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Perspective

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Blood Cancer Pain and Symptoms

Alice John*

Abstract

Patients with blood-related malignancies experience a significant symptom burden, which includes a variety of pain syndromes brought on by various pathogenic pathways and causes. Therefore, a complex clinical scenario involving pain may be seen in this situation. In fact, there are many other clinical diseases that can induce pain, including the disease itself, its consequences, iatrogenic causes, and unrelated clinical conditions. The treatment strategy, which should be based on a multidisciplinary management and necessitate the integration of etiology-targeted interventions and painkilling drugs, may be guided by a close diagnostic procedure for the assessment of the underlying causes of the pain and of its pathogenic mechanisms. Most patients with BRC on pain can achieve sufficient pain control using oral medications according to the World Health Organization's three-step analgesic ladder, but many difficult-to-treat pain syndromes that are frequently encountered in this context may require more complicated therapies.

Keywords: Hematological malignancies; Pain; Blood cancer

Introduction

The symptom burden for patients with blood-related malignancies is significant and includes several types of discomfort. In this situation, it may be possible to identify a number of pain syndromes that may be brought on by the disease itself, its consequences, diagnostic techniques, and treatments. Regarding its temporal pattern, pain is categorized as acute or chronic; from a neurobiological perspective, it is categorized as nociceptive (inflammatory) or neuropathic. Additionally, somatic (superficial and deep) and visceral categories can be used to categories nociceptive pain. Additionally, pain can sometimes manifest even in the absence of a clearly unpleasant stimulus. This is the result of a centrally maintained process linked to a complex lesion in the somatosensory pathways, which likely involves some neurobiological changes like the activation and plasticity of neuronal and glial cells. Again, in the context of malignant hematology, breakthrough pain, signifying an intermittent worsening of pain that may happen either spontaneously or induced by movements (incident pain), is frequently observed. In this regard, it's critical to remember that incident pain refers to a pain brought on by movement in any clinical condition, whereas movement breakthrough incident pain refers to a pain brought on by movement in a patient receiving ongoing opioid medication.

***Corresponding author:** Alice John, Editorial Office, Clinical Oncology: Case Reports, United Kingdom E-mail: oncologyreport@escienceopen.com

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Pain is a common presenting symptom of BRC patients; this type of pain typically responds well to causative interventions, and typically remission from this pain occurs shortly after the start of a treatment with chemotherapeutic medicines and/or steroids. On the other hand, patients who are actively receiving therapy may experience short- or long-lasting iatrogenic pains. Additionally, patients who have survived their illness may develop chronic pain as a result of consequences from their treatment. Last but not least, one of the most distressing symptoms that would be treated as part of an all-encompassing program of end-of-life care in patients with advanced-stage incurable diseases is pain. Malignant hematology has historically disregarded the treatment of pain. Onco-hematological patients' pain management practices have so far been adapted from those utilized for patients with solid tumors in the absence of explicitly tailored recommendations. Cancer pain has frequently been ignored and improperly treated, as has lately been reported. Although it has been strongly emphasized that a comprehensive pain treatment should be incorporated in the overall management of patients with BRC, the same concerns regarding an inadequate pain control may therefore also apply in the context of malignant hematology. Epidemiological information on pain syndromes in BRC patients is limited and lacking. However, the incidence of pain in the former setting has been reported to range from 37% to 90%, for which the prevalence of pain in patients affected by BRC may be considered as similar or even higher compared to patients with solid tumors. In the past, several authors have reported a much lower incidence and severity of pain in patients with BRC compared to those recorded in the setting of solid tumors. This review makes an effort to address a subject that has historically received little attention: pain in BRC patients.

Blood cancer-related pain syndromes and their complications

Bone pain, which is mainly associated to two pathological processes: osteolytic lesions and the infiltration of Bone Marrow (BM) by malignant cells, is the most significant disease-related pain experienced by patients with blood-related malignancy. Under these conditions, the periosteum, mineralized bone, and the BM are all heavily supplied by sensory and sympathetic nerve fibers, which activate to cause pain. The most distressing pain syndromes of bone origin are experienced by multiple myeloma patients with BRC. The physical deconditioning syndrome, which is characterized by muscle atrophy and physical debility and causes bedsores, constipation, and rectal and bladder spasms with a negative impact on quality of life, is one example of a condition where pain may result from complications other than skeletal involvement. As previously indicated, skeletal lesions cause localized and/or irradiation nociceptive continuous pain when at rest, which is occasionally compounded by neuropathic symptoms (mixed pain), as well as incident pain that is brought on by movement. The conventionally accepted mechanisms of pain in the absence of skeletal diseases include BM hypertension, ischemia, and the strength of the periosteum due to the involvement of malignant cells in the BM. These hypotheses have lately been challenged by experimental results from animal models, which show that the presence of malignant cells in the BM and/or the mineralized matrix alone can cause pain in the absence of periosteal tumor involvement and/or lytic lesions.

Patients who have BM infiltration frequently describe a deep, migratory discomfort that is dull or throbbing. The involvement of visceral, cutaneous, and mucous membrane tumors, as well as space-occupying masses, bulky lymph nodes, organ enlargements, and peripheral nerve injuries, are additional well-known causes of disease-related pain. Involvement of vertebral bodies with extradural spinal cord compression seen in multiple myeloma and lymphomas (less frequently in other BRC) as well as infiltration or compression by cervical, axillary, para-aortic, or retroperitoneal lymph nodes of adjacent nervous plexus are additional significant causes of neuropathic pain. Clinical consequences of BRC may be connected to some other significant pain disorders. Onco-hematological patients are in fact particularly susceptible to painful infections including post herpetic neuralgia, oral and vaginal herpes, herpes zoster, esophagitis by Candida, pneumonia, cellulitis, urinary tract infection, wound infections, and oral and gastrointestinal mucositis. Finally, depending on the associated pathogenic mechanisms and anatomical area, internal hemorrhages and deep or superficial vein thrombosis may ensue.

Discussion

Iatrogenic and care-related pain is becoming a bigger issue in onco-hematology. Almost all patients who undergo invasive diagnostic procedures, such as lumbar puncture (headache) and BM aspiration/biopsy, as well as other care-related actions, such as vein punctures, the insertion of catheters, medications, the patient's mobilization/transportation, and so on, experience discomfort and transient acute pain. Agents frequently used to treat BRC can also cause different types of pain. Due to the growth of the hematopoietic matrix and the stimulation of nerve endings in the BM, patients taking Granulocyte Colony-Stimulating Factors (G-CSFs) for neutropenia or stem cell mobilisation may have bone pain and headaches.

Assessment of pain in blood cancer patients as a diagnostic factor

Multiple types of pain, which might occasionally coexist in the same patient, can be experienced by BRC patients. For appropriate care, each pain syndrome must undergo a separate assessment. The fifth vital sign, pain, should be monitored on a regular basis. The first step in pain assessment is patient reporting of their pain experiences. Several tools, including verbal descriptions, the Visual Analogue Score (VAS), and the numerical rating scale, can be used to measure the intensity of the pain. Some patients, such as children, non-communicative patients, and unconscious adults, may not benefit from these techniques; instead, they should be observed for their facial expressions and other verbal and non-verbal cues. Based on particular tools and scales, neuropathic pain is evaluated and assessed. In order to maximize a patogenetically target-oriented treatment, the primary step should be the diagnosis of the source of pain. Electrophysiological tests and radiologic imaging can also be helpful in this direction under certain conditions. For the detection of symptomatic or asymptomatic osteolytic lesions and spinal cord compression, conventional radiology, comprising an X-ray of the skeleton, Computed Tomography (CT), and Magnetic Resonance Imaging (MRI), constitute the standard diagnostic procedures. Additionally, CT and MRI are used to evaluate jaw osteonecrosis brought on by bisphosphonates. The causes and severity of the underlying neuropathic illnesses can be determined through electrophysiological tests based on the examination of nerve conduction velocities, such as particular latency time, amplitude, duration, and configuration of sensory- and motor-evoked potentials.

Management of pain in onco-hematology

Pain should be avoided wherever possible in BRC patients. A realistic treatment plan for those who are in pain should combine causative therapies with analgesic measures. Therefore, the mainstay therapies for underlying diseases-related pain include chemotherapy and radiotherapy. In addition, infections should be controlled with antibiotics, and in certain cases, orthopedic devices, skeletal-stabilizing surgery, and physiotherapy may be helpful. The increased usage of bisphosphonates over the past ten years has offered an efficient way to stop the symptoms of myeloma bone damage. However, it is still exceedingly challenging to prevent procedural and iatrogenic discomfort. Short-term diagnostic procedures like lumbar puncture and BM aspiration/biopsy are typically carried out under local anesthetic; however some patients may find them uncomfortable. A pre-emptive analgesia with brief unconscious sedation or general anesthesia can therefore be recommended in these particular instances. Unfortunately, there is still room for improvement in the prevention of oral and gastrointestinal mucositis; the only practices that are still advised are meticulous oral hygiene and patient education. In patients receiving bortezomib, early dose reduction or the discontinuation of neurotoxic medications may prevent the progression of the neural damage and allow for at least a partial recovery of nerve dysfunction. Therapy-induced peripheral neuropathies are not preventable and require careful patient evaluation and follow-up.

Although no controlled trials have been published in patients with Blood Related Cancer (BRC), a number of nonpharmacological methods can be helpful in the management of pain and they can have some advantages. When a thorough pain management strategy is being planned, a psychological support system and multimodal cognitive behavioral therapies, including relaxation techniques, coping mechanisms, and mood-enhancement techniques, should be considered. Additionally, some types of pain and its incapacitating sequelae may be managed with physical therapies, rehabilitation, and other biomechanical interventions (such as massage and trigger point pressure). Any medication with a primary therapeutic indication other than pain reduction but the ability to help control pain is considered an adjuvant analgesic. These medications play a crucial role in the treatment of all types of pain, but they are especially useful for neuropathic pain management. In patients with Blood related Cancer, bisphosphonates, antidepressants, and anticonvulsants like gabapentin and pregabalin are the most frequently used adjuvant medications. These medications are given for a variety of neuropathic conditions, for which treatment may require an individualized approach with tricyclic antidepressants, anticonvulsants, and some opioid medications, either alone or in combination.

Conclusion

In the overall therapy of patients with active BRC as well as long-term survivors, who place a high priority on improving quality of life, pain control is a crucial component. In this regard, a multidisciplinary approach can be the foundation of an appropriate pain management strategy. Although adjuvant medications, targeted treatments, and non-pharmacological therapies may be crucial in certain situations, the WHO analgesic ladder for cancer pain is effective in the majority of patients. The current difficulty is in pain prevention. In this context, over the past ten years, we have made significant clinical progress in the diagnosis, prognosis, and therapy of myeloma bone disease. Lenalidomide and other immunomodulatory counterparts currently under development, such as pomalidomide, have also been shown to

have no neurotoxic side effects when used to treat patients, particularly those with multiple myeloma. In conclusion, a better comprehension of the factors influencing the response to analgesic therapy, enabling the identification of patients who are challenging to treat, can improve our clinical practice when dealing with malignant pain. In this context, improvements in the understanding of the molecular basis of pain may offer hope for the creation of novel diagnostic tools and focused therapeutic interventions, potentially leading to a material improvement in the treatment of pain in the near future.

Author Affiliations Top

Editorial Office, Clinical Oncology: Case Reports, United Kingdom