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The management of neuropathic pain in a patient with retroperitoneal tumour

Abstract

This paper analyses the case report of a 62-year-old man diagnosed with retroperitoneal tumour and severe intensity of neuropathic pain localized in the right lower extremity. Patient was administrated prolonged–release oxycodone/naloxone tablets as well as adjuvant analgesics. Previous pain treatment was inefficient due to inadequate dosage of prolonged–release oxycodone/naloxone tablets, lack of the use of adjuvant analgesics and unrecognition of depression. After introduction of changes in pharmacotherapy of pain and depression and psychological support satisfactory analgesic effect and significant mood improvement have been achieved.

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Key words: background pain, episodic pain, analgesics, adjuvant analgesics

Introduction

Pain prevalence in cancer patients increases with disease progression and often displays complex patomechanism, therefore it requires multidisciplinary approach. Usually a complete disappearance of pain is not possible, however, there are methods to relief the pain to the extent that is acceptable by patients. The aim of this study is to present a case report of a patient diagnosed with retroperitoneal tumour and severe neuropathic pain. Effective analgesia was achieved by using a few analgesics and adjuvant analgesics and significant mood improvement was gained by providing psychological support.

Case study

A 62-year-old patient was diagnosed with a retroperitoneal tumour in November 2015. Histopathology unveiled poorly differentiated adenocarcinoma probably metastatic (adenocarcinoma partim male differentiatum probabiliter metastaticum). Positron emission tomography (PET) showed pathological mass with the dimensions 79 × 51 × 82 mm in the right retroperitoneal space, which modelled inferior main vein. Chemotherapy was started — scheme CAV (cyclophosphamide, doxorubicin, vincristine) because of the unclear type of the tumour and lack of cancer primary focus. The first course was administered in

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February 2016. However, after 4th course it was changed to a scheme PF (cisplatin with 5-fluorouracil) due to disease progression. Further disease progression was found in graphic investigations after 6 courses. In ultrasonography two tumorous were revealed; first one with the dimension 75 × 48 mm, in the right periaortic space and the second one with the dimension 72 × 54 mm below the right kidney. Therefore, the patient was administered 3rd line chemotherapy (paclitaxel with carboplatin). However, due to the occurrence of allergic reaction, treatment was changed to carboplatin with gemcitabine. Owing to significant deterioration of the general condition of the patient chemotherapy was completed in January 2017.

In February 2017, the patient reported to Palliative Medicine Outpatient Clinic. Regarding patient's general condition, the first visit as well as all subsequent calls, were held in his place of residence. Patient complained of pain in the region of the right hip radiating to the right knee with severe intensity: 5–10 according to Numerical Rating Scale (NRS: 0 — no pain, 10 — the most severe pain). The pain exacerbated while walking and over the night disturbing the sleep. Patient described the pain as acute and lancinating („as somebody hammering nails"). Patient assessed the intensity of background pain as 5 (NRS), moreover, pain exacerbated 7–8 (episodic pain) time during the day, achieving 10 in NRS. Episodic pain intensified within less than 5 minutes, the episode lasted approximately 5–15 minutes and subsided in lying position. Background pain was treated using prolonged release oxycodone and prolonged release naloxone (OXN) at a dosage of 10 mg + 5 mg administered twice a day. The patient was not prescribed an immediate–release formulation of an opioid for the treatment of episodic pain.

Pain limited patient's activity significantly and negatively influenced his mood. The patient spends most of the day in bed, he has depressed mood and shows no interest in anything. On the day proceeding the physician's visit the patient felt very severe intensity of pain, which evoked thoughts of approaching death and made him feel vulnerable. Apart from the pain, the patient also reported constipation with painful bowel movements every 4–5 days.

In a physical examination, the following deviations from a normal stage were found: pale skin, pathological resistance with diameter approximately 10 cm in the hypogastrium on the right side and hyperesthesia of the anterior surface of the right thigh, in the area of innervation of thigh nerve. Laboratory investigations did not show anaemia either neutropenia or decrease in the number of platelets. Level of creatinine, sodium, potassium and calcium in the blood serum was at normal range.

Due to insufficient analgesia, the dose of OXN was increased to 20 mg + 10 mg twice a day. Immediate–release morphine was prescribed for the treatment of episodic pain, with starting dose of 10 mg was increased to a dose of 20 mg owing to inadequate analgesia. Because of neuropathic component of pain pregabalin was used at a starting dose of 75 mg before sleep, which was gradually increased to a dose of 75 mg in the morning and 150 mg in the evening. Additionally, treatment with dexamethasone was started at a dose of 4 mg in the morning and 2 mg on midday. Based on the history and psychological assessment conducted by the Hospital Anxiety and Depression Scale a moderate depressive syndrome was diagnosed. In this connection sertraline was started at a dose of 50 mg once a day and psychologist's consultation was recommended. Lactulose was administered at a dose of 15 mL twice a day for the treatment of constipation.

Slight decrease in background pain intensity was found (from 5 to 4 according to NRS) on the next visit. Episodic pain was less frequent (4–5 times a day) but its intensity was still assessed as 10 (NRS). Nevertheless the patient slept over the night without any disturbances and was able to walk to a toilet with the help of a walker. Due to insufficient analgesia further modification of drug therapy was required, therefore dose of OXN was increased to 40 mg + 20 mg and pregabalin to 150 mg, both administered twice a day. Psychologist stated that severe pain evokes resigned thoughts in the patient, therefore cognitive–behavioural therapy, emotional support, psychoeducation and relaxation training were introduced.

The patient assessed background pain intensity at 3 (NRS) on the following visit and reported 1–2 episodes of breakthrough pain, with intensity of 10 on NRS. Episodic pain occurred mostly in the morning when getting up. Despite of high intensity of episodic pain, due to its less frequency and effective treatment with immediate–release morphine, the patient spent more time out of bed. His mood improved significantly as well. The dose of pregabalin was increased gradually to 300 mg in the morning and 300 mg in the evening, while the dose of dexamethasone was decreased to a dose of 2 mg administered twice a day.

The patient noticed an improvement in the efficacy of the treatment of background pain (2 on NRS) and episodic pain (1–2 episodes per day with intensity of 7 on NRS) on the next visit. Thanks to psychologists support the patient felt no longer helpless when episodic pain occurred, he learned to cope with pain

exacerbations by changing position and administration rescue doses of immediate–release morphine. Psychological therapy resulted in mobilizing family support. Finally, the patient was satisfied with the treatment results.

Discussion

Pain management

Pain is a frequent symptom at each stage of cancer disease. Its prevalence equals to nearly 40% of patients after oncology treatment completed, 55% of those during anticancer therapy and over 66% of patients with advanced disease. Moderate to severe pain intensity (over 5 according to NRS) refers to nearly 40% of cancer patients [1]. Still in 56–82% of patients' treatment is inappropriate and ,in consequence, ineffective, which significantly decreases patients' quality of life [2]. Neuropathic pain component is present in approximately 20–30% of cancer patients. Moreover, in a significant percentage of patients' pain displays composite patomechanism (both receptor and neuropathic, for example in patients with bone pain) [3]. In this case pain was probably caused by compression and infiltration of adjacent tissues by the peritoneal tumour. The suspicion of bone metastasis could not have been confirmed, owing to patient's poor condition. Neuropathic pain is defined as pain that is induced by a damage or a disease of a somatosensory nervous system [4]. Four diagnostic criteria were formulated:

1. Pain has a definite neuroanatomical location.
2. The history suggests the presence of the structures' damage of peripheral or central nervous system responsible for pain appearance.
3. Positive or negative neurologic symptoms are present in physical examination that are associated with pain or positive results of tests confirming diagnosis (quantitative assessment of sensation, laboratory investigations).
4. Documented presence of a disease or presence of damage in laboratory investigations (for example neuroimaginery) responsible for pain appearance.

Neuropathic pain may be diagnosed as definitive (all 4 criteria fulfilled), probable (criteria 1 and 2 and 3 or 4) or possible (criteria 1 and 2 without confirmation in investigations) [4]. In the patients depicted neuropathic pain was found as possible.

Episodic pain according to a definition of the European Association for Palliative Care (EAPC) Research Network refers not only to the breakthrough pain, which comprises a significant increase in pain intensity during effective management of background pain with opioid analgesics, but also a significant increase in pain intensity (according to most researchers of 2 or more in NRS) during an ineffective treatment of background pain, independently of using opioid analgesics and in patients without background pain [5]. EAPC recommends morphine, oxycodone or ,unavailable in Poland, hydromorphone as a first line treatment of pain of moderate to severe intensity in cancer patients [6]. In the depicted patient, ineffective pain treatment was caused by too low dose of an opioid for the treatment of background pain as well as lack of prescription of immediate–release formulation of opioid (rescue dose) for the treatment of breakthrough pain episodes.

According to World Health Organization (WHO) analgesic ladder as well as EAPC recommendations usage of adjuvant analgesics should be considered for patients with neuropathic pain component when opioids are not fully effective [7]. Adjuvant analgesics, especially anticonvulsants — gabapentinoids play an important role in the management of neuropathic pain in cancer patients [8]. According to the Polish Association for the Study of Pain and international recommendations pregabalin and gabapentin are the first line adjuvant analgesics in the treatment of neuropathic pain in cancer patients [9,10]. Pregabalin is a derivative of gamma–aminobutyric acid (GABA), which binds to a subunit of $_2$– receptors opened through a change in voltage of membrane of calcium channel in the CNS, inducing anticonvulsant and analgesic effects. Pregabalin displays linear pharmacokinetics, significant analgesic efficacy and beneficial safety profile; the drug is most frequently administered in the dose range of 150–600 mg [11]. The most frequent adverse effects comprise excessive sedation, dizziness and sometimes peripheral oedema in patients with heart failure. In the depicted patient treatment with OXN and pregabalin was deemed effective, which is confirmed by the results of other studies conducted in cancer patients with neuropathic pain of severe intensity [12]. Along with effective analgesia and patient's satisfaction, a combined use of the drugs did not evoke a deterioration in GI tract function.

Due to the small number of conducted studies, the level of scientific evidence of recommendation of using corticosteroids as adjuvant analgesics, in the treatment of pain in cancer patients is moderate (IIB and IIC) [13]. However, corticosteroids are used in the treatment of neuropathic and bone pain in conjunction with opioids and other co-analgesics. Their mechanism of analgesic action remains unclear and most probably it is associated with anti-inflammatory and antioedema actions as well as anticancer effects (inhibition of angiogenesis) and modulation of neuroimmunology reactions [14]. Dexamethasone is a preferred corticosteroid in the treatment of pain

in cancer patients due to its strength and prolonged period of action as well as a little mineralocorticoid effect. Normally the starting dose equals to approximately 8 mg and it is recommended establishing the lowest effective dose administered by parenteral (subcutaneous or intravenous) or oral route, considering benefits and adverse effects of the treatment [15,16].

Depressive disorders

Depression is present in approximately 36% of patients with cancer pain. Although pain intensity and its period of appearance display connection with appearance of depressive disorders, there is still lack of sufficient data to establish the aforementioned dependency [17]. A connection between pain and depression seems to result from common pathophysiology mechanisms, particularly the role of serotonin and noradrenalin, which play an important role in pain transmission, especially in pain inhibitory systems. Their lower level is a cause of mood disturbances and may lead to depression development [18]. The first line drugs in the management of depression are selective serotonin reuptake inhibitors (SSRI), which efficacy and good tolerance were confirmed in clinical studies [19]. However, it should be noted that SSRI in contrast to serotonin and noradrenalin reuptake inhibitors (SNRI) are ineffective adjuvant analgesics in the treatment of neuropathic pain. Apart from pharmacotherapy the treatment of depressive disorders comprises also psychological technics: cognitive–behavioural therapy, behavioural therapy with planning and interpersonal psychotherapy [20].

Summary

Pain and depression are frequent symptoms that may concurrently appear in cancer patients and require a meticulous clinical evaluation, diagnostic procedures, classification and treatment adjusted to individual patients' needs. Due to multidimensional characteristics of pain, which often accompanies and intensifies psychological disturbances, including depression, physicians and other staff members working with cancer patients should pay appropriate attention to complex clinical assessment of patients not only in physical but also psychological, social and spiritual dimensions.

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