Medical emergencies in prostate cancer

Prostate cancer is the second biggest cause of death from cancer among men in the UK. Many patients present to doctors with complications from disease or from treatment. This review discusses common emergencies in patients with prostate cancer.

Dr Faye Lim Specialist Registrar in Clinical Oncology, University College Hospital, London NW1 2PG, UK.
Dr Heather Payne Consultant in Clinical Oncology, Meyerstein Institute of Oncology, University College Hospital, London, NW1 2PG, UK.

More than 30,000 men are diagnosed with prostate cancer each year in the UK, and this disease has overtaken lung cancer as the most common cancer in men.[1] It is also the second biggest cause of death from cancer in men in the UK at around 10,000 deaths every year. More than 60% of cases occur in men aged over 70 years and the largest proportion of cases are diagnosed in those aged 70–79 years.

Although there has been a huge rise in prostate cancer incidence over the last 20 years, this rise has not been mirrored by an increase in mortality. The increase in incidence is largely due to increased detection of prostate cancer by prostate-specific antigen (PSA) testing, and surgery for benign prostatic hyperplasia. The causes of prostate cancer are largely unknown, although risk factors have been identified including age, race, and family history. Other potential risk factors include vitamin or mineral interactions and other dietary habits. With increasing use of chemotherapy and radiotherapy, many patients now present with complications from treatment or from disease progression. This article covers common emergencies that can occur in patients with prostate cancer.

Bone metastases

Bone metastases occur in 80% of men with advanced prostate cancer and without treatment half of these patients develop painful, potentially debilitating bone complications.[2] The spine, pelvis, ribs, proximal femur, and humerus tend to be affected. Additionally, pain associated with skeletal metastases can be difficult to control with standard analgesia. Studies show that palliative radiotherapy of single sites can produce partial and total pain relief and reduction in stiffness in around 80–90% of patients.[3]

A single fraction of radiation provides good pain relief and is well tolerated. In some patients the onset of pain relief can be within 2 days of therapy, however, in others it may take up to 6 weeks for the full benefit of treatment to be realised.[4] Bone metastases can also cause other complications including spinal-cord and nerve-root compression and can increase the risk of fracture of long bones.

A recent study[2] showed that zoledronic acid 4 mg intravenously every 3 weeks significantly reduced the risk of skeletal-related events compared with placebo in men with hormone refractory prostate cancer. Skeletal-related events were defined as pathological fracture, spinal-cord compression, surgery or radiation therapy to bone, or change in antineoplastic therapy to treat bone pain. Studies investigating the role of bisphosphonates in prostate cancer are ongoing.

Box 1: Common emergencies in prostate cancer

- Spinal-cord compression
- Fractures and near fractures
- Haematuria
- Obstructive neuropathy
- Malignant hypercalcaemia
- Neutropenic sepsis secondary to chemotherapy

Spinal-cord compression

Many patients present to clinicians or are admitted acutely to hospital with symptoms and signs of spinal-cord compression. The most common site of symptomatic compression is the thoracic region (67% of patients), with 27% diagnosed in the lumbar spine and 6% in the cervical spine.[5] These patients often have a history of back pain that has not responded to analgesics, continues to worsen, and begins to cause impaired mobility and sensory loss. The natural progression of spinal-cord compression if untreated is to paraplegia or quadriplegia and loss of sphincter functioning with urinary or bowel retention, or both.

The complete loss of neurological function is irreversible and has major clinical and social consequences. Therefore, early diagnosis of spinal-cord compression and prompt treatment is essential. In the first instance, a patient suspected of having spinal-cord compression should be given both 16 mg dexamethasone daily to reduce any associated oedema and a proton pump inhibitor.

An MRI of the spine from the cervical to sacral region should be done to confirm the diagnosis and to determine the site of compression. The scan will also give information about the integrity of the surrounding bones and any other areas of impending compression or collapse. Once the diagnosis has been confirmed, the patient should be urgently referred to an oncologist for consideration of radiotherapy or surgery. Surgical decompression should always be

considered in men who are anaesthetically fit, have a solitary point of compression with normal surrounding vertebrae, a good performance status, and are either ambulant or have a short history of immobility. The decision to proceed with surgery might be dependent on the status of the prostate cancer and the availability of other systemic therapies. Radiotherapy is usually given after surgical laminectomy or anterior fixation.

A randomised study by Patchell[6] compared surgery and post-operative radiotherapy with radiotherapy alone in a group of good-performance patients with a single site of cord compression. Combined treatment was better than radiotherapy alone and patients who had both treatments were more likely to regain the ability to walk. Patients who were still ambulatory at the time of treatment retained the ability to walk for a significantly longer time. Surgery with radiotherapy also significantly improved urinary continence, muscle strength, and functional status, and decreased the need for corticosteroids and opioid analgesia compared with radiotherapy alone.

Patients who are not suitable for surgery should be treated urgently with radiotherapy. Often the fraction used is determined by prognosis and general condition of the patient.[7] All patients are treated with continued corticosteroids to reduce oedema related to radiotherapy. After treatment patients need a period of rehabilitation and input from the multidisciplinary team.

Fractures and near fractures

Metastatic bone disease causes destruction of normal bone. Prostate cancer metastases are classically osteoblastic, but alter bone strength and can increase risk of fracture. Intractable pain and loss of mobility (especially in a long bone) that is not responding to analgesia can signal pathological or impending pathological fracture. Imminent fracture causes worsening of pain with increased load on that bone.

The management of fractures or impending fractures will depend upon the life expectancy of the patient, whether the fracture is displaced or not, and whether it affects weight-bearing bones. For established fractures in weight-bearing bones, surgery should be considered even if life expectancy is short. Treatment will provide good pain relief. If life expectancy is more than 3 months, and the fracture is not in a weight-bearing bone, surgery should be considered.

For impending fractures, early diagnosis and intervention is necessary to decrease pain and prevent disability. Radiological signs include: more than 50% cortical bone destruction, a destructive lesion greater than 2·5 cm, and a pathological avulsion fracture. The use of prophylactic fixation of long bones can stabilise the bone despite continuing bone destruction and allow weight-bearing. Radiotherapy should be considered postoperatively to provide pain relief, promote bone healing, and halt local tumour progression.

Urinary complications

Haematuria

Haematuria can occur as a late complication of radiotherapy to the pelvis or because of local cancer progression within the prostate or bladder. All patients should be investigated with cystoscopy to rule out co-existing pathology in the bladder and should undergo imaging of the kidneys to exclude renal bleeding. This symptom requires evaluation and restaging of the prostate cancer with PSA measurement and imaging of the abdomen and pelvis with MRI or CT.

Radiation treatment can cause telangiectasia in the bladder mucosa that can rupture and bleed. This complication can occur from 6 months to many years after therapy. It is usually self-limiting and requires little intervention. If bleeding is persistent or causing anaemia cystoscopic diathermy is occasionally needed.

Bleeding secondary to local progression of the prostate cancer may require palliative radiotherapy if the maximum tolerance of the surrounding normal tissues has not been reached with previous irradiation. Other interventions include laser coagulation of the bleeding prostate and the use of intravesical tranexamic acid with etamsylate, a haemostatic agent.[8] The overall treatment strategy for the prostate cancer might need to be changed to halt progression.

Urinary obstruction

Obstructive uropathy is a common occurrence in patients with metastatic prostate cancer, affecting 3·3–16% of patients. Causes include bladder outlet or ureteric obstruction secondary to local progression of cancer in the prostate or bladder neck; gross pelvic lymphadenopathy; or stricture formation in the urethra following radiotherapy or surgery.

Patients can have an insidious rise in urea and creatinine and a decrease in urine output. Pain is usually absent unless there is acute obstruction. Patients may also have acute renal failure with life-threatening hyperkalaemia.

Management is dependent on the cause and site of obstruction. If local disease in the prostate is the cause then simple urethral catheterisation may relieve the problem. It is important to monitor for post-obstructive diuresis, to replace fluid according to output, and to correct any electrolyte abnormalities. Palliative trans-urethral resection of the prostate can be done for refractory urinary retention or bladder

Box 2: Management of spinal-cord compression

- Consider as a diagnosis if back pain is associated with weakness or stiffness of limbs and with associated sensory disturbance or abnormalities in bowel or bladder function.
- Urgently MRI whole spinal cord and give 16 mg dexamthasone and a proton pump inhibitor
- Refer patient to spinal unit for decompression of metastatic deposit, if appropriate.
- Give radiotherapy either as urgent first-line treatment if patient is unsuitable for surgical intervention, or after surgical decompression.

Box 3: Management of hypercalcaemia

- Consider hypercalcaemia as diagnosis in patients with non-specific symptoms such as fatigue, anorexia, polyuria, nausea, weakness, constipation, lethargy, and confusion.
- Give infusion of isotonic normal saline to encourage diuresis.
- Promptly stop calcium or vitamin D supplements and thiazide diuretics.
- Give bisphosphonate infusions—either pamidronate or zoledronic acid.

outflow obstruction with high residual volumes of urine after voiding.

A further alternative for outflow obstruction is insertion of a prostatic stent, which can be used in patients who are unfit for general anaesthesia. If the obstruction is secondary to cancer in the prostate or bladder, palliative radiotherapy can be useful for local tumour shrinkage and control, and will often alleviate obstructive symptoms. Overall treatment might need addition of hormonal therapy or chemotherapy to gain control of the cancer.[9]

Upper-urinary-tract obstruction caused by compression of the vesico-ureteric junction or invasion of the ureteric orifice requires ureteric stenting with cytoscopy. If the ureter is impossible to cannulate then a percutaneous needle nephrostomy should be done. Local treatment with radiotherapy or change in systemic treatment may achieve tumour regression and allow conversion of indwelling stents at a subsequent procedure. In the patient with a poor prognosis, the quality of life and the patient's wishes should help to determine the management.[10]

Other complications

Malignant hypercalcaemia

Malignant hypercalcaemia is the most common endocrine complication of malignant disease. It is usually caused by excessive bone resorption and increased tubular reabsorption of calcium in the kidneys. It can also be caused by the direct interaction of malignant cells within bone. Hypercalcaemia is a rare complication of prostate cancer.

Malignant hypercalcaemia can easily be overlooked because patients tend to have non-specific symptoms such as fatigue, anorexia, polyuria, nausea, weakness, constipation, lethargy, or confusion. If left untreated and calcium levels continue to rise, the patient may have neurological symptoms such as fits, altered behaviour and impaired renal function and eventually coma. There is a direct correlation between symptom severity and blood concentration of calcium.

Treatment of hypercalcaemia is aimed at improving renal function, quality of life, and mental status. Any calcium, vitamin D supplements, or thiazide diuretics should be stopped. The patient should receive isotonic saline infusion to encourage renal excretion of calcium and bisphosphonates should be considered.

Pamidronate restores normocalcaemia in 60–100% of patients and is often the bisphosphonate of choice. It is usually given as 60–90 mg infusion over 2–4 hours. Zoledronic acid, the most potent bisphosphonate, can also be given and is highly effective. The fall in calcium is very rapid and is usually maintained for several weeks.

Other therapeutic strategies include calcitonin, which acts by opposing both the physiological effects of parathyroid hormone on bone and calcium resorption at the renal tubules. Dialysis is rarely indicated in patients with hypercalcaemia complicated by renal failure.

Neutropenic sepsis

Chemotherapy can be indicated for hormone-refractory prostate cancer. Until recently, standard care has been mitoxantrone and prednisolone.[11] This regimen improved bone pain scores in 30% of men but has not been associated with increased survival. Two recent phase 3 studies changed the approach to management of hormone-refractory prostate cancer in which taxane-based chemotherapy gave a survival benefit.[12,13] Docetaxel improved time to disease progression, led to declines in PSA, and improved quality of life.

Optimum chemotherapy remains uncertain and is the subject of ongoing clinical trials. As a result of the increasing use of chemotherapy in prostate cancer, patients can be at risk of developing neutropenic sepsis. This often occurs 7–14 days after chemotherapy. Patients tend to have fever and non-specific influenza-like symptoms. These patients should have an urgent full blood count; if they are not neutropenic, they may be given oral antibiotics and allowed home provided they are stable. They should be advised to return to hospital immediately if they deteriorate. Patients with neutropenia should be admitted to hospital urgently. A full septic screen should be done, and broad spectrum antibiotics given as per local hospital policy. The use of granulocyte-colony-stimulating factor (G-CSF) should be discussed with the oncology team.

Conclusion

Most emergencies, if diagnosed early and managed promptly in the appropriate manner, result in a good outcome for the patient with minimum distress to both the patient their and family.

Box 4: Management of neutropenic sepsis

- Consider as diagnosis in all patients on chemotherapy who have influenza-like symptoms, high temperature, or signs of focal infection.
- Take full history and do a full examination of the patient. Do a septic screen including chest X-ray, and blood and urine cultures.
- Give broad spectrum antibiotics according to hospital policy.
- Consider giving granulocyte colony stimulating factor until neutrophil count is above 1x109/l.
- Liaise with microbiologist for advice about antibiotics if pyrexia does not improve after 48 hours on first-line antibiotics.

Particular emphasis should be given to neutropenic sepsis, which is common and life-threatening. Spinal-cord compression is another emergency and must be considered in all patients with back pain and neurological deficit or altered bowel and bladder function. Prompt action is essential to prevent further neurological damage.

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