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Anatomy of clinical consultation. Pain in a patient with metastasized prostate cancer. I can help when you ask me the right questions

Abstract

We are all asked for consultations to see a complex patient or to answer the telephone call and think about the patient without seeing him and without touching him. Although this type of consultation is much cheaper, faster and sometimes effective. There is a danger that we hear only a part of the story, or a story coloured in such a way that it will push the decision in one direction, intended by a doctor or nurse who requested it. In this article I describe a consultation "by a telephone". I go in the depths of the request and discuss with the doctor who asked me in consultation all pros and cons. I come to conclusion that we should teach young doctors how to request consultation, which questions to ask without suggesting the answers.

Key words: consultation, cancer pain, pain in cancer, opioid switching, morphine, fentanyl

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Introduction

I was asked to advice on pain control concerning an elderly patient with prostate cancer. This induced very interesting discussions on which I shall reflect here. Pain control in patients with prostate cancer is often difficult and some aspects of it are controversial. This case shows how important it is to gather right information before asking somebody for advice. Gathering this information only may help to solve the problem. It also helps to reflect on the case with the colleagues and the nurses, providing you can separate the clinical facts from your emotions and feelings. Here I present exact case description as I received it.

Case description

The patient was a 72 years old man. He was diagnosed 9 years ago with prostate cancer and known for 18 months with multiple bone metastases. He suffered of severe pain which in the initial presentation was named "bone pain". Initially the pain responded well to fentanyl 25 mcg/hour patch. It went so good, that the patient started slowly to decrease the dose himself, while the patch was well tolerated. However, after couple of weeks the pain intensity increased, and it was presumed by the presenting doctor that this resembled tumour progression. However, no information on the changes in bone scintigraphy or prostate specific antigen (PSA)

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were given. The dose of fentanyl was thus gradually increased to 100 mcg/hour every 3 days. Because of progressive weight loss in the last 3 weeks the patient was prescribed prednisone to stimulate his appetite and gain some energy. On the other hand it was hoped that prednisone may contribute to better analgesia, which it did not. At the moment of consultation the patient was still suffering of severe pain with frequent exacerbations, called by the presenter "breakthrough pain". He used up to 3 PRN doses of oral morphine 40 mg, but without much effect. Besides, he complained of breathlessness, again this was presumed to be due to "lung metastases", but no diagnostic imaging was performed. The dose of fentanyl was increased again to 125 mcg/hour, but to no avail. The patient became restless, could not concentrate or sleep at night and was dozing off during the day time. His daughter observed that especially in the evening, he was confused. There was no cognitive impairment diagnosed before.

Patients' medication

1. Monthly 90 mg of pamidronate IV
2. Metoclopramide 10 mg tds
3. Prednisone 10 mg od
4. Lactulose syrup 50% 20 ml od

The question asked me was: Would opioid rotation be appropriate? To which drug and which dose? Would fentanyl buccal or intranasal be a good choice for the patient's breakthrough pains?

Questions that need to be asked

To answer these questions we need to have some more information. It should be possible to obtain this information from the doctor who requested this consultation. It would be much easier, when the doctor asking for consultation would have the answers ready. However, as it frequently happens, the doctors who gather these facts properly, do not need a consultation... On the other hand many doctors who ask for consultation do not like to admit they do not know something about their patients and they try to mask it or even confabulate the truth. Another problem is going through the assumptions, like in the case above.

The case presented to me was without any details of the oncological history of this patient. It looked like it is not important to a doctor working in palliative medicine. How advanced was the tumour initially? How was the patient treated? Did he

have locally advanced cancer treated with prostatectomy and/or radiotherapy. Initial therapy, especially when tumours are less advanced can be radical and survivors may suffer of many iatrogenic damage (a.e. neuropathy).

Was there any radiotherapy given for the bone pain already? Where? With what effect? We know the patient has bone metastases, but can we review his most recent bone scintigraphy? Where does the patient localise exactly his (worst) pain? Do these localisations match with the findings on the bone scan? This is essential for the diagnosis of the "bone pain". Bone scintigrams should be performed twice a year and progression of metastases (or their regression) should be monitored. Lack of match between complains and bone scintigraphy suggest extraosseal source of pain (see below)

Are there any bones instable (hips, pelvis)? Is the pain getting worse on movement or at rest? What is the dynamics of PSA increase (if any) in comparison to increase of pain? Does this patient presents with diffuse skin hyperalgesia and/or allodynia, or localised mechanoreceptive pain (pain on pressure). Patients with prostate cancer live much longer than decades ago and they run the risk of developing many other than "malignant" pains. Among them is the osteoporosis, bone instability and fractures. Sometimes not to be seen on scintigrams. Here we should have a plain X rays. Typically the "instability" of pain are focal and are not accompanied by the PSA rise. In comparison to the bone pain due to metastases growing in the bones, the sites are also sensitive to movement and palpation.

Is the patient constipated due to the opioids? On rare occasions patients may have no analgesia from opioids, but also may be not constipated. Rotation to another opioid, may solve the problem (and cause constipation). Here we have an indirect and imprecise information that the patient uses lactulose syrup. No precise information about the defecation pattern is presented.

What does it mean that the patient has a breakthrough pains? Is the pain in general well controlled and the patient experiences sudden (on movements?) exacerbations? Is there any radiation of pain or localized hyperalgesia area suggesting nerve or nerve root compression? This is very important as "breakthrough pains" are defined as pains against the background of well controlled pain.

We were told the patient was prescribed morphine orally, 40 mg PRN. Was there any response to the PRN doses after administration? We were told that the patient was still in pain, but the response

to oral morphine was poor, but this was not specified enough.

Were there laboratory tests done, especially the renal function, plasma electrolytes including Mg⁺⁺ and Ca⁺⁺ and full blood count are of importance for pain control.

Differential diagnosis

The differential diagnosis is a summary of clinical thinking and answering the above questions. Answering the clinical questions one may make one possibility more probable than the other.

1. Pain due to bone metastases. This pain is usually worse at rest. Sometimes patients report that the pain is getting less during the movement. The pain is usually not mechanoreceptive, this means it will not increase on pressuring with finger. Progression of pain would coincide with hormonal unresponsiveness and progression of the PSA. By itself this pain responds well to combination of opioids and if possible paracetamol and/or NSAID.
2. Pain due to bone instability, especially of the hips and lumbar spine. This pain is getting worse on movement and on weight bearing. It is getting less at night while resting in bed. The patient may even have discrete bone fractures which should be diagnosed with X rays. The instable or fractured sites may be sensitive to pressure (mechanoreceptive pain). The pain due to bone fractures may be associated with a neuropathic pain (see below). Due to iatrogenic hypogonadism and many years of anti-androgen therapy, the patient could suffer osteoporosis and bone instability or fractures. The pain due to osteoporosis and fractures is usually not associated with rising PSA.
3. Pain due to bone metastases that cause compression of the nerve roots (hyperalgesia of the dermatomal distribution) or peripheral nerves (hyperalgesia in discrete areas served by the nerves). However, most of the peripheral nerve compression is of not "malignant" origin. It depends on general deterioration, loss of tissue supporting and protecting nerves, compression against bones etc. Also, typically, this pain is not associated with the PSA rise.
4. Pain due to the opioids themselves; the so called opioid-induced hyperalgesia (OIH). This pain would be indeed diffuse, would not be explained by anatomical changes (negative match between the complains and bone scan findings). The dy-

namics of this pain may be unrelated to the increase of PSA. It would be important here to know the renal function as some metabolites of morphine may accumulate in renal insufficiency and may provoke neurotoxicity. Also fentanyl is the most OIH-genic opioid, in comparison to methadone or buprenorphine.

5. The pain may be related to dietary deficiencies as the patient is cachexic and is not eating well. Among the most important is hypomagnesaemia, which can present as an increasing insensitivity to the opioids. Magnesium increases opioid binding to mu receptors [1]. Previous chemotherapy including cis-platin may be responsible for renal function impairment but also for magnesium losing nephropathy [2].
6. If the pain intensity is increasing at the third day of the patch, this would suggest that fentanyl is rapidly absorbed from the patch and/or rapidly metabolised and the patch becomes "empty" at the third day. This can be easily seen when the frequency of the oral morphine PRN medication is analysed in time. The need for additional doses is clustered at the third day of the patch. However, this phenomenon occurs usually with the reservoir patches, but is much less often seen with the new matrix patches. This phenomenon is called "end-of-dose" pain and can be even defined as pseudoaddiction.

Discussion

Many patients, nearly automatically, would assume that the pain suffered by this patient is a typical "cancer pain". However, this patient, thanks to the modern oncological treatment, lives so much longer than decades ago, that it is probable that he suffers also other, "non-malignant pain" like osteoporosis, bone instability, nerve compression or opioid induced hyperalgesia. Most of these "non-malignant" pains share couple of characteristics. They may be less opioid sensitive than pain due to bone metastases and the patients easily develop tolerance when the pain is treated with opioids only. Patients may present with toxic effects of opioids, while being still in pain.

This is also the reason, why the pain should be diagnosed and treated specifically with multiple modalities, not only with opioids. This patient, I understood was at home and refused any other diagnostic procedures and visits to hospital specialists. However, generic treatment with opioids, with or without adjuvant drugs is highly improbable to

help here. Gathering right information should be an on-going process. Severe pain, many trials and changes of medication, may demotivate patient to do anything and push the doctor into the scenario of "generic pain" treatment.

Switch to other opioids would help for a short while. However, nothing is suggesting that the patient is actually dying and his prognosis may be weeks or even months. So the question the doctor should ask is not to which opioid he should switch, but what is the diagnosis of pain and are there any, non-invasive, ways to get the diagnosis as sharp as possible and start specific treatment.

This case also shows how much are we influenced by the Industry and their advertisements on new and improved drugs. Many "breakthrough pains" are in reality poorly diagnosed and controlled pains. Treatment of these pains with the modern rapid acting fentanyl preparations will probably affect only the budget of your institution, but will not help the patient.

What do we need to think of prednisone treatment? Prednisone treatment is often used as an adjuvant in the treatment of hormone escaped prostate cancer. There is good evidence saying that in such patients there is still some additional anti-androgen effect, by addressing a different route of androgen metabolism [3–5]. Corticosteroids may increase patient's appetite, but they are at the same time katabolic and provoke nitrogen losses [6]. In the longer term this results in poorer patient's condition and mobility. Prednisone can be used as adjuvant in pain treatment like in liver capsule tension, but none of this was specified in patients' history. Again, using such a "generic" drug for the unspecified symptoms will probably not help, but only trouble the view and interpretation of clinical facts.

Why is the pain control in prostate cancer typically a big problem? One of the reasons for this is iatrogenic hypogonadism. Longstanding antiandrogen therapy is not only responsible for muscle wasting, poor appetite and fatigue, but also for decreased pain threshold. Substitution with testosterone, fea-

sible in all other non-hormone dependent cancers, is not possible here. Unfortunately.

In truly "bone pain" due to metastases the treatment of choice is radiotherapy. Opioids and adjuvants are only a bridge to analgesia resulting from radiotherapy. In bone instability pain the patient should be consulted with orthopaedic surgeon and bone scan and plain films should be carefully examined. In many cases bone instability can be treated operatively. Fractures of the vertebrae can be treated with vertebroplasty [7].

Conclusion

The intention of this article was not to solve the problem of this patient but to show the complexity of the case and a structure for step-by-step solution to the problem. Crucial here is gathering clinical facts, abstinence from assumptions and formulating and asking clear and specific questions. Without this process, a consultation by an experienced colleague may prove to be useless.

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