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REVIEW ARTICLE

Symptomatic spinal cord involvement in prostate cancer

N EKE

Abstract

The literature on spinal cord involvement in prostate cancer is reviewed by searching the Medline from 1965 to 1997 and references in publications on the subject. The objective was to identify the clinical characteristics and treatment modalities of the disease.

Prostate cancer is the leading cause of metastatic spinal cord disease in men. The tumour reaches the spinal column mainly by the venous route. The frequency of involvement in decreasing order is thoracic spine, lumbar spine and cervical spine. The tumour usually exerts compression of the cord from the extradural space. However, intradural and intramedullary metastases have devastating effects. The patients have other neurological and urological symptoms prior to the onset of paraplegia. But in some, spinal cord compression may be the first symptom of prostate cancer. Plain X-rays may suffice in diagnosis but MRI is the single most valuable investigation for anatomic definition or localization of spinal cord secondaries. All forms of treatment are palliative.

Treatment options, singly or in combination, include hormonal manipulation, radiotherapy and laminectomy each often with high dose corticosteroids. Recurrence of symptoms after an initial relief with hormonal manipulation signifies escape of the tumour from endocrine control and portends a poor prognosis.

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Introduction

Prostate cancer is a leading cause of cancer death in men, second only to lung cancer.[1] The highest incidence of prostate cancer is recorded in African Caribbeans [2] and in black Americans in whom the prevalence has been described as a public health epidemic.[3] Contrary to previous views, a high prevalence of prostate cancer has been documented in Africans.[4,5] The lowest incidence in the world is recorded among the Chinese and Asiatics.[6]

Spinal cord involvement in prostate cancer is a major manifestation of advanced disease. The incidence varies from one to 12% of patients with prostate cancer.[7-10] While some reports indicate that prostate cancer is the second highest spinal metastatic tumour,[11] others have identified it as the leading source of spinal metastases in men.[12,13] The literature is reviewed to define the clinical characteristics and the treatment modalities of patients with advanced prostate cancer and symptomatic spinal cord involvement.

Pathology.

Prostate cancer is clinically graded from one to five on the basis of morphologic abnormalities in the architecture of the glandular system, the differentiation of the cancer cells, and the definition of the tumour margin.[14] Histologically, primary prostate cancer is mainly an adenocarcinoma which constitutes 95% of prostate cancer.[15]

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Other malignant primary prostatic diseases include rhabdomyosarcoma,[16] squamous cell cancer and leiomyosarcoma.[17] The broad grades range from well-differentiated to anaplastic tumours.

All patients with spinal cord compression from prostate cancer have multiple bone secondaries at presentation as shown by ^{99}Technitium scan.[18] Metastasis to the spine is thought to be by venous spread.[19] Most cord secondaries occur in the thoracic spine followed by the lumbar spine and cervical spines.[18,20] In 5% of patients, the secondaries are confined to the spinal extradural space. Most commonly the vertebral body and the pedicles are affected. The tumour thence spreads to the spinal canal.[11] Prostatic bone secondaries are usually osteoblastic although lytic lesions occur.[21] The disc space is maintained even when the vertebral body collapses. The lesions may be multiple and non-contiguous.[9,22] Their effect is spinal cord compression. Rarely and more devastatingly, intradural and intramedullary metastases may occur.[23] The spinal cord may also be damaged when the metastatic tumour causes occlusion of the blood supply to a segment.[24] Other tumours of the spinal canal to be excluded are lymphoma and multiple myeloma [19] as well as primary tumours of the lung, kidney and breast.

Presentation.

Early prostate cancer is largely asymptomatic [6] and may be detected by Prostate Specific Antigen (PSA) estimation, especially where screening for the disease is a policy. A high proportion of black African patients in the diaspora present with advanced disease.[3,4] The manifestations of advanced disease in prostate cancer include: weight loss, bladder outflow obstruction, anaemia, alteration of bowel habit, bone pains and the features of spinal cord compression. Spinal cord compression presents initially with back pain. Compression occurs more in high grade tumours.[9,25] Spinal cord compression may be the first manifestation of prostate cancer.[7,8,18] Paraplegia is usually preceded by other neurological or urological symptoms or rarely, bowel symptoms.[18,19] The other neurological symptoms include paraparesis, sensory deficits, muscle weakness and paraplegia or quadriplegia. In one series of patients with neurological symptoms, the frequency of these were: pain (75%), sensory symptoms (68%), bladder dysfunction (40%), while 46% were bed-ridden.[20]

The urological symptoms are usually those of the lower urinary tract such as retention, frequency, nocturia, urgency, haematuria and incontinence. These symptoms often lead to the investigation and diagnosis of prostate cancer before the onset of paraplegia. Paraplegia, in addition to loss of motor function, is usually accompanied by sensory loss. The level of neurological symptoms and signs may not correspond with the anatomical level of the spinal compression.[26] Cord compression from prostate cancer has been reported to manifest up to 100 months from the time of diagnosis of prostate cancer.[18,20]

Investigations.

The modalities for early detection of prostate cancer include digital rectal examination, PSA estimates, transrectal ultrasound scan (TRUS) and biopsy of the prostate. PSA levels are used to monitor the response or relapse of the disease following treatment. Investigations of localizing diagnostic importance in spinal cord involvement in prostate cancer include:

1. *Plain spinal X-rays.* These may show (a) typical osteoblastic lesions or osteolytic lesions in adjacent vertebrae, (b) vertebral body collapse, and (c) the involvement of the vertebral body and the pedicles on X-ray which shows as the "winking owl sign".[20] The radiographic pattern of metastatic prostate cancer is often classic enough to make tissue biopsy unnecessary for diagnosis.[23] However, pathological shadows are evident on plain X-rays only when about 50% of the vertebra has been destroyed.[27]
2. *CT scan (specifically CT myelography).* This clearly defines the extent of bone involvement and enables planning for the route of surgical access to the lesion (anterior, posterior or lateral).[19,28] It is more sensitive in showing bone destruction once the level of the lesion has been identified.
3. *Magnetic resonance imaging (MRI).* This is the most valuable single investigation. Its accuracy matches that of myelography. It has an advantage over myelography in being non-invasive.[29] The study should cover the entire spine because of the frequency of multiple spinal metastases.[30,31] It shows the actual spinal cord compression. MRI shows bone marrow but does not show cortical bone well. Furthermore, sclerotic lesions may be missed.
4. *Myelography.* This is a useful alternative option if MRI is not possible from unavailability or from difficulty with the positioning of the patient.[32] Observed complications include deterioration of the neurological status of the patient.[7,33]
5. *Fine needle biopsy of identified spinal lesions.* This is indicated when the primary site in the prostate has not been identified.[19] It is useful between T5 and L5 vertebrae when guided by biplanar image intensifier. CT guided needle biopsy for all levels is an alternative. Reported complications include haemothorax, pneumothorax, haemorrhage and neurologic deterioration.[23]
6. *Radionuclide scanning.* Radionuclide whole-body bone scintigraphy is universally preferred for detecting bony involvement in prostate cancer [34] and should be employed in the evaluation of patients suspected to have spinal cord compression from prostate cancer.

Treatment.

Spinal cord involvement in prostate cancer has been described as an oncologic emergency.[32] Urgent treatment is essential to prevent irreversible cord damage[19,32,35] and requires early diagnosis.[36,37] The immediate aim of treatment is to decompress the spinal cord and to preserve the stability of the spine. The treatment modalities are hormonal manipulation,[38,39] radiotherapy[40-42] and laminectomy[19,23,43] either singly or in combination. High dose corticosteroids are added to any of these modalities.[18,20] Hormonal manipulation involves androgen deprivation. This may be

achieved by the use of drugs or by orchidectomy. The drugs such as the antiandrogens flutamide and bicalutamide (Casodex) or the LH-RH Analog goserelin (Zoladex) are rarely available and are often unaffordable to most patients in developing countries. Orchidectomy is effective although usually only temporarily so. Urgent orchidectomy with high dose intravenous steroids is effective in some individuals with paraplegia.[18,32]

Local radiotherapy by external beam irradiation provides prompt and durable relief of compression at a specific spinal lesion site. Systemic radiation may be applied in multiple spinal lesions.[41]

The most rapid effective treatment of spinal cord compression is laminectomy during which a compressing tumour or collapsed vertebra may be removed.[19] Such treatment should take into account the expected life expectancy of the patient. Terminally ill patients are unlikely to benefit from laminectomy. If a combination of tumour, bone, and disc compresses the spinal cord, laminectomy is the only remedy with hope of successful palliation.[23] Indications for laminectomy in spinal cord compression from prostate cancer include severe myelopathy, spinal instability and rapid neurological deterioration during or after radiotherapy.[10] However, laminectomy is ineffective in the presence of vertebral body disease and may worsen the neurological status as well as the stability of the spine.[19,36] Other complications include failure of treatment in the short or long term with recurrence of compression.[18,44]

There is no clearly established superiority of laminectomy with radiotherapy over radiotherapy alone.[43] When available, combined radiotherapy and androgen blockade may precede laminectomy.[20] High dose corticosteroids (Dexamethasone) are used to reduce spinal cord oedema resulting from the initial cause of compression and from tumour infarction from hormonal and radiotherapeutic treatments.[10,32]

Inhibitors of bone turnover like mithramycin used in Paget's disease of bone have been found effective in prostatic metastatic bone disease.[45]

The results of treatment of spinal cord involvement in prostate cancer range from full recovery through partial relief of motor and/or sensory deficits[35] to total failure in paraplegic patients.[18,36] Relief in paraplegic patients has been sustained for up to two years with hormonal treatment alone.[38] Survival up to eight years following combination treatment for an intradural lesion has been recorded.[9] Spinal cord compression may relapse after an initial response to treatment.[18,44,46] Such recurrent compression may be at a different leve[l.8]

Discussion

Paraplegia is a serious complication of metastatic stage D2 adenocarcinoma of the prostate.[20] The diagnosis is not difficult to make. Localization of the compression site by MRI or myelography is essential for such treatment modalities as local radiotherapy and laminectomy. Distressingly, apart from plain X-rays, the investigations essential in the evaluation of these patients are not readily accessible to patients in developing countries.

All forms of treatment of spinal cord involvement in prostate cancer can only be palliative.[10] The prognosis in spinal cord invasion by prostate cancer is poor even with the combination therapies.[18] While local spread of tumour is associated with high morbidity, distant metastasis have worse prognosis at all ages. The poorer the differentiation, the worse the prognosis.[7-9,11,47,48] Several prognostic factors have been identified by various authors but these do not apply universally to all patients. It has been suggested from one study that no patient who was paraplegic prior to treatment regained full function.[7] Also recently, it was concluded that pretreatment ambulatory function is the main determinant of post treatment gait function.[49] This point was refuted in other studies in which some quadriplegic and paraplegic patients regained full powers in the limbs after bilateral subcapsular orchidectomy.[31,46] Treatment at an early stage of prostate cancer with hormonal manipulation is expected to reduce the occurrence of serious complications such as spinal cord involvement.[50] Patients with spinal cord compression who improve with treatment have a longer survival than those who fail to respond.

Careful selection of patients for laminectomy is essential. Laminectomy as a palliative procedure is a major operation.[18] However, bilateral subcapsular orchiectomy (BSO) for hormonal manipulation is a simple procedure. Moreover, as the spinal lesions may be multiple and non-contiguous, BSO may be preferred to laminectomy.

Recurrence of spinal cord compression after an initial successful endocrine treatment connotes escape of prostate cancer from endocrine control and is associated with a poor prognosis.[46,51] An effort to explain this escape has been made by Isaacs.[52] Recent studies have demonstrated that the normal prostate is heterogenous, composed of stem cell units hierarchically containing androgen-independent stem cells, androgen-sensitive amplifying cells, and androgen-dependent transit epithelial cells. Cancer cells arising from each of these subsets may display a characteristic response with respect to hormonal manipulations. Although patients with prostate cancer bony metastasis (D2 disease) respond well to first-line hormonal therapy with orchiectomy, antiandrogens or LH-RH analogs, hormone refractory metastatic disease (D3 disease) will ultimately develop in most patients.[41]

Conclusion

In view of the unpredictable course of advanced prostate cancer as in spinal cord involvement, it is considered worthwhile to offer such patients hormonal treatment irrespective of the delay in presentation. It has been suggested that many patients with prostate cancer die ***with*** the disease but not from it.[53,54] Until a reliable cure is found for this epidemic, most patients with spinal cord involvement in prostate cancer will die ***from*** the disease.

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