However, loss of BAP-1 expression in the Malignant pleural mesothelioma, frequent (≈60% of cases), is much more often acquired than germinal [6].

Chemotherapy of malignant pleural mesothelioma The interest of chemotherapy in malignant pleural mesothelioma has long remained a subject of controversial. Indeed, its evaluation proved to be difficult: publication on small numbers of patients, factors prognosis not taken into account, evaluation of the response to treatment difficult before the era of computed tomography, effect on survival not studied compared to a control group. Also, many cytotoxic agents, alone or in combination, have not been correctly evaluated in this pathology. The development of pemetrexed has brought renewed interest in the chemotherapy of pleural mesothelioma malignant and allowed to define the association cisplatin-pemetrexed as a therapeutic standard of the MPM chemotherapy.

Monochemotherapy

Malignant pleural mesothelioma is a relatively insensitive tumor. Certain drugs possess an activity: anthracyclines (the new molecules not obtaining results superior to thedoxorubicin), cisplatin and carboplatin, mitomycin, ifosfamide, antimetabolites (gemcitabine and antifolates: methotrexate, pemetrexed [7], raltitrexed [8], and more recently vinorelbine [9]. The recent studies, methodologically safer, highlight the interest of antimetabolites, and more particularly recent antifolates such as raltitrexed and pemetrexed, which offer a ratio interesting efficacy-tolerance. The only study carried out comparing chemotherapy with supportive care alone [10] confirmed the activity of vinorelbine monotherapy, although the survival benefit does not reach not meet statistical significance.

Polychemotherapy

The European Lung Cancer Working Party (ELCWP) team conducted an analysis of studies of chemotherapy carried out in malignant pleural mesothelioma from 1983 to 2001 [11] and highlights the role cisplatin, which clearly appears to be the most active drug in terms of response rate.

The superiority of cisplatin over carboplatin is probable on these data. The antitumor activity of combination chemotherapy is superior to that of monotherapy, taking into account that the majority of combinations included a platinum salt.

The more recent associations based on the association of a platinum salt and an antimetabolite seem be endowed with a superior activity (cisplatin - gemcitabine, cisplatin - pemetrexed, cisplatin or oxaliplatin - raltitrexed).

Intra-Pleural Treatments

Intra-Pleural Chemotherapy

Intracavitary chemotherapy offers the advantage of high local concentrations of cytotoxics with reduced systemic side effects [12]. The limiting factors are penetration limited to a few millimeters; therefore, the administration of intrapleural chemotherapy only seems logical after performing surgical cytoreduction.

Intra-pleural chemotherapy used after pleurectomy-decortication does not seem sufficient to reduce the frequency of local relapses [13-15], despite the addition of chemotherapy system thereafter. The administration of intrapleural chemotherapy under conditions hyperthermia is likely to increase its effectiveness. Hyperthermia, endowed with cytotoxic properties by itself, potentiates the cytotoxicity of anti-mitotics and their tissue penetration. The studies performed [16-18] involved too few patients to be able to formally assess the potential benefit of this technique (median survival of 11 to 15 months); toxicity is not negligible. It is therefore not routinely validated in MPM, unlike peritoneal MM, and must, only be considered in the context of a clinical trial.

Intra-pleural immunotherapy

Historical trials with Interferon Gamma [19] or Interleukin 2 [20] have shown the ability of the administration of these immunomodulators to obtain objective responses on pleural lesions small

corresponding to the early stages of mesothelioma. The impact on patient survival treated is difficult to determine; this type of therapeutic approach is currently abandoned.

Targeted Therapies

Malignant mesothelioma is a highly angiogenic tumour; circulating VEGF levels usually very high in this tumor appears to be an unfavorable prognostic factor [21]. Receptor blockers VEGF (vatalanib, sorafenib, vandetanib, sunitinib, cediranib) have not demonstrated significant efficacy justifying their continued development in this indication. Bevacizumab has demonstrated its effectiveness in combination with cisplatin-pemetrexed chemotherapy [25] but not in combination with the regimen cisplatin-gemcitabine [26] (see chemotherapy). Nintedanib, anti-angiogenic inhibitor of VEGFR, PDGFR and FGFR, showed in a phase II trial in combination with cisplatin-pemetrexed chemotherapy a significant improvement in progression-free survival and no significant improvement in survival compared to chemotherapy alone [22]. This led to the completion of a phase III trial, the results of which reported to ASCO 2018 show no benefit of nintedanib in combination with chemotherapy in terms of PFS (6.8 months in the nintedanib arm vs 7 months) or overall survival (14.4 months vs 16.1 months in the placebo arm) [23, 24].

The activity of EGFR tyrosine kinase inhibitors as well as imatinib seems almost nil in monotherapy.

Immunotherapy with checkpoint inhibitors of the immune response

Tumor expression of PD-L1 appears to be greater in mesothelioma with non-epithelioid histology and thus seems correlated with a worse prognosis. Interesting response rates and durations (27-28%) were obtained with anti-PD(L)1 antibodies.

Pembrolizumab Showed in Phase II Keynote 028 Trial a 20% Response Rate in 25 Patients pre-treated for pleural mesothelioma expressing PD-L1 in at least 1% of tumor cells, a duration median response of 12 months, a median progression-free survival of 5.4 months and a median survival of 18 months [27]. S. PopatF reported the Phase 3 ETOP [28, 29] PROMISE-meso study at ESMO 2019.

One hundred and forty-four platinum-experienced patients were randomized between PEMBROLIZUMAB and GEMCITABINE / VINORELBINE. While the response rate is 22% as expected, an independent operator does not achieve the main objective: no improvement in PFS with review. Overall survival with 63% crossover does not show any difference.

Surveillance

No consensus exists concerning the methods and frequency of monitoring, whether the patient has been treated by chemotherapy and/or surgery.

CONCLUSION

Malignant mesothelioma is one of the most aggressive cancers, we recall the role of occupational and environmental exposure to asbestos in its genesis its prognosis is poor despite the development of new treatments including immunotherapy.

RÉFÉRENCES

1. Robinson, B. W., & Lake, R. A. (2005). Advances in malignant mesothelioma. *New England Journal of Medicine*, *353*(15), 1591-1603.
2. Peto, J., Decarli, A., La Vecchia, C., Levi, F., & Negri, E. (1999). The European mesothelioma epidemic. *British journal of cancer*, *79*(3), 666-672.
3. Wagner, J. C., Sleggs, C. A., & Marchand, P. (1960). Diffuse pleural mesothelioma and asbestos exposure in the North Western Cape Province. *Occupational and Environmental Medicine*, *17*(4), 260-271.
4. Panou, V., Gadiraju, M., Wolin, A., Weipert, C. M., Skarda, E., Husain, A. N., ... & Churpek, J. E. (2018). Frequency of germline mutations in cancer susceptibility genes in malignant mesothelioma. *Journal of Clinical Oncology*, *36*(28), 2863-2871.
5. Klebe, S., Driml, J., Nasu, M., Pastorino, S., Zangiabadi, A., Henderson, D., & Carbone, M. (2015). BAP1 hereditary cancer predisposition syndrome: a case report and review of literature. *Biomarker research*, *3*(1), 1-7.
6. Husain, A. N., Colby, T. V., Ordóñez, N. G., Allen, T. C., Attanoos, R. L., Beasley, M. B., ... & Wick, M. R. (2018). Guidelines for pathologic diagnosis of malignant mesothelioma 2017 update of the consensus statement from the International Mesothelioma Interest Group. *Archives of pathology & laboratory medicine*, *142*(1), 89-108.
7. Scagliotti, G. V., Shin, D. M., Kindler, H. L., Vasconcelles, M. J., Keppler, U., Manegold, C., ... & Rusthoven, J. J. (2003). Phase II study of pemetrexed with and without folic acid and vitamin B12 as front-line therapy in malignant pleural mesothelioma. *Journal of clinical oncology*, *21*(8), 1556-1561.
8. Baas, P., Ardizzoni, A., Grossi, F., Nackaerts, K., Numico, G., Van Marck, E., ... & Giaccone, G. (2003). The activity of raltitrexed (Tomudex®) in malignant pleural mesothelioma: an EORTC phase II study (08992). *European Journal of Cancer*, *39*(3), 353-357.
9. Steele, J. P., Shamash, J., Evans, M. T., Gower, N. H., Tischkowitz, M. D., & Rudd, R. M. (2000). Phase II study of vinorelbine in patients with

malignant pleural mesothelioma. *Journal of clinical oncology*, *18*(23), 3912-3917.
10. Muers, M. F., Stephens, R. J., Fisher, P., Darlison, L., Higgs, C. M., Lowry, E., ... & MS01 Trial Management Group. (2008). Active symptom control with or without chemotherapy in the treatment of patients with malignant pleural mesothelioma (MS01): a multicentre randomised trial. *The Lancet*, *371*(9625), 1685-1694.
11. Berghmans, T., Paesmans, M., Lalami, Y., Louviaux, I., Luce, S., Mascaux, C., ... & Sculier, J. P. (2002). Activity of chemotherapy and immunotherapy on malignant mesothelioma: a systematic review of the literature with meta-analysis. *Lung cancer*, *38*(2), 111-121.
12. Ratto, G. B., Civalleri, D., Esposito, M., Spessa, E., Alloisio, A., De Cian, F., & Vannozzi, M. O. (1999). Pleural space perfusion with cisplatin in the multimodality treatment of malignant mesothelioma: a feasibility and pharmacokinetic study. *The Journal of Thoracic and Cardiovascular Surgery*, *117*(4), 759-765.
13. Colleoni, M., Sartori, F., Calabrò, F., Nelli, P., Vicario, G., Sgarbossa, G., ... & Manente, P. (1996). Surgery followed by intracavitary plus systemic chemotherapy in malignant pleural mesothelioma. *Tumori Journal*, *82*(1), 53-56.
14. Sauter, E. R., Langer, C., Coia, L. R., Goldberg, M., & Keller, S. M. (1995). Optimal management of malignant mesothelioma after subtotal pleurectomy: revisiting the role of intrapleural chemotherapy and postoperative radiation. *Journal of surgical oncology*, *60*(2), 100-105.
15. Rusch, V., Saltz, L., Venkatraman, E., Ginsberg, R., McCormack, P., Burt, M., ... & Kelsen, D. (1994). A phase II trial of pleurectomy/decortication followed by intrapleural and systemic chemotherapy for malignant pleural mesothelioma. *Journal of clinical oncology*, *12*(6), 1156-1163.
16. Richards, W. G., Zellos, L., Bueno, R., Jaklitsch, M. T., Jänne, P. A., Chirieac, L. R., ... & Sugarbaker, D. J. (2006). Phase I to II study of pleurectomy/decortication and intraoperative intracavitary hyperthermic cisplatin lavage for mesothelioma. *Journal of clinical oncology*, *24*(10), 1561-1567.
17. Rice, T. W., Adelstein, D. J., Kirby, T. J., Saltarelli, M. G., Murthy, S. R., Van Kirk, M. A., ... & Weick, J. K. (1994). Aggressive multimodality therapy for malignant pleural mesothelioma. *The Annals of thoracic surgery*, *58*(1), 24-29.
18. Yellin, A., Simansky, D. A., Paley, M., & Refaely, Y. (2001). Hyperthermic pleural perfusion with cisplatin: early clinical experience. *Cancer*, *92*(8), 2197-2203.
19. Boutin, C., Nussbaum, E., Monnet, I., Bignon, J., Vanderschueren, R., Guerin, J. C., ... & Douillard, J. Y. (1994). Intrapleural treatment with recombinant gamma-interferon in early stage malignant pleural mesothelioma. *Cancer*, *74*(9), 2460-2467.
20. Astoul, P., Picat-Joossen, D., Viallat, J. R., & Boutin, C. (1998). Intrapleural administration of interleukin-2 for the treatment of patients with malignant pleural mesothelioma: a Phase II study. *Cancer: Interdisciplinary International Journal of the American Cancer Society*, *83*(10), 2099-2104.
21. Scherpereel, A., Wallyn, F., Albelda, S. M., & Munck, C. (2018). Novel therapies for malignant pleural mesothelioma. *The Lancet Oncology*, *19*(3), e161-e172.
22. Grosso, F., Steele, N., Novello, S., Nowak, A. K., Popat, S., Greillier, L., ... & Scagliotti, G. (2017). Nintedanib plus pemetrexed/cisplatin in patients with malignant pleural mesothelioma: phase II results from the randomized, placebo-controlled LUME-Meso trial. *J Clin Oncol Off J Am Soc Clin Oncol*, 35(31), 3591-600.
23. Scagliotti, G. V., Gaafar, R., Nowak, A. K., Nakano, T., van Meerbeeck, J., Popat, S., ... & Tsao, A. S. (2019). Nintedanib in combination with pemetrexed and cisplatin for chemotherapy-naive patients with advanced malignant pleural mesothelioma (LUME-Meso): a double-blind, randomised, placebo-controlled phase 3 trial. *The Lancet Respiratory Medicine*, *7*(7), 569-580.
24. Tsao, A. S., Miao, J., Wistuba, I. I., Vogelzang, N. J., Heymach, J. V., Fossella, F. V., ... & Kelly, K. (2019). Phase II trial of cediranib in combination with cisplatin and pemetrexed in chemotherapy-naïve patients with unresectable malignant pleural mesothelioma (SWOG S0905). *Journal of Clinical Oncology*, *37*(28), 2537-2547.
25. Kindler, H. L., Karrison, T. G., Gandara, D. R., Lu, C., Krug, L. M., Stevenson, J. P., ... & Vokes, E. E. (2012). Multicenter, double-blind, placebo-controlled, randomized phase II trial of gemcitabine/cisplatin plus bevacizumab or placebo in patients with malignant mesothelioma. *Journal of clinical oncology*, *30*(20), 2509-2515.
26. Zalcman, G., Mazieres, J., Margery, J., Greillier, L., Audigier-Valette, C., Moro-Sibilot, D., ... & Intergroup, F. C. T. (2016). Bevacizumab for newly diagnosed pleural mesothelioma in the Mesothelioma Avastin Cisplatin Pemetrexed Study (MAPS): a randomised, controlled, open-label, phase 3 trial. *The Lancet*, *387*(10026), 1405-1414.
27. Alley, E. W., Lopez, J., Santoro, A., Morosky, A., Saraf, S., Piperdi, B., & van Brummelen, E. (2017). 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. *The Lancet Oncology*, *18*(5), 623-630.
28. Galateau-Salle, F., Churg, A., Roggli, V., Travis, W. D., & for Tumors, W. H. O. C. (2016). The 2015 World Health Organization classification of

tumors of the pleura: advances since the 2004 classification. *Journal of thoracic oncology*, *11*(2), 142-154.

29. Nowak, A. K., Chansky, K., Rice, D. C., Pass, H. I., Kindler, H. L., Shemanski, L., ... & Yoshimura, M. (2016). The IASLC mesothelioma staging project: proposals for revisions of the T descriptors in the forthcoming eighth edition of the TNM classification for pleural mesothelioma. *Journal of Thoracic Oncology*, *11*(12), 2089-2099.