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COMMENTARY

Pain and related complaints in patients with acute leukemia: time for simultaneous care in hemato-oncology

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Abstract

This commentary deals with the need of an early integration between hematologist and palliative care specialists as well as pain therapists as a routine basis in order to ensure the best management of patients affected by acute leukemia from the onset of the disease and in the stages of causal therapy. This strategy could limit the burden of painful symptoms and, in addition, avoid unnecessary suffering to patients, ensuring the best conditions for optimal outcome of these patients with extremely high clinical complexity and symptomatology who receive intensive treatments or who are managed with novel treatment approaches.

Keywords Pain · Acute leukemia · Opioids · Quality of life · Managed care

Introduction

While a wealth of information is available on symptom burden reported by patients with solid tumors, substantially less empirical data is available for patients with leukemia, and this is particularly true for patients with acute leukemia (AL) [1–3]. Although pain and related distressing complaints are common in the daily clinical practice of hematologists, these are not always adequately reported and appropriately treated [4]. Pain and its related symptom complications following AL treatment are important causes of morbidity and health-related quality of life (HRQOL) impairments. In the setting of AL, pain may be a troublesome symptom and may be due to very different causes and pathogenic factors in all disease phases [4]. The lack of uniformity and guidelines in pain management in this challenging setting also represents an important problem, as outlined by a recently published study [5] which reported a high variability across institutions in the use of pain medication among pediatric AL patients. Although some data regarding pain in patients with more advanced patients with AL are available [1], there is paucity of data on pain during active AL therapies [2, 3]. Therefore, the recent paper by Shaulov et al. [6] is an important one providing novel information in this research area. In a large population of 318 AL patients (of whom some 90% were newly diagnosed), the authors documented that about half reported pain, and in one-third of them, this was of severe intensity [6]. In their sample, they included patients with acute myeloid leukemia (AML), acute promyelocytic leukemia (APL), and acute lymphoblastic leukemia (ALL) and basically included only patients receiving intensive chemotherapy treatments. For example, APL patients receiving a chemotherapy-free treatment (i.e., all-trans retinoic acid plus arsenic trioxide) were excluded [6]. This percentage of patients reporting pain is in line with what was found in a previously reported observations [2, 3], and, interestingly, it is basically the same percentage found in a recent study documenting long-term HRQOL and symptom burden in APL patients treated with standard chemotherapy several years after treatment [7]. This might suggest that pain could also be a persistent problem over the long-term period in AL patients treated with intensive regimens. In the study by Shauolov et al. [6], the three most common sites of pain were oropharynx, head, and abdomen, and severe pain was associated with younger age, performance status, and longer time from the start of chemotherapy [6]. Although the authors used a validated patient-reported symptom measure, this only allowed examining the relationship between pain with other physical and psychological symptoms. The inclusion of an

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additional cancer-specific HRQOL questionnaire could have been of value, for example, to better understand not only the relationships between pain severity and specific symptoms but also other more general HRQOL aspects, such as overall quality of life, social or emotional functioning. An important data emerging from this study was that, although all medical available measures were applied in order to mitigate symptom burden by the hematology team, the authors reported that only less than 1% of patients receiving aggressive induction chemotherapy were referred to palliative care (PC) specialists in the early phase of disease, such as soon after the diagnosis or before the start of treatment [6]. The predictability of pain and related distressing symptom burden in patients undergoing induction chemotherapy for AL highlights the need to implementing measures of prevention, starting with early supportive care [8, 9], as suggested by the authors [6]. The application of early supportive care as well as an integrated multidisciplinary team approach in this patient population could be critical to optimize patient management and avoid unnecessary (or at least partly avoidable) suffering. This is indeed a major challenge of modern hematology [8, 9]. The spectrum and complexity of pain in this setting can be dynamic and continuously changing (fluctuating pain) according to a pattern of sustained/persistent acute pain, often with negatively prognostic pathophysiological components, such as the incident and neuropathic features [1, 4], rather than chronic pain, as observed in patients with solid tumors. Hence, there is a need to continuously adapt and modify the pain management in relation to the fluctuations of pain as well as the analgesic responses. The latter may include non-opioid agents, opioids, and adjuvant drugs, such as anticonvulsants. In this context, the choice of the appropriate route of administration and titration of therapeutic agents as well as the prevention and treatment of the side effects induced by pain medication are of crucial importance. All these aspects involve delicate attention to polypharmacy management, also given the possibility of drug interactions among commonly administered drugs (such as chemotherapeutic agents and anti-infective compounds) and analgesics [4]. In addition, a timely interplay between different specialists, beyond the mere consultation visit, such as the hematologists and PC and pain medicine specialists was facilitated since the onset of illness may have crucial value in improving outcomes of patients [8, 9]. Indeed, patients with hematologic malignancies have unique PC needs, and the potential value of early integration of PC in these patients has already been acknowledged [8]. However, the relative lack of knowledge regarding pain and related symptom burden in the AL setting, together with the general attitude of hematologists to continue treatments, sometimes even futilely aggressive, up to the most advanced stages of illness, could represent an important barrier to the patient's referral to PC services [10]. As result, despite many unmet PC needs related to the symptom burden and the general sufferance afflicting, often severely, patients with hematological malignancies are rarely treated by hematologists in collaboration to PC services [8–10], although the beneficial role of an early referral and of an integrated and simultaneous care approach has been claimed [9, 10]. To conclude, Shaulov et al. [6] should be applauded for having provided novel empirical data that underscore the important problem of pain management during active treatment and for having noted the need to test the value of early PC interventions in AL patients with ultimate goal to improve symptom control.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Niscola P, Cartoni C, Romani C, Brunetti GA, D'Elia GM, Cupelli L, Tendas A, de Fabritiis P, Mandelli F, Foà R (2007) Epidemiology, features and outcome of pain in patients with advanced hematological malignancies followed in a home care program: an Italian survey. Ann Hematol 86:671–676
2. Niscola P, Romani C, Cartoni C, Cupelli L, Piccioni D, Dentamaro T, Tendas A, Giovannini M, Scaramucci L, Tolu B, Perrotti AP, de Fabritiis P (2008) Epidemiology of pain in hospital haematological setting: an Italian survey. Leuk Res 32(1):197–198
3. Zimmermann C, Yuen D, Mischitelle A, Minden MD, Brandwein JM, Schimmer A, Gagliese L, Lo C, Rydall A, Rodin G (2013) Symptom burden and supportive care in patients with acute leukemia. Leuk Res 37(7):731–736
4. Niscola P, Tendas A, Scaramucci L et al (2011) Pain in malignant hematology. Expert Rev Hematol 4(1):81–93
5. Getz KD, Miller TP, Seif AE et al (2018) Opioid utilization among pediatric patients treated for newly diagnosed acute myeloid leukemia. PLoS One; 8 13(2):e0192529
6. Shaulov A, Rodin G, Popovic G, Caraiscos VB, le LW, Rydall A, Schimmer AD, Zimmermann C (2018) Pain in patients with newly diagnosed or relapsed acute leukemia. Support Care Cancer. https://doi.org/10.1007/s00520-018-4583-5
7. Efficace F, Breccia M, Avvisati G, Cottone F, Intermesoli T, Borlenghi E, Carluccio P, Rodeghiero F, Fabbiano F, Luppi M, Romani C, Sborgia M, D'Ardia S, Nobile F, Cantore N, Crugnola M, Nadali G, Vignetti M, Amadori S, Lo Coco F (2018) Health-related quality of life, symptom burden, and comorbidity in long-term survivors of acute promyelocytic leukemia. Leukemia. https://doi.org/10.1038/s41375-018-0325-4
8. Niscola P, Tendas A, Efficace F (2018) Early palliative care in patients with hematological malignancies: where do we go from here? J Pain Symptom Manag 55(4):e1–e2
9. Boucher NA, Johnson KS, LeBlanc TW (2018) Acute leukemia patients' needs: qualitative findings and opportunities for early palliative care. J Pain Symptom Manag 55(2):433–439
10. Wadhwa D, Popovic G, Pope A, Swami N, Le LW, Zimmermann C (2018) Factors associated with early referral to palliative care in outpatients with advanced cancer. J Palliat Med 21(9):1322–1328