CASE REPORT

Intrapleural cisplatin for management of malignant pleural effusion in a patient with plasma cell leukaemia

Abhishek Agarwal,¹ Jagpal Klair,² Setu Patolia,³ Nikhil K Meena⁴

¹Cooper University Hospital, Camden, New Jersey, USA

²Department of Internal Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

³University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

⁴Department of Pulmonary and Critical Care Medicine, University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA

Correspondence to

Dr Abhishek Agarwal, agarwal-abhishek@cooperhealth.edu

Accepted 6 June 2015

SUMMARY

Plasma cell leukaemia (PCL) is a rare aggressive form of multiple myeloma. It occasionally involves the pleura, causing malignant pleural effusion (MPE). MPE presents a management dilemma for physicians, given the different treatment options available with varying efficacy and side effects. We report a case of a 64-year-old man with MPE due to PCL, successfully managed with intrapleural cisplatin and a tunneled pleural catheter. We believe this to be the first report of management of PCL-associated MPE with intrapleural cisplatin.

BACKGROUND

Plasma cell leukaemia (PCL) is an uncommon and aggressive variant of myeloma. This is defined by the presence of >20% plasma cells in the peripheral blood and an absolute plasma cell count of $>2 \times 10^9/L$.^{1,2} Management of PCL requires early induction therapy with intensive chemotherapy regimens to control the disease activity and decrease the risk of early death.³ This is followed with autologous stem cell transplantation, if feasible.³ Malignant pleural effusion (MPE), when associated with PCL, portends a poorer prognosis. One of the reasons for poor prognosis may be the lack of standard treatment for MPE associated with multiple myeloma (MM).⁴

Richardson *et al*, in 2005, showed that bortezomib, either intrapleural or intravenous, could be used as a management option for PCL-associated MPE.⁵ However, there have been no further developments in the area. We report a case of a 64-year-old man with MPE due to PCL, who showed a dramatic improvement with intrapleural cisplatin. To the best of our knowledge, this is the first reported case of intrapleural cisplatin used through a tunneled pleural catheter (TPC) to successfully treat PCL-associated MPE.

CASE PRESENTATION

A 64-year-old man with medical history of PCL, receiving chemotherapy of cytarabine (Ara-C) 750 mg/m², etoposide 200 mg/m²/day, adriamycin 20 mg/m²/day, decitabine at 20 mg/m² (he also received 9 cycles of vidaza (azacitidine) followed by decitabine), was admitted for treatment of osteomyelitis due to *Enterococcus faecium*. His hospital course was extremely turbulent; he required multiple intensive care unit admissions for hypercarbic respiratory failure, likely stemming in part from a large recurrent left-sided pleural effusion. The

pleural fluid was exudative, with lactate dehydrogenase of 350 IU/L and protein of 6.2 g/dL. On sampling, the pleural fluid had 85% plasma cells while the plasma cells comprised 5% of the peripheral blood; consistent with aggressive local disease. Approximately 1.5 L were drained twice a week for a total of 3 weeks prior to the pulmonary consultation, to avoid respiratory decline. Pulmonology was consulted for options to address the pleural effusion. An indwelling pleural catheter was placed with cisplatin (20 mg/m²) instilled via the catheter to (1) treat the local disease and (2) assure easy drainage without repeated thoracentesis. The pleural fluid was removed daily for a week via the TPC, and the fluid sample was studied twice after the cisplatin administration. The pleural plasma cell count and output decreased to zero within a week. During the same period, the patient's plasma cells in peripheral blood increased from 5% to 34% and his general debilitation precluded systemic chemotherapy or autologous stem cell transplantation. With this knowledge, even though there was significant improvement in his symptoms, he elected comfort as his primary goal.

DISCUSSION

Gluzinski and Reichenstein described PCL over a century.⁶ It is a rare but aggressive form of MM. It is defined by the presence of more than 20% plasma cells in peripheral blood and absolute plasma cell count greater than 2×10^9 .¹ Incidence of PCL ranges from 2% to 4% of patients with MM.¹ PCL can originate de novo (primary PCL) or can occur secondary to leukaemic transformation of MM (secondary PCL).² Primary PCL is more aggressive with higher tumour burden, rapid clinical course, extra medullary involvement and marked bone marrow infiltration, and portends poorer prognosis.² These patients have a median survival of 4–11 months.² Treatment involves induction therapy with bortezomib-based regimens followed by haematopoietic cell transplantation in appropriate candidates. As virtually all patients who achieve complete remission relapse, maintenance therapy with lenalidomide can be considered.^{3,4,7}

PCL can also, rarely, involve pleura, causing MPE. Although pleural effusions occur in 6% of MM patients, effusions due to pleural myelomatous involvement are very rare, occurring in less than 1% of patients. Similar to other malignancies, presence of pleural effusion is associated with worse prognosis in patients with PCL.⁸

CrossMark

To cite: Agarwal A, Klair J, Patolia S, *et al*. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-210044

Treatment of MPE depends on the size of pleural effusion, the rate of accumulation, the patient's symptoms and overall prognosis. In some cases, systemic chemotherapy for the primary cancer can completely resolve the MPE.⁹ But in most cases, given the functional status of the patient, it may not be feasible. Symptomatic patients are usually managed by therapeutic thoracentesis, sometimes every other day. For rapidly re-accumulating pleural effusion, such as that seen in our patient, pleurodesis has been used. Numerous sclerosing agents have been studied, including talc, doxycycline, biologicals such as interferon, *Staphylococcus* superantigen and *Streptococcus pyogenes*, and antineoplastics such as bleomycin and doxorubicin.^{10–11} Success rates for these treatments range between 40% and 100%. Intrapleural chemotherapy and gene vectors for management of MPEs are an emerging area of research, and they may provide loco-region control of underlying malignancy as well as relief from symptoms due to the effusion.^{12–13} A local level of therapeutic agent, many fold higher than serum levels, can be achieved with intrapleural administration and in theory should more effectively manage the local disease while decreasing the systemic toxicity. Randomised trials have demonstrated efficacy in achieving a decrease in MPE but without a survival benefit.¹³

We presented a case of PCL with pleural involvement causing repeated hypercarbic respiratory failure, in which the patient got symptomatic relief but was unable to extend life. To the best of our knowledge, this is the first case of pleural involvement of PCL managed by intrapleural cisplatin instilled via a TPC. Iannitto *et al* successfully used intravenous and intrapleural bortezomib in a patient of MM with pleural involvement.⁵ Ichinose *et al*¹⁴ showed that intrapleural cisplatin decreased incidence of carcinomatous pleuritis without an impact on survival. Rusch *et al*¹⁵ showed that intrapleural cisplatin-based chemotherapies achieved 49% response rate in control of MPE associated with solid cancers. These studies highlight that even though there is no survival benefit, there may be an improvement in quality of life measure.

Learning points

- ▶ Multiple myeloma can, rarely, involve pleura and cause myelomatous pleural effusion.
- ▶ Intrapleural chemotherapy with agents such as cisplatin can be used for local control of the disease.
- ▶ Intrapleural chemotherapy with cisplatin can improve quality of life by decreasing pleural effusions despite no survival benefit.

Further randomised controlled trials are needed to evaluate the efficacy of intrapleural antineoplastic agents and their impact on quality of life. But for the time being, it is important for physicians to recognise intrapleural chemotherapy as an option in their armamentarium to manage MPEs.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Fernández de Larrea C, Kyle RA, Durie BG, *et al*. Plasma cell leukemia: consensus statement on diagnostic requirements, response criteria and treatment recommendations by the International Myeloma Working Group. *Leukemia* 2013;27:780–91.
- 2 Ramsingh G, Mehan P, Luo J, *et al*. Primary plasma cell leukemia: a surveillance, epidemiology, and end results database analysis between 1973 and 2004. *Cancer* 2009;115:5734–9.
- 3 Mahindra A, Kalaycio ME, Vela-Ojeda J, *et al*. Hematopoietic cell transplantation for primary plasma cell leukemia: results from the Center for International Blood and Marrow Transplant Research. *Leukemia* 2012;26:1091–7.
- 4 Katodritou E, Terpos E, Kelaïdi C, *et al*. Treatment with bortezomib-based regimens improves overall response and predicts for survival in patients with primary or secondary plasma cell leukemia: analysis of the Greek myeloma study group. *Am J Hematol* 2014;89:145–50.
- 5 Pemmaraju N, Chang E, Daver N, *et al*. Extramedullary acute myeloid leukemia: leukemic pleural effusion, case report and review of the literature. *Front Oncol* 2014;4:130.
- 6 Gluzinski A, Reichentein M. Myeloma und leucaemia lymphatica plasmocellularis. *Wien Klin Wschr* 1906;19:336–9.
- 7 D'Arena G, Valentini CG, Pietrantonio G, *et al*. Frontline chemotherapy with bortezomib-containing combinations improves response rate and survival in primary plasma cell leukemia: a retrospective study from GIMEMA Multiple Myeloma Working Party. *Ann Oncol* 2012;23:1499–502.
- 8 Nam HS. Malignant pleural effusion: medical approaches for diagnosis and management. *Tuberc Respir Dis (Seoul)* 2014;76:211–17.
- 9 Shaw P, Agarwal R. Pleurodesis for malignant pleural effusions. *Cochrane Database Syst Rev* 2004;(1):CD002916.
- 10 Ren S, Terman DS, Bohach G, *et al*. Intrapleural staphylococcal superantigen induces resolution of malignant pleural effusions and a survival benefit in non-small cell lung cancer. *Chest* 2004;126:1529–39.
- 11 Ong KC, Indumathi V, Raghuram J, *et al*. A comparative study of pleurodesis using talc slurry and bleomycin in the management of malignant pleural effusions. *Respirology* 2000;5:99–103.
- 12 Iannitto E, Minardi V, Tripodo C. Use of intrapleural bortezomib in myelomatous pleural effusion. *Br J Haematol* 2007;139:621–2.
- 13 Serman D, Recio A, Haas A, *et al*. A phase I trial of repeated intrapleural adenoviral-mediated interferon- β gene transfer for mesothelioma and metastatic pleural effusions. *Mol Ther* 2010;18:852–60.
- 14 Ichinose Y, Tsuchiya R, Koike T, *et al*. A prematurely terminated phase III trial of intraoperative intrapleural hypotonic cisplatin treatment in patients with resected non-small cell lung cancer with positive pleural lavage cytology: the incidence of carcinomatous pleuritis after surgical intervention. *J Thoracic Cardiovasc Surg* 2002;123:695–9.
- 15 Rusch VW, Figlin R, Godwin D, *et al*. Intrapleural cisplatin and cytarabine in the management of malignant pleural effusion: a Lung Cancer Study Group trial. *J Clin Oncol* 1991;9:313–19.

Copyright 2015 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow