Thoracic and Cardiovascular Surgery

Palliative Care for the Patient With Mesothelioma

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The role of palliative care in the medical management of malignant mesothelioma is multifaceted, requiring proficiency in multiple disciplines. Pain management is a key aspect of this care. The most common sources of pain are postthoracotomy syndrome, chemotherapy-induced peripheral neuropathy, involvement of the intercostal nerves by tumor invading the chest wall, and dyspnea. The palliative care provider also must be prepared to recognize and treat psychological disorders, to identify other social and spiritual sources of distress, including anxiety and depression, and to provide or arrange for counseling to patient and family for advance care planning, as well as grief and bereavement.
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Providing palliative care to newly diagnosed patients with malignant pleural mesothelioma, which is almost always fatal, presents a significant challenge. Palliative care practitioners, who are members of the multidisciplinary treatment team, play an important role. They not only detect and provide advice regarding pain, symptom management, and psychological and spiritual distress but also help oncology clinicians communicate prognostic information. Additionally, they often help mesothelioma patients define goals of care and craft advance care plans to guide their families and their clinicians in carrying out their wishes.

The most common symptoms reported by pleural mesothelioma patients are shortness of breath (39%), tiredness (36%), general pain (34%), worry (29%), chest pain (25%), cough (22%), sweating (22%), and constipation (22%).[1]

Pain

Etiology

Patients with mesothelioma can have chest pain from several sources, as follows: (a) tumor infiltration of the intercostal nerves causes a difficult-to-treat neuropathic pain syndrome; (b) patients who undergo a palliative pleurectomy/decortication or extrapleural pneumonectomy can develop postthoracotomy pain, a neuropathic pain syndrome presenting as pain in the area of the surgical scar, and hyperesthesia so severe that even clothing is painful[2]; and (c) cis-platinum (or cisplatin) causes painful peripheral neuropathies, and patients who receive it through an abdominal port can experience pain at the port insertion site as well as diffuse abdominal pain. Recurrent comprehensive pain assessment and ascertainment of whether the pain level is acceptable are cornerstones of pain management. Techniques for assessing and measuring pain are described elsewhere.[2,3]

Management

Anesthetics

Lidocaine patches are particularly useful when placed on areas of hyperesthesia. In the postthoracotomy syndrome, for example, patients experience a burning, constricting pain in the posterior arm and chest wall or over the surgical scar.[2] A lidocaine patch can relieve that pain. The patches can be cut to size and applied to the affected area for no more than 12 consecutive hours a day. Use should be avoided over areas of broken skin and in patients undergoing radiation therapy. Extended application of lidocaine patches has been safely applied for up to 24 hours/day for up to 4 days with minimal systemic absorption in healthy volunteers and in postherpetic neuralgia patients.

Trigger-point injections, nerve blocks, and neurolytic procedures also can be effective.[2] Because the doses of systemic opioids needed to relieve pain often cause unacceptable side effects, patients with active mesothelioma that invades the chest wall are likely to need a temporary or permanent indwelling epidural or intrathecal catheter, with the option of patient-controlled epidural analgesia to deliver opioids, local anesthetic agents, clonidine, or combinations of these and

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Table 1 Adjuvants for Neuropathic Pain

Class	Agent	Dose (PO unless otherwise specified)
Anti-convulsants	Gabapentin	Initial dose: 100 mg tid or 100/100/300 mg 100 bid renal insufficiency (RI) Incr by 100 tid to 900-5400 mg/d (max 200 mg bid RI)
	Pregabalin	Initial dose: 50 mg tid; incr to 300 mg qd (max 600 mg/d)
	Phenytoin	1000 mg load; 200-300 mg qd
	Carbamazepine	200 mg hs, increase q3d (tic-doloruex type pain)
	Lamotrigine	100-200 mg qd (initial dose 25 mg/d; incr by 25 mg q2wks)
	Topiramate	200-400 mg qd (start 25-50 mg/d; incr by 25-50 mg q2wks)
Corticosteroids	Dexamethasone	10 mg bolus; 4-6 mg PO/IV bid to qid, then taper
	Prednisone	40-60 mg in divided doses; taper to lowest dose tolerated
Tricyclic antidepressants	Amitriptyline, nortriptyline	Begin 10-25 mg hs; incr to 50-150 mg/d in divided doses
Alpha-2 agonist	Clonidine	0.1-0.3 mg patch
Other	Duloxetine	Initial dose 20 mg qd; max 60 mg; to d/c taper gradually

other agents.[2,4] The infused opioids block pain transmission by binding to receptors in the dorsal horn of the spinal cord. Epidural catheters are used when the expected survival is less than 3 months, whereas implanted pumps connected to intrathecal catheters are used for patients with an expected survival of greater than or equal to 3 months.[2] Those interested in the indications for and techniques of the anesthetic and neurolytic procedures are referred to an excellent review.[5]

Ketorolac

Ketorolac tromethamine (Toradol) is a nonsteroidal anti-inflammatory drug of particular value in relieving moderate-to-severe acute somatic pain, such as pain at the chest tube insertion site. A dose of 30 mg ketorolac given intravenously equals the pain-relieving potency of 15 mg morphine intravenously, and acute toxicity is minimal if the total daily dose is under 100 mg.

Adjuvants for Neuropathic Pain

Neuropathic pain has a burning, shooting, numb, deeply aching quality. Cis-platinum, used in the treatment of mesothelioma, usually causes painful peripheral neuropathy. The most common mechanism of neuropathy is damage to the axons starting with the most distal branches. Amifostine and leukemia-inhibitory factor do not prevent neurotoxicity induced by cisplatin.[6] Vitamin E has been shown to prevent neurotoxicity associated with cisplatin in small open-label evaluations.[6]

Treatment of chemotherapy-induced painful peripheral neuropathy includes the usual agents used for patients with neuropathic pain from any etiology (Table 1).[6] In addition to treating these painful symptoms of neuropathy, it is often necessary to reduce the dose of chemotherapy or even discontinue it.

Opioids

When patients have not previously received opioids, patient and family misconceptions about opioids must often be overcome. These include fears about becoming an addict, "feeling high," "using up" the effective agents and having nothing left if the pain gets worse, and developing refractory constipation. Even families who want the patient to be comfortable can be worried that the opioid is "killing" the patient.

Opioids can be delivered noninvasively (orally, rectally, transmucosally, or transdermally) or invasively (subcutaneously, intravenously, or by spinal infusion). For patients switched from oral or rectal to parenteral or spinal medication, or vice versa, the dose must be altered accordingly to avoid overdose or undertreatment (Table 2). Regardless of the route of administration, patients who are experiencing continuous pain should receive the analgesics regularly and be awakened, if necessary, to administer medications that will prevent recurrence of the pain.[7]

Fentanyl. The transdermal fentanyl patch delivers lipophilic fentanyl into the fat-containing areas of the skin. The drug diffuses continuously from the patch reservoir through a rate-controlling membrane and is absorbed from the skin depot into the bloodstream, where it is rapidly metabolized.[2] The onset of pain relief is delayed by about 12 hours and a relatively constant plasma concentration of fentanyl is not reached until about 14-20 hours after the initial patch is placed. Liberal rescue medication must therefore be provided during the first 24 hours after application of the patch. About 50% of the drug is still present 24 hours after patch removal. Converting patients from oral or parenteral medication to the patch is easily accomplished (Table 3). A new patch is applied every 72 hours, although up to 25% of patients require a new patch every 48 hours. The transdermal system is an

Table 2 Relative Potencies of Commonly Used Opioids[3]

Drug	Epidural	SC/IV(mg)	PO (mg)
Morphine	1	10	30
Codeine		130	200
Oxycodone		NA	20
Hydromorphone	0.15	1.5	7.5
Methadone		*	
Oxymorphone		1	10
Levorphanol		2	4
Fentanyl		0.1	?
Meperidine (Demerol)†		75	300

*Methadone is approximately half as potent orally as it is intravenously. It is usually not given SC because of local irritation. Consult a pain or palliative care specialist when initiating methadone therapy (see text).

†Not recommended for patients with chronic pain.

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