Painful bone metastases – Can we do better?

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The treatment of painful osseous metastases (POM) remains extremely challenging for the clinician. Richard Payne and Nora Janjan recognized how complex these patients are and as a result they recommended setting up specialized interdisciplinary cancer center bone metastasis clinics specific for patients with painful osseous metastases (1). Despite advances in the understanding of the pathophysiology of POM, new and improved analgesics/analgesic techniques, and a greater appreciation of how to approach the evaluation and management of patients with POM, it appears that a significant proportion of patients with POM continue to suffer. Some patients, while experiencing these intense painful episodes have stated they "would rather be dead than continue like this". Potential reasons why clinicians may have difficulty optimally treating this pain; especially cancer-related pain could include: (I) Clinicians usually are uncertain of the precise nociceptive mechanisms contributing to a patient's pain (e.g., TRPV1, $Nav_{1.7}$, P2X3), and (II) Even if clinicians were able to know which nociceptive mechanism was largely responsible for a patient's pain complaints, there may not be any currently available agents to combat this particular receptor/channel/signaling pathway. There are currently available therapeutic strategies that may be at least partially beneficial for patients with painful osseous metastases; however, unfortunately these patients may not always receive the optimum analgesia that can be provided. I would like to bring attention to what I believe are some reasons why even experienced clinicians may continue to prescribe treatment strategies providing suboptimal analgesia.

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First, like most issues related to complaints of pain; the clinician should make every reasonable effort to reach a diagnosis [e.g., "find the pain generator(s)"]. All too often, when patients that are near the end of life or labeled as "comfort care", complain of increased pain intensity or even a new pain; clinicians reflexly increase the opioid dose that they are receiving. Although this may be appropriate more times than not, occasionally it also may be appropriate to go back and perform a focused history and physical examination or even in certain infrequent instances utilize noninvasive diagnostic imaging (e.g., ultrasound)/investigations, since if there is something causing the pain that can be relatively easily treated; then the patient may be able to live the last few months of their life with improved quality of life and less pain/suffering.

A potential example of this may be the 84 year-old man with advanced prostate cancer with extensive metastatic disease involving many areas of the body including the ribs on both sides complaining of severe bilateral anterior chest pain. This pain has been assumed to be bilateral rib pain from metastases, treated by increasing opioids. The high doses of opioid only mildly diminished his pain but left him somnolent and less communicative with his family. However, on closer evaluation/investigation, the pain complaints were actually compatable with thoracic radiculopathy from spinal metastases and he was treated with single fraction external beam radiation therapy to the thoracic spine with excellent results.

Second, I feel that there is underutilization of radiation therapy (external beam or radiopharmaceutical administration). This may be due in part to knowledge deficits, and/or possibly due to irrational fear on the part of radiation oncologists/nuclear medicine physicians that administering small "palliative" amounts of radiation may lead to adverse effects or may wind up delivering "over the limit of radiation" that is "allowed" despite that these are "palliative care" patients at near the end of life or in "comfort care" situations.

Third, I feel that there is underutilization of rapid onset opioids (ROOs), since many patients (roughly half) with POM have rapid onset breakthrough pain (ROBTP). ROBTP

episodes tend to have short spiking characteristics with rapid onset (<5 minutes) and short duration (<15 minutes). Thus, these ROBTP episodes need to be treated with ROOs which may have an onset if roughly 5 minutes and peak quickly with short duration; matching the characteristics of the ROBTP episode. However, I feel that ROOs are not being prescribed all that much for these patients with POM and ROBTP. Unfortunately, often patients with ROBTP episodes are given immediate release formulations [e.g., morphine sulfate immediate release (MSIR), oxycodone immediate release (OxyIR)]. Hopefully the "suboptimal" terminology transmucosal immediate release fentanyl (TIRF) instead of ROOs as well as the United States Food & Drug Administration (US FDA) Risk Evaluation Mitigation Strategy (REMS) program is not contributing to this underutilization of ROOs; however I am not confident that this is the case.

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