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Neuropsychiatric disorders in patient with end-of-life stage of cancer disease — a case report

Abstract

Advanced cancer disease often results in many unpleasant physical and psychological symptoms. They may have an important impact on the patients' quality of life. Acute psychotic disorders like cognitive failure, and delirium in particular, are quite common in patients referred to oncologists and palliative care units. Here we describe the case of a man, 63 years of age, with squamous cell lung cancer, treated for severe pain due to bone metastases, who developed cognitive failure and delirium. We discuss delirium, its diagnosis and treatment which may help the clinician to improve their skills.

Key words: acute psychic disorders, pulmonary cancer, end-of-life stage of cancer disease

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Introduction

Cognitive disorders are second most common group of psychiatric symptoms in oncologic and palliative care patients. The Diagnostic and Statistical Manual of Mental Disorders, Fourth edition (DSM-IV) divides cognitive disorders into some sub-categories. One of them is: delirium, dementia, amnesic and other cognitive disorders [1]. Prevalence of delirium is increasing as the general population including patients with cancer, live longer. Delirium contributes to increased morbidity and mortality, substantial treatment costs, and a lot of stress in the family and professional carers. Diagnosis, assessment and treatment of delirium is quite difficult and complicated because of imprecise concepts, subtle, inconsistent, and overlapping symptoms, and multiple causes.

Case report

A 63-years-old male patient was referred to Palliative Care In-Patient Unit in January 2009 due to persistent pain of left lower extremity and right shoulder region. He was diagnosed with squamous cell lung cancer in September 2007 and started systemic treatment with four cycles of cisplatin, vinorelbine and fractionated radiotherapy. He was well during all check ups in the clinic until January 2009. Few days before admission to the Palliative Care Unit he had a fall. The X-ray showed extensive metastatic deposits and bone losses in the left femur, but no fracture. The patient was treated conservatively and was administered a single dose of 90 mg Pamidronate IV. He became bedbound. On admission to Palliative Care Unit he was commenced on analgesics which reduced substantially his pain.

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The effective regime consisted of oxycodone SR 20 mg bid, oxycodone IR 5 mg prn for break-through pain, ketoprofen 100 mg bid and gabapentin 100 mg tid. He was offered palliative radiotherapy, but refused it. Unfortunately, a while later he developed chest infection and periodotal abscess necessitating IV antibiotics and drainage. Drainage by the maxillofacial surgeon was partially successful and another session was planned in the future. Because in the same time patient's pain, especially of the right shoulder, has increased, dose of oxycodone was increased to 25 mg bid, gabapentin 300 mg tid, and two new drugs were added: paracetamol 500 mg tid and fluoxetine 20 mg once daily because of increasing psychological depression. This approach resulted in general improvement. The laboratory tests did not show significant abnormalities. He was started with some gentle physiotherapy. A couple of days later he felt unwell, weak and sweating. His body temperature was 38.7°C, and pulse rate 110/min, BP was 90/60 mm Hg. There were crepitations in the lower parts of the lungs. The metastatic pneumonia with the focus in the jaw suspected. The same day, during the physiotherapeutic exercises, patient experienced severe, stabbing, lancinating and excruciating pain of the left leg. Clinically fracture of the femur was diagnosed and the leg was stabilized in a Brown's device. SR oxycodone was switched to SR morphine titrated up to 60 mg bid and dexamethazone 4 mg once daily IV was added. Opioid switch was unfortunately needed due to supply problems and temporary lack of oxycodon in the setting. Gabapentin and ketoprofen were continued. With occasional IR morphine 20–40 mg prn the pain at rest was quite well controlled. Later IV ketamine 30 mg was added to this regime. In the same time discrete cognitive disorders like slight confusion with lucid intervals were observed. The symptoms of cognitive failure exacerbated dramatically in a short time. The patient was time and disorientated in time and place, restless, anxious, very agitated which exacerbated the pain. Severe hypercalcaemia (12.1 mg/dL, total calcium, ref. range 8.5–10.6 mg/dL) was diagnosed. At that stage acute delirium was diagnosed and the patient was treated with 12.5 mg of levomepromazine IV with stat dose of 5 mg midazolam IV, continued 2 mg every 1 hour to dose 6mg. This therapy, which was chose to achieve a bit more sedation for a while, settled him for a period of 2 hours. Patient received an indwelling bladder catheter. After that the patient was given IV Levomepromazine 12.5 mg qid, i.v. midazolam 3 mg qid, dexamethasone was discontinued. The patient was settled, relatively lucid before he passed away two days later.

Discussion

People often say that they fear more the dying than being dead. Indeed, the quality of dying can be challenged by the unrelieved symptoms, both physical and psychological. On the other hand management of many mental disorders like delirium, depression, anxiety, suicidal ideation, may be challenging even for a most experienced palliative medicine specialists [2, 3].

Cognitive failure is unfortunately very common in patients with advanced stage of chronic disease. The prevalence of delirium is ranging from 25 to 40% of cancer patients, growing up enormously to almost 85% of terminal cancer patients [2, 4–6]. Although not much is known about the mechanisms of this disorder, observed symptoms suggest multifocal malfunction of different brain regions. Delirium has been defined as non-specific cerebral dysfunction characterized by concurrent disturbances of level of consciousness, attention, thinking, perception, memory, psychomotor behaviour, emotion and the sleep-wake cycle [7]. Among clinical features of delirium one can find acute onset, confusion, disorientation (in time, place and/or person), distractibility, psychomotor agitation or retardation, illusions (misperceptions) and hallucinations (usually visual), delusions (especially with paranoid themes), fear and anxiety, autonomic dysfunctions, diurnal variation (worse at night and early morning, with lucid intervals especially during the day). Delirium is being divided into three sub-types, based on arousal disturbances and psychomotor behaviour, which include "hyperactive", "hypoactive" and "mixed" sub-types. Most common are hypoactive and mixed sub-types, but hyperactive delirium is the most feared one and one the most clinicians are familiar with [8]. Early signs of delirium may be misdiagnosed as depression, dementia, fear, anxiety, anger or manic episode [9]. The most common differential diagnostic issue is whether the patient actually has delirium or preexistent dementia, which are both the cognitive disorders. Dementia appears in relatively alert persons with little or no clouding of consciousness. The onset of symptoms is more chronic, and one's sleep-wake cycle seems less impaired. Most prominent in dementia are difficulties in short and long-term memory, impaired judgement and abstract thinking, disturbances of higher

cortical functions (aphasia, apraxia). Delirium, in contrast to dementia, is being considered as reversible even in patients with advanced chronic disease, although it may not be fully reversible in terminally ill patients who develop delirium in the last days or hours of their life (terminal delirium). This is due to multiple organs irreversible failure [2, 10].

The standard approach to the managing delirium includes searching for underlying causes, correction of these factors, and management of the symptoms of delirium. In the terminally ill patients, whatsoever, who develop delirium in last days of life, the management of this disorder is quite unique, presenting a number of dilemmas, and desired clinical outcome may be significantly altered by the dying process. There is an ongoing debate as to the appropriate extent of diagnostic evaluation that should be pursued in a dying patient with terminal delirium. Most clinicians would undertake diagnostic procedures only when a suspected aetiology can be identified easily, with minimal use of invasive procedures, and treated effectively with simple interventions that carry minimal risk and burden to the patient. Most often, however, the aetiology of terminal delirium is multifactorial or remains obscure. In patients with advanced cancer, delirium may be due to both direct effect of disease on central nervous system (primary or metastatic tumours) and indirect effects of cancer or treatment on the CNS. These indirect effects may be caused by metabolic disturbances: hypoxia, hypercapnia, hypo- or hyperglycaemia, electrolyte disturbances (including hypercalcaemia), impaired liver and kidney functions, infections, drugs (CNS depressants, gluco-corticosteroids, sympathomimetics, anticholinergics, opioids, benzodiazepines), chemo and radiotherapy, but also uncontrolled pain [3, 11–15].

In symptomatic treatment one can use pharmacologic and non-pharmacologic interventions. It is important to provide quiet, well-lit room, filled with familiar objects, with calendar and clock being visible. The presence of the family cannot be underestimated [16]. These interventions are important but frequently insufficient and needs to be accompanied by appropriate pharmacological treatment. In delirium the drugs of choice in the treatment of delirium are antipsychotics (haloperidol, chlorpromazine, levomepromazine, thioridazine). Atypical antipsychotics (olanzapine, risperidone, quetiapine) are effective but not always available in injectable formulations. They are usually seen as alternatives in case of extrapyramidal side effects or tardive dyskinesia caused by the first line drugs. Although the aim of therapy is to diminish agitation, to clear sensorium and improve cognition in the delirious patient, this is not always possible in the terminally ill and dying patients. Sometimes the symptoms can be controlled only by decreasing of consciousness and sedation. The latter can be achieved by addition of benzodiazepines (lorazepam, midazolam) [2, 5, 13–15, 17].

In our case the underlying aetiology of delirium was clearly multifactorial. Among the factors that certainly contributed to delirium was: pneumonia, severe pain, opioids and steroids, as well as hypercalcaemia and possibly hepatic failure. Due to this advanced disease phase, it was decided to abandon aggressive treatment with IV antibiotics and bisphosphonates, as well as aggressive treatment of metabolic abnormalities. The analgesic drugs were continued, while the corticosteroids were withdrawn. The antipsychotic drug, together with short acting benzodiazepine, helped to settle agitation. For a while the patient was lucid which was important to the family. The family was all the time informed about the developments and was participating in decision making truly representing patient's interests. Both patient and the family fully accepted proposed therapy and the moment when the patient needed to be sedated. With this agreement the therapy was continued till the end. In that way the best possible quality of dying was achieved.

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