

IN THE NAME OF ALLAH

Cancer Pain Syndromes

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overview

- **Acute**
- **Chronic**

- CANCER PAIN is one of the most common and problematic symptoms faced in palliative care.
- Despite advances in cancer treatment and palliative care, pain has been reported to be moderate to severe in as many as 51.9% of patients with advanced disease and 38% of all patients.
- Uncontrolled pain often results in unnecessary suffering; it can have an impact on quality of life and interfere with activities of daily living, even affecting basic functions such as mobility and sleep.

Acute pain syndromes

ETHIOLOGY

- Acute pain associated with diagnostic interventions
- Acute pain associated with therapeutic interventions
- Acute pain associated with anticancer therapies
- Acute pain associated with chemotherapy toxicity
- Acute pain associated with infection
- Acute pain associated with vascular events

Acute pain associated with diagnostic interventions

Diagnostic Interventions

- **Lumbar puncture headache:** positional headache, which is precipitated or markedly exacerbated by upright posture, usually develops hours to several days after the procedure, is typically described as a dull occipital discomfort that may radiate to the frontal region or to the shoulders, and routine management relies on rest, hydration, and analgesics.
- **Transthoracic needle biopsy**
- **Transrectal prostatic biopsy**
- **Mammography pain:** Breast compression associated with mammography can cause moderate, and rarely severe pain. duration of the pain is generally short.

Acute pain associated with therapeutic interventions

therapeutic interventions

- **Postoperative pain:** Acute postoperative pain is universal unless adequately treated. Unfortunately, under treatment is endemic despite the availability of adequate analgesic and anaesthetic techniques.
- **Radiofrequency tumour ablation:** is commonly used in the management of liver metastases.
- **Cryosurgery:** Cryotherapy is commonly applied in the management of skin, cervical, and prostatic tumours
- **Other interventions:** include the pains associated with tumour embolization techniques, radioembolization of liver tumours and chemical pleurodesis.

Acute pain associated with analgesic techniques

- **Local anaesthetic infiltration pain:** Intradermal and subcutaneous infiltration of lidocaine produces a transient burning sensation before the onset of analgesia.
- **Opioid injection pain:** Intramuscular (IM) and subcutaneous (SC) injections are painful.
- **Opioid headache:** very rare
- **Spinal opioid hyperalgesia syndrome:** Intrathecal and epidural injection of high opioid doses is occasionally complicated by pain (typically perineal, buttock, or leg)
- **Spinal injection pain:** Back, pelvic, or leg pain may be precipitated by epidural injection or infusion.

Acute pain associated with anticancer therapies

Anticancer therapies

- **Intravenous chemotherapy infusion pain:** Four pain syndromes related to intravenous infusion of chemotherapeutic agents are recognized: venous spasm, chemical phlebitis, vesicant extravasation, and anthracycline-associated flare.
- **Intraperitoneal chemotherapy pain:** A transient mild abdominal pain, associated with sensations of fullness or bloating is reported by approximately 25% of patients after intraperitoneal chemotherapy. opioid analgesia or discontinuation of therapy was recommended.
- **Intravesical chemo- or immunotherapy:** BCG therapy for transitional cell carcinoma of the urinary bladder usually causes a transient bladder irritability syndrome.

Acute pain associated with chemotherapy toxicity

○ Mucositis:

- Pretreatment oral pathology and poor dental hygiene increase the risk of chemotherapy-induced mucositis.
- Younger patients have a relatively greater risk
- Damaged mucosal surfaces may become superinfected with microorganisms, such as *Candida albicans* and herpes simplex.

○ Corticosteroid-induced perineal discomfort:

- A transient burning sensation in the perineum is described by some patients following rapid infusion of large doses (20–100 mg) of dexamethasone

Acute pain associated with chemotherapy toxicity

- Painful peripheral neuropathy
- Headache
- Diffuse bone pain
- Palmar–plantar erythrodysesthesia syndrome: This is a painful rash
- Post-chemotherapy gynaecomastia:
 - Testis cancer is the most common underlying disorder
 - typically develops after a latency of 2–9 months and resolves spontaneously
- Chemotherapy-induced tumour pain

- **Acute pain associated with hormonal therapy:** diffuse musculoskeletal pain, bone pain, arthralgia syndrome
- **Acute pain associated with immunotherapy**
- **Acute pain associated with bisphosphonates:** associated with the development of multifocal bone pain and/or myalgia. pain occurs within 24 hours of infusion and may last up to 3 days.
- **Acute pain associated with growth factors (GM-CSF/ G-CSF):** commonly produce mild to moderate bone pain and constitutional symptoms such as fever, headache, and myalgias during the period of administration. Co administration of dexamethasone may reduce the prevalence and severity of bone pain

Acute pain associated with radiotherapy

- Can be due to transport and positioning of the patient for radiotherapy.
- can be caused by acute radiation toxicity:
 - *Oropharyngeal mucositis*
 - *Acute radiation enteritis and proctocolitis*: occurs in as many as 50% of patients receiving abdominal or pelvic radiotherapy. These complications typically resolve shortly after completion of therapy, but may have a slow resolution over 2–6 months.
- *Early-onset brachial plexopathy*: breast cancer, Hodgkin's disease
- *Radiotherapy-induced pain flare*: Palliative radiotherapy of bone metastases causes a temporary increase in bone pain in 30–40% of patients immediately after radiotherapy and A single 8 mg dose of dexamethasone before radiotherapy has been effective
- *cystitis-urethritis, vaginal ulceration, or radiation dermatitis*

○ **Acute pain associated with infection:** Acute herpetic neuralgia

○ **Acute pain associated with vascular events:**

- *upper or Lower-extremity deep venous thrombosis,*
- *Superior vena cava obstruction*
- *Acute mesenteric vein thrombosis,*
- *Superficial thrombophlebitis*

Chronic pain syndromes

- Most chronic cancer-related pains are caused directly by tumour
- almost one-quarter of the patients experienced two or more pains.
- Over 90% of the patients had one or more tumour related pains.
- 21% had one or more pains caused by cancer therapies.
- Somatic pains (71%) were more common than neuropathic (39%) or visceral pains (34%).

Cancer-induced bone pain (CIBP)

- Bone is the third most common site of metastatic disease.
- approximately 75% of these patients suffering from related pain.
- It is important to understand the underlying mechanisms of CIBP

Mechanisms of cancer-induced bone pain

○ **Peripheral factors:**

- The relationship between the site of bone metastasis, the sensory nerves, and the surrounding microenvironment plays a key role in CIBP.
- CIBP may occur prior to evidence of bony destruction.

1. Local changes in sensory neurons:

- Direct pressure and compression of surrounding structures, including the sensory nerves innervating the bone and periosteum, will occur with tumour growth.

2. Inflammation:

- In the area of bony metastases, a range of pro-hyperalgesic mediators, commonly associated with inflammation, is released from the tumour and associated immune system cells.

3. Bone microenvironment:

- When tumour cells spread to bone, the balance of bone turnover is disrupted
- An increase in osteoclasts and their activity results in increased degradation of bone matrix

Mechanisms of cancer-induced bone pain

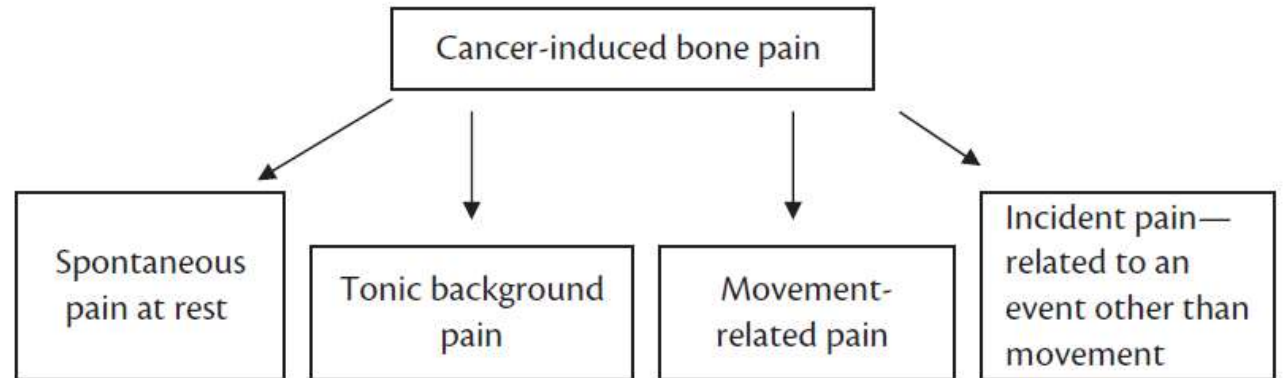
○ Central factors:

- it is not understood at all how much the central changes contribute to the degree of severity of the pain syndrome.
- changes in spinal pain processing, with central sensitization ,play a major role in the development of chronic pain.

Clinical features

- Bone pain can have a significant impact on physical, psychological, and social functioning.
- The optimum use of the World Health Organization (WHO) analgesic ladder is critical for successful management of CIBP.
- Bone is the most common source of pain in patients with malignant disease.
- Lesions in bone account for 30–35% of all cancer pains in patients with advanced disease.

Clinical characteristics



Background pain

- Background pain can be intermittent initially, but rapidly progresses to become constant in nature.
- **Site of pain:** The skeleton was affected in slightly different patterns depending on the primary site of the tumour
- **Radiation of pain:**
 - Usually the pain is localized to a specific area (there is point tenderness over the affected area of bone)
 - migratory pattern of pain: pain might appear in one area of the body at a given time, then move to a completely different part of the body with total resolution of the pain at the original site.
- **Quality (character) of pain:** described as a dull ache
- **Intensity (severity) of pain:** is independent of tumour type, location, number and size of metastases, gender, and age of patient

Background pain

○ Exacerbating factors of pain:

- exacerbation of pain is often related to specific events ('incident pain'). Incident pain can be further divided into:

- (a) volitional pain—precipitated by a voluntary act (e.g. walking)

- (b) non-volitional—precipitated by an involuntary act (e.g. coughing)

○ Relieving factors of pain:

- A variety of different non-pharmacological, pharmacological, oncological, and other types of interventions have been used to treat bone pain.

Breakthrough pain

- Breakthrough pain is referred to as 'transitory exacerbation of pain experienced by the patient who has relatively stable and adequately controlled baseline pain'
- Bone pain is a major source of breakthrough pain
- The clinical features of breakthrough pain vary from individual to individual and often mirror the clinical features of the background pain;
- between onset and peak of pain to be 3 minutes, with a range of 1 second to 30 minutes.
- Patients with breakthrough pain have significantly increased levels of depression and anxiety

Spontaneous pain vs movement-related pain

- Spontaneous pain refers to episodes of breakthrough pain that occur unexpectedly at rest.
- In contrast, movement-related pain (also known as incident pain or 'precipitated pain') refers to episodes of breakthrough pain that are related to specific events.
- Movement-related pain is the more common form of incident pain in patients with CIBP

Neuropathic pain

- Neuropathic pain is a heterogeneous group of chronic pain conditions arising from a lesion or disease of the peripheral or central somatosensory nervous system.
- is commonly divided into peripheral and central neuropathic pain.
- Treatment often is difficult and may involve interventions distinct from those typically used for nociceptive pains.

Classification of neuropathic pain

Peripheral	Central
Mono- and polyneuropathy diabetes alcohol HIV chemotherapy other	Multiple sclerosis
Plexopathy	Neoplasms
Radiculopathy	Spinal cord injury
Nerve injury: postsurgical post-traumatic	Syringomyelia
Amputation: phantom limb pain stump pain	Myelopathy
Root avulsion	Stroke
Post-herpetic neuralgia	
Trigeminal neuralgia	
Neoplasms	

Clinical characteristics

- Neuropathic pain may develop immediately after a nerve injury or disease or occur as a late effect, often after several months.
- types of pain perceived in areas of sensory abnormality, either hyposensitivity and/or hypersensitivity.
- Other sensations, such as paraesthesia (abnormal sensation that is not painful or unpleasant) and dysaesthesia (unpleasant abnormal sensation) may be present spontaneously or occur only when evoked by a stimulus.
- Allodynia is a type of evoked pain that is elicited by a non-noxious stimulation
- Hyperalgesia, which describes an increased response to a stimulus that is normally painful

Neuropathic pain syndromes

- Neuropathic pain syndromes have become an increasing problem in cancer patients.
- affecting up to 40% of patients
- neuropathic pain in cancer patients is caused by cancer treatment or comorbid disease compared with all cancer pain.
- Neuropathic pain conditions may persist independently of the cancer and affect the quality of life in disease-free cancer survivors
- painful mononeuropathy or plexopathy often is caused by direct infiltration of peripheral nerves by the cancer.
- Polyneuropathy may occur in association with malnutrition or paraneoplastic syndromes, may affect 5% of patients

Chemotherapy-induced neuropathy

- usually is a dose-dependent
- Symptoms include sensory loss, paraesthesia, dysaesthesia, and pain sometimes accompanied with muscle weakness.
- Cold allodynia and pricking dysaesthesia affecting hands and feet

Visceral pain

Visceral pain is pain that arises from in or around internal organs.

Pathophysiology of visceral pain

- **Peripheral activation:** Physiologic stimuli include distention, inflammation, torsion, and ischaemia.
- **Peripheral sensitization:**
 - refers to changes in the functioning of a primary afferent nerve
 - This phenomenon may be relevant to the concept of visceral hyperalgesia.
- **Central sensitization:** Examples of visceral pain that are believed to be related to central sensitization include oesophageal non-cardiac chest pain and chronic pancreatitis

Visceral pain syndromes

Pain related to thoracic disorders

- Many serious illnesses affect thoracic viscera, including the heart, its blood supply, and the great vessels; the lungs, airways, and pleura; or other mediastinal structures such as lymph nodes.
- Pain syndromes related to thoracic disease often have a time course determined by the progression of the underlying illness.

Pain related to intra-abdominal disorders

- Risk factors for the development of abdominal pain are tumour size, invasion of the anterior capsule, and invasion of intrapancreatic nerves.
- **pain related to a neoplasm in the upper mid-retroperitoneum, such as the pancreas;**
- **Bowel obstruction:** The pain is usually crampy and may rise and fall during the day.
- **capsular injury:** include the hepatic distention syndrome , pain from large adrenal masses and rapid enlargement of the spleen and lymph nodes.
- **related to antineoplastic therapies:** e.g. tumour embolization procedures involving lesions in the liver, kidney, spleen, or uterus
- Radiation-related pain syndromes include radiation enteritis, proctitis, and prostatitis.
- Associated with placement of oesophageal stents

Pain related to pelvic disorders

- Due to intra-pelvic pathology, such as chronic bowel obstruction
- locally advanced neoplasms affecting gynaecological structures, prostate, or rectum.
- These disorders may cause persistent perineal or deep pelvic pain, and may be accompanied by tenesmus or by urinary urgency or bladder spasms.

Conclusion

- Adequate assessment is a necessary precondition for effective pain management.
- In the cancer population, assessment must recognize the dynamic relationship between the symptom, the illness, and larger concerns related to quality of life.
- Syndrome identification and inferences about pain pathophysiology are useful elements that may simplify this complex undertaking.

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