doi:10.1111/imj.15436

LETTER TO THE EDITOR

Clinical-scientific notes

COVID-19 unmasks the critical role of primary healthcare providers in the timely diagnosis of multiple myeloma

The Coronavirus disease 2019 (COVID-19) pandemic has caused major disruptions to healthcare provision in Australia and globally. On 25 January 2020, the first COVID-19 case was announced in Australia,[1] diagnosed at Monash Medical Centre, Victoria. In March, the first confirmed cases of community transmission were documented and soon after Victoria went into statewide lockdown. In July, a second wave triggered a subsequent extended lockdown. Presentations in both primary care and emergency settings fell significantly.[2,3] In the cancer setting, between April and October 2020, there were 10% fewer notifications than predicted to the Victorian Cancer Registry.[4] Haematological cancers were similarly affected, with a 6.9% decrease in expected notifications.

Multiple myeloma (MM) is a neoplasm characterised by monoclonal plasma cells and usually a monoclonal protein in the presence of end-organ damage or myeloma-defining event.[5] MM is almost always preceded by an asymptomatic pre-malignant stage known as a monoclonal gammopathy of undetermined significance and paraprotein burden has been shown to correlate with disease progression.[6] In the absence of advanced disease, diagnosis and management can usually be delivered in the outpatient setting. During the COVID-19 pandemic, we anecdotally observed more frequent aggressive presentations compared with previous years, and notably more patients with advanced bony disease. To investigate, we conducted a retrospective review of all patients with newly diagnosed symptomatic MM who commenced therapy at Monash Health, Victoria, between January 2017 and January 2020. We compared patients diagnosed following the first confirmed Australian COVID-19 case (at our institution) on 25 January 2020, with patients diagnosed in the preceding 3 years.

A total of 40 patients was diagnosed post-COVID-19 compared with 104 in the 3 years previous (Table 1). Patients diagnosed post-COVID-19 were slightly younger, but the two groups were otherwise comparable at

Table 1 Clinical characteristics of patients with symptomatic multiple myeloma diagnosed between January 2017 and January 2020, pre- and post-the first confirmed case of Coronavirus disease 2019 (COVID-19) in Australia

Characteristic	Post-COVID-19	Pre-COVID-19	*P*-value
n (%)	40 (28)	104 (72)	
Median age (range) (years)	64.5 (39–85)	70 (34–91)	0.049
Sex			
Male/female (%)	26/14 (65)	67/37 (64)	1.00
International staging system stage, *n* (%)			
I	7 (18)	16 (15)	0.81
II	9 (23)	27 (26)	
III	24 (60)	54 (52)	
Incomplete	0 (0)	7 (7)	
Revised international staging system stage, *n* (%)			
I	3 (8)	13 (13)	0.41
II	15 (38)	45 (43)	
III	11 (28)	20 (19)	
Incomplete	11 (28)	26 (25)	
Cytogenetics			
High risk, *n* (%)	4 (10)	8 (9)	0.74
t (4;14)	2 (5)	4 (4)	
t (14;16)	0 (0)	1 (1)	
del17p13	2 (5)	3 (3)	
Median paraprotein (g/L)	36	23	0.03
Bony disease, *n* (%)	25 (63)	61 (60)	0.71
Severe bone disease requiring radiotherapy or surgery, *n* (%)	14 (35)	14 (13)	0.008
Emergency department presentation, *n* (%)	31 (78)	55 (53)	0.008

baseline assessment, including traditional prospective risk factors (Table 1). Patients diagnosed post-COVID-19 had significantly higher paraprotein levels at diagnosis (mean paraprotein 36 g/L vs 23 g/L; $P = 0.03$). Despite similar frequencies of end-organ manifestations, they were more likely to present through the emergency department, require initial hospitalisation and were more likely to require radiotherapy or surgery for symptomatic or unstable bony disease (35% vs 13%; $P = 0.008$).

Within the limitations of a retrospective study, these findings suggest that patients diagnosed with MM during the COVID-19 pandemic presented with more advanced disease, despite comparable traditional staging criteria and risk stratification. In the absence of adverse prognostic factors, the higher paraprotein burden, more extensive skeletal disease and greater need for initial hospitalisation likely reflect delayed diagnosis and the impact of COVID-19, rather than innately aggressive biology.

With an anticipated surge in cancer presentations following COVID-19-related delays, our findings support the critical role that general practitioners play during COVID-19 in recognition of these patients. Consideration of MM in patients with new or unexplained bone pain will avoid morbidity related to further treatment delay. It is critical that public health messaging emphasises the importance of seeking timely medical care amidst a return to COVID-19 normal.

Received 11 June 2021; accepted 17 June 2021.

Adrian Chee [1], Michael S. Y. Low,[1,2] Shahla Vilcassim,[1,2,3] George Grigoriadis[1,2,3,†] and Pasquale L. Fedele [1,2,†]

[1]Monash Haematology, Monash Health, [2]School of Clinical Sciences at Monash Health, Monash University, and [3]Centre for Cancer Research, Hudson Institute of Medical Research, Melbourne, Victoria, Australia

[†]These authors contributed equally to the work.

References

1 Department of Health and Human Services (Victoria). Coronavirus update for Victoria – 25 Jan 2020 (media release). [cited 2021 May 1] Available from URL: https://www2.health.vic.gov.au/about/media-centre/MediaReleases/first-novel-coronavirus-case-in-victoria

2 Kam AW, Chaudhry SG, Gunasekaran N, White AJR, Vukasovic M, Fung AT. Fewer presentations to metropolitan emergency departments during the COVID-19 pandemic. *Med J Aust* 2020; **213**: 370–1.

3 Scott A. The Impact of COVID-19 on GPs on Non-GP Specialists in Private Practice. Melbourne: The University of Melbourne; 2020. Available from URL: https://melbourneinstitute.unimelb.edu.au/__data/assets/pdf_file/0003/3436014/UoM-MI-ANZ_Brochure-FV.pdf

4 Marvelde L, Wolfe R, McArthur G, Blake LA, Evans SM. Decline in cancer pathology notifications during the 2020 COVID-19 related restrictions in Victoria. *Med J Aust* 2021; **214**: 281–3.

5 Rajkumar SV, Dimopoulos MA, Paulumba A, Blade J, Merlini G, Mateos M *et al*. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol* 2014; **15**: e538–48.

6 Kyle RA, Therneau TM, Rajkumar SJ, Offord JR, Larson DR, Plevak MF *et al*. A long-term study of prognosis in monoclonal gammopathy of undetermined significance. *N Engl J Med* 2002; **346**: 564–9.