Drab Marcin, Szymczyk Agnieszka, Tomczak Waldemar, Drab-Urbanek Elżbieta, Łapacz Katarzyna, Hus Marek, Podhorecka Monika. Chest pain in the course of multiple myeloma - a clinical case study. Journal of Education, Health and Sport. 2018;8(7):11-18. eISNN 2391-8306. DOI http://dx.doi.org/10.5281/zenodo.1256175
http://ojs.ukw.edu.pl/index.php/johs/article/view/5537

The journal has had 7 points in Ministry of Science and Higher Education parametric evaluation. Part b item 1223 (26/01/2017).
1223 Journal of Education, Health and Sport eissn 2391-8306 7

The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 02.05.2018. Revised: 18.05.2018. Accepted: 30.05.2018.

Chest pain in the course of multiple myeloma - a clinical case study

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Key words: multiple myeloma, chest pain, cancer pain

Abstract:

Introduction: Multiple myeloma (MM) is a rare blood cell proliferative disease characterized by the accumulation and proliferation of monoclonal plasmocytes. Clinical picture of MM includes bone pain, underlying osteolytic lesions, osteopenia or osteoporosis that often lead to pathological fractures.

Aim: To draw attention to the unusual cause of chest pain and the holistic approach to analgesic therapy in patients with MM.

Case report: A clinical case of a 66-year-old patient with chest pain intensified when moving and deep breathing was presented and cardiological and gastroenterological reasons were excluded. Initially, non-steroidal analgesics and weak opioids were used in the treatment with good effect, however, as time was passing the pain symptoms progressed. Diagnostic imaging was complemented by computed tomography which revealed massive destructive changes within the ribs with the presence of soft tissue masses infiltrating adjacent muscles. Based on additional tests, the patient was diagnosed with MM. Optimization of analgesic therapy has brought permanent pain relief and improved his quality of life.

Summary: The modern approach to anelgesia in patients with MM includes not only the use of analgesics, but also radiotherapy, bisphosphonates/zoledronic acid, orthopaedic treatment and chemotherapy.

Introduction:

Multiple myeloma (MM) constitutes about 1% of all human neoplastic diseases, the third most common proliferative disease in adults (19%). Most of the diagnosed cases are symptomatic, while the isolated myeloma of bones and extraskeletal form represents only 3-5% of all cases [1, 2].

Symptoms of MM result mainly from:

• replacing normal bone marrow formation with pathological plasmocytes, resulting in haematopoiesis failure;

• a monoclonal protein produced by plasmocytes, which may lead to renal failure and hyperviscosity syndrome;

• plasmocyte secretion of pro-inflammatory cytokines stimulating osteoclasts, which leads to excessive bone resorption [3].

Bone pains are the most typical clinical manifestation of MM (approximately 70% of patients at the time of diagnosis), which are results of osteolytic lesions, osteopenia or osteoporosis, often leading to pathological fractures [3, 4].

According to the definition by the *International Association for the Study of Pain* (IASP), pain is an unpleasant and negative sensory and emotional impression, which arises as a result of stimuli that damage tissues or threaten their damage [5]. It is estimated that this problem affects about 75% of patients with advanced cancer disease, whereas standard pharmacotherapy is effective in approximately 70-90% of cases [6].

For the majority of patients, pains are the result of healthy tissues' infiltration with neoplastic cells, in 1/3 of cases there are secondary pains to cancer resulting from cachexia and physical activity' limitation, and for 20% of patients they are the result of oncological treatment. Among the causes of iatrogenic pain, we can distinguish neuralgia pains within the postoperative scar, patients' neuropathy, lumbosacral or brachial plexopathy after radiotherapy and peripheral neuropathy resulting from the neurotoxic effect of cytostatics [7].

In terms of pathogenesis, we can distinguish two types of pain:

• receptor (nociceptive), which is the result of pain receptors' stimulation,

• neuropathic, caused by the nervous system structures' dysfunction or damage [5, 6, 7].

Nowadays, the complexity of the perception process of pain sensations is emphasized - the sensations are often not related to the degree of tissue damage - and the feelings and their expression are very individual in each patient (Figure 1), therefore a reliable analysis of

reported ailments and determination of pathomechanism pains constitutes the basis of effective treatment [8, 9].

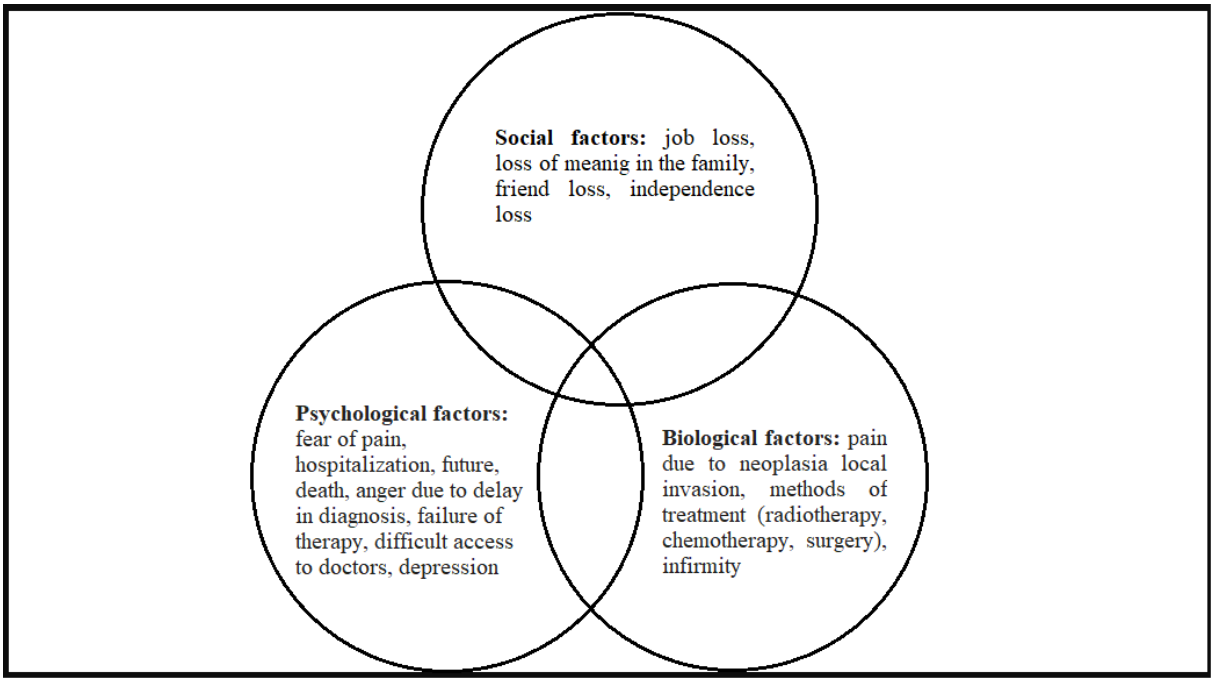

Figure 1. Pain components.

Aim of the work:

Paying attention to the atypical cause of chest pain, i.e. massive destructive changes within the ribs with the presence of soft tissue masses infiltrating adjacent muscles and a holistic approach to the analgesic therapy in MM patients.

Case report:

A 66-year-old patient reported severe chest pain (at the VAS scale initially 4, followed by progression of pain, up to a maximum of 8 at the VAS scale). The pain was dull, intensified when moving and deep breathing, radiating from the spine to the front chest. In outpatient settings, cardiological (ECG without features of myocardial ischemia, without enzymatic features of myocardial injury) and gastroenterological (gastroscopy without abnormalities) reasons of chest pain were excluded.

Initially, the pain was decreased after acetaminophen was administered by the oral route at a dose of 500 mg-1000 mg/day and the local use of ketoprofen (VAS 2-3 after the drugs). Despite the applied treatment, progression of pain was still observed (VAS 6-7). Therefore, ketoprofen at a dose of 50 mg-200 mg/day and diclofenac at a dose of 75 mg-150 mg/day was used initially, then tramadol at a dose 50-200mg/day given by the oral route,

initially achieving reduction of pain (VAS 3-4). Diagnostics were extended to thorax CT, where at the L1/L2 level in the right intervertebral foramen the pathological mass that filled it was revealed. In the bone parts of the ribs disseminated focuses of destruction were revealed with the presence of smoothly contoured pulmonary, strengthening-contrasting soft-tissue masses, infiltrating adjacent muscle structures. In the 1st right rib, there was a change of 54x43 mm, the 7th right rib 51x27 mm, the 8th right rib 16mm, the 3rd left rib 20 mm, the 7th left rib 82x31 mm and 75x39 mm, and the 11th left rib 36x26 mm. Moreover, the bone structure was diluted by 2 cm within the left hip bone in the area of the joint space of the sacroiliac joint and there were numerous degenerative changes in the lumbar region of the spine. Based on the radiological image multiple myeloma was suspected.

The patient was admitted to the Hematooncology Clinic to complete the hematological diagnosis. In the performed biochemical tests the following was found: creatinine 1.27 mg/dl (N 0.7-1.2 mg/dl), calcium 2.47 mmol/l (N 2.15-2.5 mmol/l), LDH 356 IU/l (N 10-480 IU/l), β-2-microglobulin 2.68 mg/l (N 0.7-3 mg/l), IgG 9.97 g/l (N 7-16 g/l)), IgM 0.25 g/l (N 0.4-2.3 g/l), IgA 21.9 g/l (N 0.7-4 g/l), free kappa chains 222.16 mg/l (N 3.3-19.4 mg/l), free lambda chains 15.51 mg/l (N 5.71-26.3 mg/l), lambda IgA monoclonal protein in electrophoresis of serum proteins 1.24 g/dl. Besides, an open biopsy of the chest wall was performed. In the histopathological picture of the infiltration of the rib the presence of diffused infiltration from CD138+, MUM1+, CD56+ plasmocytes, kappa+, lambda-, CD45-, CD20-, CD3-, Ki67 60% light chain immunoglobulins was demonstrated. Based on the clinical picture and additional examinations carried out, the diagnosis of myeloma with stage III according to Durie and Salmon, stage I according to ISS was confirmed.

Due to persistent pain (VAS 8), oxycodone was used at a 40 mg/day, fentanyl 50 μg/h in the transdermal patch and acetaminophen at a 1500 mg/day and ketoprofen was used pro tempore. VTD chemotherapy was initiated (bortezomib in combination with thalidomide and dexamethasone) and zoledronic acid treatment in due doses. Moreover, after the first cycle of chemotherapy, radical radiotherapy with the 3D technique was conducted - the infiltration of the 1st right rib and infiltration of the 7th left rib was given a dose of 30 Gy. It was during the first treatment cycle when the pain reduction was achieved (VAS 3), and after the third treatment cycle oxycodone doses were reduced to 20 mg/day. The patient did not require additional doses of non-steroidal analgesics and the fentanyl was discontinued. The patient received a total of 6 cycles of chemotherapy. After induction therapy, the patient underwent autologous transplantation of hematopoietic cells. As a result of the treatment, complete remission was achieved. Currently, the patient does not require any painkillers.

Discussion:

In 2/3 of patients who have been diagnosed with the cancer, pain's intensity is moderate to severe, and its etiology is mixed, therefore accurate assessment of the patient's clinical condition should take into account the likely cause of pain and the choice of appropriate treatment [5, 6, 7].

In 1986, the principles of pharmacotherapy of cancer pain, which were developed by the team of experts of the World Health Organization (WHO), were published for the first time. In recent years, this document has been supplemented with studies prepared by IASP experts and the *European Association for Palliative Care* (EAPC) [10,11].

Detailed imaging diagnostics allows a doctor to detect bone changes in as many as 80-90% of patients with symptomatic MM. The clinical picture of MM includes also anaemia, renal failure, hypercalcemia and recurrent infections with bacterial and viral aetiology [2, 3]. In the patient described, the first symptom of MM was non-specific, worsening pain in the chest. This type of pain is usually the first symptom of cardiovascular disease, but it may be connected with other organs and systems disorders. The pain coming from the chest wall (sensory nerves, cartilage-bone connections, spine, skin), the inside of the chest (aorta, pulmonary artery, mediastinum, oesophagus, trachea, bronchi, pleura) and the abdominal cavity (stomach, duodenum, pancreas, gallbladder) and psychogenic disorders should be taken into consideration in differential diagnosis [12]. Therefore, the first diagnostic step was to exclude the causes of cardiological and gastroenterological pain, and then to begin analgesic therapy in accordance with the analgesic ladder. The treatment was started with paracetamol and non-opioid analgesics (ketoprofen and diclofenac), followed by weak opioids (tramadol). Initially, the therapy brought clinical improvement, but the lack of causative treatment led to the progression of the disease process and increased pain.

Scientific reports confirm that analgesic treatment is an integral part of cancer therapy, and poorly controlled pain causes many adverse physical, psychological, social and spiritual effects [6, 13]. In the clinical picture of MM, renal failure is included, therefore the chronic use of non-steroidal anti-inflammatory drugs in patients with MM is not recommended. Oxycodone is one of the therapeutic options in patients with severe pain [2]. In comparison with morphine, it shows a higher rate of penetration of the blood-brain barrier, which makes it similar to lipophilic drugs, such as fentanyl. The drug is characterized by high efficacy of nociceptive and neuropathic pain therapy with a small number of clinically significant side

effects. The oral form of the drug is convenient to use. In the case of severe bone destruction, high analgesic efficacy with a relatively small number of complications is also showed by radiotherapy. The analgesic effect is observed in as many as 50-80% of patients, and 20-50% results in complete resolution of the symptoms [14]. Radiotherapy helps to achieve not only an analgesic effect, but also to accelerate healing [15]. Also, drugs used in MM therapy directly or indirectly inhibit osteoclast activity. In the case of bortezomib, an additional effect of osteoblast stimulation and the effect of bone reconstruction in patients was also demonstrated in vitro. The documented osteoclast-inhibiting activity is shown by bisphosphonates and zoledronic acid [2].

In case of the described patient, the use of a combination therapy based on chemotherapy in the VTD system (bortezomin, thalidomide, dexamethasone), zoledronic acid, radiotherapy and opioid analgesics initially reduced the pain and brought subsequent relief. This type of therapy significantly improved the patient's quality of life.

Summary:

The key element in the treatment of pain in the course of MM is the individualization of therapy and the essential role is played by appropriately selected analgesics. The therapy should be conducted adequately to the severity of pain, gradually increasing analgesia until it is mastered. It should be remembered that a modern approach to treating pain in patients with MM includes not only standard analgesia, but also radiation therapy, bisphosphonates/zoledronic acid, orthopaedic treatment and chemotherapy in patients with the progression.

References

1. Curado MP, Oliveira MM, Silva DRM, et al. Epidemiology of multiple myeloma in 17 Latin American countries: an update. Cancer Med. 2018;7:2101-2108.
2. Dmoszyńska A, Usnarska-Zubkiewicz L, Walewski J, et al. Zalecenia Polskiej Grupy Szpiczakowej dotyczące rozpoznawania i leczenia szpiczaka plazmocytowego oraz innych dyskrazji plazmocytowych na rok 2017. Acta Haematol Pol. 2017;48:55-103.
3. Gerecke C, Fuhrmann S, Strifler S, et al. The Diagnosis and Treatment of Multiple Myeloma. Dtsch Arztebl Int. 2016;113:470-476.
4. O'Donnell EK, Raje NS. Myeloma bone disease: pathogenesis and treatment. Clin Adv Hematol Oncol. 2017;15:285-295.
5. Kumar KH, Elavarasi P. Definition of pain and classification of pain disorders. J Adv Clin Res Insights 2016;3:87–90.

6. Thapa D, Ahuja V. Cancer pain management-current status. J Anaesthesiol Clin Pharmacol. 2011;27:162–168.
7. Glare PA, Davies PS, Finlay E, et al. Pain in cancer survivors. J Clin Oncol. 2014;32:1739-1747.
8. Shute C. The challenges of cancer pain assessment and management. Ulster Med J. 2013; 82: 40–42.
9. May C, Brcic V, Lau B. Characteristics and complexity of chronic pain patients referred to a community-based multidisciplinary chronic pain clinic. Can J Pain 2018;2: 125–134.
10. Mercadante S, Fulfaro F. World health organization guidelines for cancer pain: A reappraisal. Ann Oncol. 2005;16(Suppl 4):132–135.
11. Mercadante S, Fulfaro F. World health organization guidelines for cancer pain: A reappraisal. Ann Oncol. 2005;16(Suppl 4):132–135.
12. Kaźmierczak-Dziuk A, Grzęda M, Kowal J, et al. Ból w klatce piersiowej – podobne objawy, a różne rozpoznania i przebieg kliniczny – opisy przypadków. Pediatr Med Rodz 2011;7:401-408.
13. Figura N, Smith J, Yu HM. Mechanisms of, and adjuvants for, bone pain. Hematol Oncol Clin North Am. 2018;32:447–458.
14. Severino AL, Shadfar A, Hakimian JK, et al. Pain therapy guided by purpose and perspective in light of the opioid epidemic. Front Psychiatry. 2018;9:119.
15. Matuschek C, Ochtrop TA, Bölke E, et al. Effects of Radiotherapy in the treatment of multiple myeloma: a retrospective analysis of a single institution. Radiat Oncol. 2015;10:71.