Aggressive Approach to Pain and Symptom Management is a key For Effective Palliation in Terminally-ill Pediatric Patients

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Abstract

Palliative care for children represents a special field. The authors are presenting a diagnosed case of Ewing's sarcoma as an example of comprehensive management of pain and symptoms. Patient's pain was managed with oral morphine along with NSAIDs, amitriptyline and gabapentin. The patient was kept engaged in different activities during the day keeping in mind that no one disturbed him during sleep. High-quality palliative care is now an expected standard at the end of life. It has to be emphasized that prescribing morphine and gabapentin in optimum doses was good enough for the patient to control his pain as far as his pharmacological treatment was considered. With the aggressive use of psychosocial management, morphine and other pain-relieving interventions, palliation can be made more effective in children.

INTRODUCTION

Palliative care for children represents a special field of generalized palliative care. The World Health Organization (WHO) defines palliative care for children and their families as: 1) Active total care of child's body, mind and spirit, and also involve giving support to family. 2) Begins when illness is diagnosed, and continues regardless of whether or not a child receives treatment directed at the disease. 3) Evaluation and alleviation of a child's physical, psychological, and social distress. 4) Broad multidisciplinary approach that includes the family and makes use of available, what so ever, community resources.

Pain management is an essential part of effective palliative care, which is the right of every patient and his family.

The authors are presenting a terminally-ill pediatric patient whose management is a good example of total active palliative care with emphasis on aggressive comprehensive management of pain and symptoms.

CASE HISTORY

HISTORY OF PRESENT ILLNESS

A 6-year-old, 20 kg male patient a diagnosed case of metastatic malignant round cell tumor (Ewing's sarcoma) was in Pain and Palliative Care follow up. He had undergone left-sided above knee amputation for his primary disease. However, he had developed bilateral lung metastasis and skull bone metastasis with soft tissue element on left parietal region with poor prognosis of his disease status. He was being followed up on outpatient basis because hospital-based inpatient palliative care facility was not available initially and patient and family was reluctant to get an admission in hospice. However, in January 2007, he was admitted to Palliative Care Unit (PCU) for management of intractable pain and palliative care. He had pain in the left limb stump and right leg. Pain score on visual analogue scale (VAS) was 10/10 and pain relief was 30% on 180 mg/day morphine.

PAST MEDICAL HISTORY

In April 2005, his mother noticed a lemon sized swelling on the posterior aspect of his left knee region after a fall. It was associated with pain and difficulty in movement. Gradually swelling increased in size and involved the anterior lower third of thigh.

X-ray left lower limb showed ill defined osteolytic and expansile lesion at the junction of the middle and lower third of the femur (metaphyseal) with permeative pattern of bone destruction. Radiologically tumor had features suggestive of osteogenic sarcoma; however on histopathological examination rit was diagnosed as Ewings' sarcoma. There were no clinical and radiological signs and symptoms of metastasis at that time.

The patient received 6 cycles of pre-operative radiotherapy and 3 cycles of pre-operative chemotherapy followed by high transfemoral amputation in private hospital in December 2005.

The patient presented to oncology institute for pain at local site in October 2006. Bone scan, CT chest and MRI spine were suggestive of bone metastasis at eleventh dorsal thoracic and fourth lumbar levels with associated vertebral collapse and thecal sac compression; skull bone metastasis and bilateral lung metastasis were the other new signs of progression of disease. He was given palliative radiotherapy to scalp and referred to pain and palliative care outpatient department (OPD) for pain management.

At the first presentation in pain and palliative care OPD, skull bone metastasis had developed a 7-cm soft tissue element on left parietal region which was painless with prominent superficial veins. There was painful generalized swelling in right foot, scrotum and penis suggestive of inferior vena cava (IVC) obstruction. Subsequent CT abdomen and pelvis confirmed the presence of retroperitoneal lymphadenopathy as the cause of IVC obstruction. VAS was 10/10. Over a period of six-weeks oral morphine dose was increased from 30 mg/day to 180 mg/day. However, pain relief achieved was never more than 50%. Therefore, he was admitted to PCU in January 2007.

COURSE OF ILLNESS DURING PCU STAY

Stump pain slowly progressed to phantom limb pain of moderate to severe intensity, burning in quality with allodynia and cutaneous vasodilatation. Pain was worse in the night time and aggravated with the change in position. The patient was more comfortable in sitting position and used to sleep in semi recumbent position only. He had dysuria and hesitancy also. Initially, the patient's pain was managed with oral morphine 30 mg 4 hourly along with non-steroidal anti-inflammatory drugs (NSAIDs), amitriptyline and gabapentin; however, he often needed morphine 10 mg prn because of breakthrough pains. Severe constipation was initially managed with bedtime bisacodyl 10 mg and milk of magnesia and liquid paraffin; however, his constipation was eventually relieved with suppository and enema. Proper skin care, massage, limb elevation and scrotal support were planned for lymphedema. He was also given frusemide and spironolactone, and steroids which were gradually withdrawn as lymphedema and penile swelling had reduced.

Within one week, morphine dose could be reduced to 20 mg 4 hourly with further reduction to 15 mg 4 hourly in subsequent three days. This dose reduction subsided his drowsiness. But by next day he started having severe pain and headache. His scalp swelling became very tense for which intravenous morphine infusion along with dexamethasone and mannitol were started. Morphine infusion was gradually increased up to 3 mg per hour. Four days later he was switched over to oral morphine 40 mg 4 hourly. Within next two days his pain could be controlled with morphine 20 mg 4 hourly. Mannitol (20 %) 30 ml 8 hourly was given for 5 days and tapered over next 4 days. Intravenous dexamethasone 2 mg 8 hourly was given for 3 days. Thereafter he was shifted to oral methylprednisolone 16 mg twice a day. With this aggressive treatment his headache and skull pain could be controlled successfully. He had shooting neuropathic pain in his amputated limb; hence amitriptyline 25 mg and gabapentin 300 mg thrice-a-day were continued. He was very reluctant to move from the bed because of difficulty in movement so he had to be catheterized. A small-size bed sore developed on the back. Proper training was given to his parents for urinary catheter care and bed sore management so that they can manage the child after discharge. Morphine dose was gradually reduced to 10 mg 4 hourly over a period of 10 days, as pain relief could be maintained on this reduced dose. He was discharged to his home with smiling faces and parental satisfaction.

The PCU team intends to send patients to home after a certain level of comfort is achieved but the presented 6-year-old child was very reluctant to go home because of a very peculiar problem of his siblings making fun of his scalp swelling. Rather he was quite happy in his later days of his hospital stay. With adequate and aggressive pain management, this patient was surprisingly free from other cancer-related complications like air hunger, nausea, anorexia and agitation. Sleep deprivation can cause anger, depression and anxiety so sleep-wake cycle must be preserved in the hospital and thus preserving social relationships. So the patient was kept engaged in different activities during the day like playing with dolls, making stories and chatting, keeping in mind that no one (including nursing staff) disturbed him during nighttime sleep. In spite of these efforts his pain had contributory elements of anger, maladjustment with siblings and family. Discussing the disease and prognosis issues with him was a big challenge as he always used to avoid these discussions. Although some

palliative care physicians can argue against telling prognosis to a small child, it is always advisable to initiate discussion of illness with the child depending on the understanding and expectation of the child.

His psychological assessment was done by a psychiatrist. It was suggested that child probably had understood that he was suffering from some serious illness and expected attention from family members. The psychiatrist advised to keep him engaged in plays which he liked and to cut down his unrealistic demands. The patient was reviewed by a psychiatrist after 5 days and the family was advised to start talking about his illness and anticipation of his death with his elder siblings. The intention was that the elder children of family would help in adjustment of child in home once they understood the reasons behind the sick child getting all parental attention. Disclosing the news of poor prognosis to the patient remained a challenge till the end.

DISCUSSION

It was very difficult to manage a dying child like him and even more difficult to manage his pain. High-quality palliative care is now an expected standard at the end of life. Yet it is not known whether the care of children with cancer meets this standard ([1]). The present patient, a 6 year old child, was a case of terminal cancer. He had substantial sufferings at the end of his life, and attempts to control his symptoms were not successful. To accomplish total pain management, a multimodal approach was chosen that consisted of morphine, NSAIDS, gabapentin, amitriptyline, steroids, mannitol in addition to psychological modalities and social support services to child and family.

Controlling physical pain was an important part of patient's overall management. It has to be emphasized that prescribing morphine and gabapentin in optimum doses was good enough for the patient to control his pain as far as his pharmacological treatment was considered. Pain score (VAS) reduced from 9 to 3 after taking oral morphine 30 mg 4 hourly. And later on morphine dose could be reduced to 10 mg 4 hourly over a period of 20 days. This dose was comparable to a study of Sirkia et al ([2]) in which out of total 62 children parenteral morphine was administered to 40 children; 30 of them received morphine as a continuous infusion through a central venous line. The dose of intravenous morphine was 0.8 mg/kg/day initially and was increased to 4.9 (range, 0.2-55) mg/kg/day. Dougherty M et al ([3]) identified eighteen patients: 12 with neuropathic pain and 6 without neuropathic pain. In the neuropathic group, the average dose of morphine 72 hours before death was 231 mg/kg per day and increased to 380 mg/kg per day on the day of death (P =.009). The average benzodiazepine dosage 72 hours before death was 6.0 mg/kg per day and increased to 25.0 mg/kg per day on the day of death (P =.018). In the non-neuropathic pain group, the average dose of morphine and benzodiazepine 72 hours before death was 3.0 mg/kg per day and 0.08 mg/kg per day, respectively, and did not increase substantially on the day of death. They concluded that dying children with cancer and neuropathic pain have higher baseline requirements of morphine and benzodiazepines and require rapid increases of both drugs in the last 72 hours of life than dying children without neuropathic pain. Similarly Collins JJ et al ([4]) retrospectively reviewed the records of the 199 patients who died of malignancy after treatment at Children's Hospital. Maximal intravenous opioid dosing ranged from 3.8 to 518 mg/kg per hour of morphine equivalent. They concluded that standard dosing of opioids adequately treats most cancer pain in children; however, a significant group requires more extensive management. These problems occur more commonly among patients with solid tumors metastatic to spine and major nerves.

No major side effects related to morphine like nausea, vomiting, sedation were observed in present patient. Incidence of side effects of morphine is quite low as shown by Sittl R et al ([5]). In their study the average age of the patients treated was 12 years (1.5-19 years), who were suffering from malignant tumors. The doses of morphine required for pain relief varied substantially (1-25 mg/kg per day orally and 0.05 mg-1 mg/kg per hour intravenously). In their patients they did not observe extreme sedation or respiratory depression or opioid-induced nausea. All children needed laxatives. In 2 children, intolerable itching was experienced. For reasons as fear of respiratory depression, primary physician's reluctance, drug addiction and giving up too soon, pain in terminally ill patients is an undertreated problem. Respiratory depression is extremely rare in children more than 2 months of age ([6]). The present case report also supports this fact.

Adjuvant drugs, like anticonvulsants and antidepressants may be necessary to treat difficult-to-treat pain, as pain can persist even after children are well enough to go home. In present patient stump pain slowly progressed to phantom limb pain of moderate to severe intensity, burning in quality with allodynia and cutaneous vasodilatation. These

symptoms were satisfactorily controlled over several days with the help of gabapentin 300 mg thrice-a-day and amitriptyline 25 mg at bed time as a part of multimodal approach. Moreover, an opioid-sparing effect was observed. Increasing gabapentin dose gradually over several days was associated with mild side effects, dizziness and mild sedation. Tricyclic antidepressants (TCAs) are generally considered to be effective for neuropathic pain ([7]). Due to its proven analgesic effect in several types of neuropathic pain, its good tolerability, and a rarity of drug-drug interactions, gabapentin is being used for the treatment of neuropathic pain of diverse etiologies, especially in the medically ill population ([8]). In a report of five cases, Butkovic et al ([9]) concluded that gabapentin should be included earlier in the treatment of neuropathic pain in adolescents because it rapidly improves analgesia and has minimal side effects.

No discussion on pain management is complete without comment on the difference between addiction and physical dependence. Children treated with opioids can become tolerant and physically dependent. However, the pervasive notion that use of opioids and other potentially abusive agents will cause a child to become an addict either at the time of treatment or in the future, means that many children may not receive adequate attention to their pain in light of this concern. Parents may refuse to allow their child to receive adequate treatment. Therefore it is helpful to anticipate this question and begin education regarding the outweighing benefits and minimal theoretical risks of aggressive cancer pain management.

Children dying from cancer should receive aggressive and active palliation. Though total pain definition stresses on the multifactorial origin of pain, and psychological, social and spiritual support interventions remain integral part of pain management, the physical pain is the most unbearable to the patient. With the aggressive use of morphine and other pain-relieving interventions, including psycosocial management of the symptoms, palliation can be made more effective, especially in children.

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