

ADVANCES IN ONCOLOGY

Current Developments in the Management of Solid Tumor Malignancies

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Management of Cancer Pain



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H&O About how many cancer patients experience pain?

JH Cancer pain is common, especially in patients with advanced cancer and metastatic disease. There are reports of pain in 70–90% of patients with advanced disease or metastatic spread. Pain is a major fear of patients when they are facing a battle with cancer; they are concerned about how much pain they will experience and how they will cope with it.

H&O What are the risk factors for the development of pain in cancer patients?

JH Cancer pain may relate to the extent of the cancer, both in terms of local spread and invasion, distant metastatic spread, and lymph node involvement. These factors typically relate to the intensity of pain. For example, local invasion may result in nerve compression, tissue inflammatory changes, or stretching of visceral structures. Metastatic spread can also cause local tissue damage or nerve compression at distant sites. In addition to tumor-related causes of pain, certain treatments related to cancer therapy can produce chronic pain. Chemotherapeutic agents (eg, platinum-based agents, vinca alkaloids, taxanes, and bortezomib [Velcade, Millennium]) and surgical procedures (eg, mastectomy, thoracotomy, and neck dissections) have been associated with the development of chronic, neuropathic pain.

H&O What are the potential consequences of pain in cancer patients?

JH An obvious consequence is the patient's suffering. As physicians, we are charged with keeping patients from

harm and injustice. There even has been a discussion surrounding the idea that untreated pain is a human rights violation. Another possible consequence of poorly treated pain is patient dissatisfaction; even if the cancer treatments are going well, the patient's experience with his or her care may be markedly negative.

Also, patients who are experiencing pain will have elevated levels of stress hormones and physiologic activation. There are data suggesting that breast and prostate cancer have earlier recurrence or progression of disease when the body is exposed to exogenous opioids in the perioperative period. It also has been documented in both in vitro and in vivo animal models that opioids cause immunosuppression. But, it is not known if the use of exogenous opioids in routine care or higher circulating levels of endogenous opioids (due to untreated pain) also results in acceleration of cancer recurrence or disease progression. It is best to treat and evaluate a patient's pain with appropriate medications (either opioids or adjuvant pain medications).

H&O What are the different types of cancer pain?

JH When evaluating a pain complaint, it is important to try and deduce the cause and source of a patient's pain. There are 3 main sources: somatic, visceral, and neuropathic. The somatic type is what most patients think of when they think of pain. It is an unpleasant experience that is the direct result of stimulation of nociceptive fibers. For example, a cut on the skin or a break in a bone will trigger typical somatic pain. It is usually well localized and is often described as aching, stabbing, or throbbing. Somatic pain is the most common experience that people have had with pain. Visceral pain is a little different. It can come from

the deep visceral structures of the thorax, abdomen, or pelvis. The pain is usually harder to localize, and it is often described as aching, sharp, or gnawing. The third component to consider is a neuropathic element to the pain. Neuropathic pain does not come from nociceptive stimulation of the pain system, but rather it arises from pathology in the peripheral or central nervous system. Neuropathic pain is particularly important to diagnose because it tends to respond to slightly different medications; it responds better to adjuvant agents and less well to opioids.

H&O What are the challenges in the management of cancer pain?

JH Reports in the pain literature and the hematology/oncology literature suggest that 75–85% of cancer patients receive inadequate treatment for their pain. Poorly or inadequately treated pain is a significant problem facing many cancer patients. Clinicians are in a difficult position concerning pain management in today's climate. Prescription opioids are becoming more frequently illegally sold and abused on the streets, and people have presented to physicians with false pain complaints with the main purpose of diverting opioid medications. There have also been high-profile cases of physicians who have been accused and prosecuted for illegal distribution of opioid medications for personal gains. Due to both of these factors, a stigma is developing over the use of opioid pain medications, and this may result in a reluctance to treat patients who need pain medications, especially opioids. In addition, with the rise of opioid diversion, practitioners may be concerned about the societal impact of the overuse of opioids.

The other side of that issue is that oftentimes patients with severe pain require an aggressive titration of opioid medications, which can be daunting for clinicians with less experience titrating these medications. Because opioids can cause significant sedation, respiratory depression, and respiratory failure, aggressive titration makes some practitioners uneasy, and many practitioners are reluctant to take that risk. There is always the option to admit a patient to the hospital and aggressively titrate opioids with the use of patient-controlled analgesia with more intensive nursing care, but given the cost of hospital admissions, pain problems are most often addressed on an outpatient basis. Patients who come to our pain clinic are often on an appropriate pain medication regimen, but they require more aggressive titration of both opioids and adjuvant agents.

H&O When should pain medication be offered to patients?

JH Pain medication should be offered any time a patient is reporting pain. Any new report of pain should be

investigated through history, physical examination, and, possibly, radiologic imaging. While reports of pain should be treated at face value, the concern over the diversion of opioid medications must also be recognized. Unfortunately, it is difficult to verify pain complaints with objective tests, and, ultimately, pain is a subjective experience. Imaging can help verify the source of pain, but it does not correlate well with severity. While we must take subjective pain complaints at face value, other behaviors can signal aberrant behavior (eg, lost/stolen medications, early completion of supply due to increased pain, frequent early refills, or inappropriate urine toxicology results).

H&O What are the typical approaches to pain management in cancer patients?

JH The National Comprehensive Cancer Network has published comprehensive guidelines for the assessment and treatment of cancer-related pain. Their guidelines help instruct on various approaches given the patient's opioid history and the severity of the presenting pain. Typically, mild pain can be addressed with nonsteroidal anti-inflammatory drugs and acetaminophen. Escalation of medications follows the World Health Organization guidelines, which recommend weak opioids (tramadol, codeine), followed by strong opioids (eg, morphine, oxycodone). If there is a neuropathic component, then antidepressants (tricyclic antidepressants, duloxetine, or milnacipran) or anticonvulsants (eg, gabapentin, pregabalin, oxcarbazepine) can be used.

H&O Are there any novel approaches to the management of pain in cancer patients?

JH The mainstays of therapy and pain management—including opioids and adjuvant medications, such as antidepressants and anticonvulsants—have not changed very much. In our clinic, the newest approach is the use of intrathecal drug delivery systems. This method is mostly for patients who have failed oral pharmacotherapy due either to side effects or suboptimal treatment. As a last resort, for localized pain that is not widespread throughout the body or significant pain from multiple distant sites in the body, an intrathecal pump can deliver opioid medications, local anesthetics, and even other neuropathic agents right to the spinal cord itself. This technology is gaining more use, but it is expensive and limited to patients who fail oral therapy.

H&O Are fears of addiction to pain medication warranted in cancer patients?

JH Any patient who is exposed to opioids has a risk of misusing the medications or becoming addicted. Patients frequently express fear of addiction, but they sometimes

confuse the terms *addiction* and *dependence*. Addiction refers to the use of these medications for the sole purpose of a euphoric effect, essentially getting high. Dependence refers to the experience of withdrawal symptoms if the agents are abruptly discontinued. It is common among patients on chronic opioids to become dependent on the opioid, such that abrupt discontinuation will cause withdrawal symptoms. Patients sometimes view this physical dependence as “addiction,” but it is easy to overcome by slowly titrating opioids when they are no longer needed.

There are other problems associated with these medications. In addition to addiction or misuse of the medications, there is also the possibility of diversion. Some patients with legitimate pain complaints may overstate their pain to obtain extra medication that they do not truly need, and then divert that medication to others. All patients receiving pain medication should be screened for inappropriate behavior, through both questioning and urine toxicology testing to assess compliance, but partial diversion is difficult to detect because the patients are taking some of the prescribed medication, resulting in appropriate urine toxicology results. Diversion is particularly concerning because powerful opioids end up on the street for sale and could fuel illicit opioid abuse.

To further cloud the issue, patients with undertreated pain may present with similar behaviors to patients who misuse, abuse, or divert opioid medications. They will need frequent increases in opioid medications, and may often take more opioids than prescribed and run out early. In the complex decision-making process in a pain clinic, clinicians must distinguish patients who are being undertreated from patients who are misusing or abusing medications.

H&O Are cancer patients likely to develop tolerance to pain medication?

JH Anyone on chronic opioid therapy can develop tolerance to opioid medications. In some senses, tolerance is a good thing. Opioid-naïve patients who require relatively high doses of opioids to be comfortable may struggle with side effects like sedation, and it is beneficial for them to develop tolerance to the side effects of opioids relatively quickly (ie, sedation and respiratory depression).

In addition to tolerance of side effects, patients may also develop reduced analgesic benefit, a situation often seen in the cancer population. This typically results in dose escalation, and some patients may experience dose-limiting side effects before adequate pain control is achieved. If a patient has a localized pain source and has exhausted the oral pharmacotherapy options, an intrathecal pump may be the next step to provide good analgesia.

H&O At what point is referral to a pain management specialist recommended?

JH It appears that many patients are undertreated and could benefit from either closer adherence to the guidelines or referral to a pain management specialist. Referral should be considered any time a patient is not responding to reasonable attempts to control pain according to guidelines. Practitioners can also consider referral if they have limited experience prescribing higher doses of opioids, given the risk of oversedation and respiratory depression.

Another indication for referral may be when there is concern over misuse or diversion of medications, or if a patient’s behavior is concerning. Referral can be beneficial to identify patients who might be abusing or diverting medications. At our hospital, the pain clinic utilizes an outside urine toxicology laboratory that conducts very detailed and sensitive analysis for both opioids and their metabolites. This allows for detailed assessment of medication compliance. This service is not available to other clinics in our hospital, and may not be routine for outpatient hematology-oncology clinics.

Suggested Readings

National Comprehensive Care Network. *NCCN Clinical Practice Guidelines in Oncology: Adult Cancer Pain, Version 2.2012*. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed December 10, 2012.

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