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Total Pain in Advanced Cancer: Are We Doing Enough?

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Abstract

Introduction: Pain in cancer patients is multidimensional and can be contributed by physical, psychological, social and spiritual components resulting in the concept of "Total Pain". Despite availability of a number of advanced therapeutic procedures for pain management, not all pain can be controlled with medications.

Case Summary: We reported a case of a 38-year-old gentleman diagnosed with advanced carcinoma of the colon with subacute intestinal obstruction. He presented with severe complex pain not controlled with usually available modalities. Insight into physical, psycho-social and spiritual components helped to control his symptoms to some extent.

Conclusion: Attention and appropriate approach to psycho-social and spiritual components along with physical symptoms (Total Pain) are highly recommended for a holistic and good end of life care. Changing goals of care should always be kept in mind while providing end of life care.

Keywords: Total pain • Palliative care • Ketamine • Opioid • End of Life care

Introduction

Pain is one of the most common and most distressing symptoms in advanced cancer. Around two-thirds of patients reported moderate to severe pain, significantly affecting their quality of life. Pain in cancer patients is multidimensional and can be contributed by physical, psychological, social and spiritual components [1]. The combination of these elements is believed to result in a "Total Pain" experience that is individualized and specific to each patient`s particular situation. A biopsychosocial model to pain assessment and management recognizes the role of idiosyncratic patient thoughts and beliefs in his response to pain.

The algorithm proposed by the World Health Organization (WHO) and the National Cancer Care Network (NCCN) showed 70%-90% of patients have effective analgesia [2-4]. Various treatment modalities are available for cancer pain management that includes the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), opioids, adjuvant analgesics and complex interventions like neurolytic procedures, epidural and intrathecal infusions.

The purpose of this article is to highlight the unique aspects and multimodality approach for complex cancer pain within the context of palliative care. Here we report a case of a 38-year-old gentleman suffering from complex cancer pain due to advanced carcinoma of the colon.

Case Summary

A 38-year-old gentleman, known hypertensive, hypersensitive to tramadol and ondansetron, a diagnosed case of signet ring cell carcinoma of the colon (splenic flexure) with serosal and nodal deposits, absent KRAS 12 and 13 mutations, has undergone left radical hemicolectomy followed by 12 cycles of chemotherapy with oxaliplatin and 5-fluorouracil as disease-modifying treatment. Post-treatment he presented with subacute intestinal obstruction (SAIO) which was managed conservatively. A response Positron Emission Tomography (PET) scan was done which showed low-grade metabolic activity in nodular soft tissue/peritoneal deposits suspicious of metastases. In view of his disease limited to left upper quadrant, staging laparoscopy with SOS cytoreduction and HIPEC (Hyperthermic Intraperitoneal Chemotherapy) was planned. He underwent exploratory laparotomy with ileo-ileal and jejuno-jejunal bypass with appendicectomy and transverse colostomy. Intraoperative findings showed few peritoneal deposits along the anterior abdominal wall, local recurrence at the rectosigmoid junction with large para-aortic node encasing left ureter. Hence, options of cytoreduction and HIPEC was deferred and was planned for palliative chemotherapy. He re-developed bowel obstruction with high-grade fever. The focus of infection could not be identified and his serology for dengue and malarial parasites was negative. Blood and urine cultures were also negative. So he was managed conservatively for bowel obstruction and fever. He was started on Fentanyl transdermal patch 12.5 mcg/hr, intravenous (IV) hyoscine butylbromide, paracetamol, antibiotics and other supportive measures. Continuous nasogastric tube aspiration helped to decrease symptom burden and vomiting. Patient was better for the next 4 days, followed by which he developed severe pain over the lumbosacral area, dragging type without any history of back stiffness, soreness or aggravation with movement. PET CT was done and showed metastatic deposits anterior to the left kidney and left psoas muscle. Fentanyl strength was escalated to 25 mcg/hr with adequate analgesia. Meanwhile, his bowel obstruction got resolved and was advised to start on clear oral fluids till tolerable level. Oral intake increased to tolerable semisolids and solids levels. He was discharged on oral medications with a tab. Morphine 10 mg four times a day, tab. Paracetamol 650 mg three times a day and other supportive measures.

A few days later, he presented with a history of non-bilious vomiting, 3-4 episodes/day with similar moderate to severe pain over the lumbosacral area, disturbing sleep and thus leading to severe distress. Transverse stoma was well functioning with no history of constipation.

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The pain was settled with 2 mg of IV morphine. His morphine dose was rescheduled to 10 mg every 4 hourly and was advised to take 10 mg PRN for breakthrough pain. Domperidone was prescribed for his vomiting. In view of raised creatinine to 1.3 mg/dl and need of multiple breakthrough doses, the opioid rotation was done with an application of Fentanyl TD patch 50 mcg/hr. A formal psychiatric opinion was taken to rule out drug dependence. Psycho-education and active distractions techniques were suggested. A computed tomography (CT) scan abdomen and pelvis were ordered and it showed multiple peritoneal and para-aortic deposits on the left side with left-sided moderate hydroureteronephrosis and psoas muscle infiltration. He was planned for left-sided Percutaneous Nephrostomy (PCN). Routine investigations were ordered and it showed serum sodium of 128 mmol/L and potassium raised to 6.0 mmol/L. Electrocardiogram (ECG) done which showed no significant changes. He was given potassium binders and salbutamol nebulization. Repeat electrolytes showed normal levels of serum sodium and potassium. So, He underwent left Percutaneous Nephrostomy (PCN) and was started on higher antibiotics according to his urine culture and sensitivity pattern. He was kept under observation and managed conservatively with good symptom control. After stabilization, PCN removal followed by internalization was done. The patient was discharged on Fentanyl 50 mcg/hr TD patch and other supportive medications and was advised for a short follow up.

On the next follow up visit, he complained of persistent, severe back pain over the lumbosacral area, which used to subside for 3-4 hours with tab. Morphine 10 mg. Injection morphine 3 mg was given immediately with a good analgesic effect. He was started on oral morphine 10 mg q 4 hourly and then changed to 30 mg sustained-release preparation (SR) twice a day. Adjuvant medications- pregabalin, amitriptyline and dexamethasone were added. With good symptom control on current medications, he received 1 cycle of second-line chemotherapy FOLFIRI (Leucovorin, 5-FU, Irinotecan) at a reduced dose. Post chemotherapy, he developed grade III toxicities in the form of diarrhea and vomiting (CINV). He was admitted and managed conservatively. After a hospital stay of 10 days, he was discharged with stable vitals and symptoms under control. A repeat CT scan showed disease progression. In view of severe toxicity with palliative chemotherapy and short disease-free interval, the patient was referred for the best supportive care.

On the first contact with palliative care services, he was found to have severe backache (Lt lumbar area), NRS 9-10/10, diffuse colicky abdominal pain, obstipation and 10-12 episodes per day of mixed (bilious and non-bilious) vomiting. He was on T. Morphine 30 mg SR thrice a day with other supportive medications. X-ray abdomen erect was ordered and was suggestive of multiple air-fluid levels. Routine labs were normal. On examination, the abdomen was soft, tender over left renal angle area with hyper peristaltic bowel sounds and empty rectum on PR. Oral medications were stopped. He was kept nil per oral. Nasogastric tube (NGT) was put to provide gastric decompression. Dietician reference was done and the patient was started on total parenteral nutrition (TPN) over 18 hrs per day. He was started on Fentanyl TD patch 50 mcg/hr with inj. Morphine 3 mg PRN IV for breakthrough pain, IV Hyoscine butyl bromide, Octreotide, Dexamethasone and Paracetamol. Antibiotic and proton pump inhibitor cover was given. With these interventions, his vomiting subsided significantly. His pain over the left lumbar area persisted even after continuous breakthrough dosages, which warranted escalation of Fentanyl to 75 mcg/hr. In spite of all these interventions, his pain persisted. A decision regarding starting a Continuous Intravenous Infusion (CIVI) pump was taken after consultation with the patient and family. CT scan abdomen and pelvis were ordered. He was started on Fentanyl and midazolam (20 mg/day @ 4 ml/hr) infusions. Fentanyl was started @ 20 mcg/hr with 20 mcg for BTP. CT scan showed 8.1 × 5 cm large intraperitoneal mass infiltrating kidney and causing obstruction of the upper pelvicalyceal system with left DJ stent in situ. Mass also found to infiltrate the duodenum near DJ flexure. There was no evidence of any acute obstruction.

Radiotherapy opinion was taken for palliative radiotherapy to mass. Due to persisting pain, fentanyl infusion was increased to 40 mcg/hr with 40 mcg for BTP. Separate IV lines were secured and Inj. Ketamine 25 mg and inj. Midazolam 20mg/day were started @ 4 ml/hr. Meanwhile, the patient received 8 Gy/SF palliative radiation to mass. His pain still persisted with NRS 6-7/10. Injection ketamine was increased to a maximum of 400 mg @ 4 ml/hr over a period of 6 days. The patient remains alert, active and oriented with good response to commands. Pain control was adequate with Fentanyl, Midazolam and Ketamine infusions. The breakthrough dose requirement was decreased significantly to 1 per day. Discussion regarding poor prognosis, practical restrictions on the continuation of ketamine infusion for longer duration and need for epidural analgesia started with the patient and his wife. Ketamine was stopped post 6 days. An epidural catheter was inserted and epidural analgesia with 0.0625% Bupivacaine and 2 mcg/hr Fentanyl @ 5 ml/hr. Fentanyl TD patch 25 mcg/hr was also applied. Midazolam infusion (20 mg/day) @ 4 ml/hr and TPN was continued. Following the insertion of the epidural catheter, his pain subsided significantly. Two days later, he started complaining of lower limb numbness and tingling which increased gradually over the next day. Hence a collective decision to remove epidural catheter and re-starting patient on Fentanyl infusion was taken and was followed upon.

During all these interventions, his NGT aspirate continuously increased and reached up to 2400 ml per day. Inj. Octreotide increased subsequently to a dose of 400 mcg every 8 hours (total=1200 mcg/day). His output decreased and remained to 300-400 ml/day. His bowels opened and stool passed every alternate days. He was on inj. Dexamethasone 4 mg twice a day which resulted in suspected oesophageal candidiasis, severe retrosternal burning, severe gastritis, uncontrolled blood sugars. Candidiasis resolved with antifungals, while a mixture of antacid and lignocaine viscous was given orally for burning pain. CIVI of pantoprazole 80 mg escalated to 160 mg per day relieved his gastritis significantly. His blood sugars were controlled with regular and glargine insulin.

In spite of all the above measures, the patient expressed unsatisfactory pain control. Though he did not complain of any physical pain, the thorough evaluation showed persisting psychological and spiritual concerns even after help from community chaplains. Hence a decision regarding the addition of haloperidol to continuous infusion taken after discussing with family. The addition of haloperidol reduced his distress significantly. During the last days of his life, his pain was well controlled. Acceptance of disease and prognosis helped to resolve his psychological and spiritual issues. He died peacefully with symptoms well under control and all family members by his side during his last breath.

Discussion

World Health Organization (WHO) had developed a three-step ladder for analgesic use in the management of pain [5]. With the amendment to the fourth step involving interventional procedures like neurolytic blocks, spinal/epidural/intrathecal analgesia, modalities have progressed further for complex cancer pain management. Opioid remains the mainstay for the treatment of moderate to severe pain in palliative care settings, with morphine considered as the gold standard. Changes in the NDPS act and with the availability of more potent opioids, patients with advanced cancer are ensured to get better analgesia.

Ketamine in low (sub-anesthetic) dose acts primarily as a non-competitive antagonist of the NMDA receptor. Ketamine was found to have its role as an adjuvant analgesic in the treatment of pain associated with central sensitization [6], acute severe neuropathic pain [7] and in opioid resistant pain [5]. A study by Urban et al. proved that continuous ketamine infusion resulted in significantly less pain in opioid-tolerant patients [8].

Various neuromodulation techniques involve infusion of one or more drugs into epidural or intrathecal space. The use of epidural space drug delivery is generally reserved for patients with a life expectancy of days to weeks as long term infusion is associated with catheter-related problems and side effects [9,10]. Previous studies showed the effectiveness of epidural analgesia in patients with terminal cancer-related pain [11-13]. Burton et al. reported there was a significant reduction in the proportion of patients with severe pain from 86% to 17% after neuraxial analgesia [14]. However, some studies proved decreased efficacy of epidural analgesia over time due to tumor progression, psychological factors, development of pseudo tolerance caused by dural thickening, the impedance of transdural diffusion, epidural metastases with the invasion of nerve roots, and reactive fibrosis [9,15].

Our patient presented with complex pain with the involvement of more than one component. Considering all possible etiologies for his pain, we have treated him with the use of multimodal analgesia. Various contributing factors for his complex pain were: poly-pharmacy and its associated adverse events; continuous vomiting; unable to tolerate oral fluids; bowel obstruction; involvement of multiple organs; unrealistic hopes of getting better; depression and other psychological factors; spiritual distress; existential distress. Interventions were introduced to resolving each contributing factor. A multidisciplinary team approach involving palliative care physicians, nurses, counselors, psychiatrists, physiotherapists, occupational therapists, chaplains, family members, etc. helped to reduce his symptom burden, to relieve patients' and family's distress and to provide a better quality of life. Hence, we recommend the use of a holistic care approach for a better quality of life to the patient and his family.

Conflicts of Interest

There are no conflicts of interest in this study.

Ethical Approval

Not applicable

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