Palliative Medicine Doctors' Meeting

Palliation of Bone Metastases:
Pharmacological approach and Radiotherapeutic approach

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Introduction

Bone is the third most common metastatic site after the lung and the liver\(^1\). As revealed by autopsy series, up to 85% of patients who are dying from breast, prostate, and lung cancer have bone involvement\(^2\). Other than pain, bone metastases causes significant complications, including pathological fracture, spinal cord compression, nerve root compression and hypercalcaemia. These greatly affect the functional aspect and quality of life of patients. Multidisciplinary approaches are usually adopted in the palliation of bone metastases. Pharmacological treatment, radiotherapeutic treatment and orthopaedic treatment are three main components in the palliative treatment of bone metastases.

Pharmacological Approach

Analgesia, specific anti-cancer drugs and bisphosphonates are the three main groups of pharmacological agents that are useful in palliative treatment of bone metastases.

Analgesia

Analgesia is usually the first treatment that is used to palliate malignant bone pain and the associated neuropathic pain due to compression and infiltration of the nerve by bone metastases. The basic principle is to use the right drug in the right dose at the right time intervals, guided by the World Health Organisation 3-step analgesic ladder with appropriate use of adjuvant drugs\(^3\).

NSAIDs are believed to be particularly effective in bone metastases. They act by inhibiting the prostaglandin synthesis, and lead to a reduction in prostaglandin-induced pain sensitisation and a reduction in edema, which if present, can increase intraosseous pressure and the stretching of the periosteum\(^4\). The choice of NSAIDs depends on availability, cost, frequency of administration, individual toxicity and response\(^3\).

As compared to NSAIDs, selective COX-2 inhibitors have a similar effectiveness in pain control, but have the advantage of less gastrointestinal effects and less interference with platelet aggregation\(^5\). These drugs may be useful for patients with a high risk of gastrointestinal complications, and for patients who have to avoid the risk of bleeding. Cost-effectiveness should be a concern when using these agents as substitute for NSAIDs.

For moderate to severe malignant bone pain, opioids are the mainstay of drug therapy. If patient has moderate to severe malignant bone pain at presentation, then we can jump over step 1 of the WHO analgesic ladder and start at step 2 or 3, using combination of opioids and non-opioids to achieve prompt relief of pain. In contrast to non-opioids, strong opioids have no ceiling dose. The clinical use of opioids has been discussed in a comprehensive palliative medicine textbook\(^6\).

Cancer Specific Agents

Hormonal therapy should be considered as a treatment modality in the palliation of bone metastases for patients with hormonal-dependent tumours, including breast and prostate cancers, especially for those who have a slow progression of the disease. Sustained symptom relief may be achieved in these groups of patients after hormonal therapy. However, it takes time for the therapeutic effect to work. Toxicity is usually minimal.

For patients with chemosensitive tumours, such as lymphoma, germ cell tumour, small cell carcinoma of the lung and carcinoma of the breast, chemotherapy can be considered for the palliation of bone metastases if the patients are in good general condition. With the shrinkage of tumour by chemotherapy, the symptoms can be relieved rapidly. However, palliative chemotherapy brings with it significant physical and psychosocial burdens. The radiological response of bone metastases is difficult to monitor. The benefits and potential risks should be weighed thoroughly before palliative chemotherapy begins.

Bisphophonates

Bisphosphonates are pyrophosphate analogues and are potent inhibitors of osteoclast-mediated bone resorption. The exact mode of action has not been completely elucidated. The inhibition of bone resorption may act by inhibiting osteoclasto-