Clinical Reports

Cerebellar manifestations of prostatic carcinoma

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Summary: We present two patients known to have prostate cancer who presented with acute cerebellar signs. The neurological deficit of the first patient was due to a paraneoplastic cerebellar manifestation and progressed, despite evidence of response of the primary prostate tumour to hormonal manipulation. The second case, resulting from a solitary cerebellar metastasis, was amenable to surgical intervention and subsequent hormonal manipulation. This latter patient has experienced no recurrent neurological signs after a period of 7 years follow-up. This is the first report of a paraneoplastic cerebellar deficit and, to our knowledge, only the sixth case of parenchymatous cerebellar metastasis of prostatic origin to appear in the literature.

Introduction

Intracranial deposits develop in 12–25% of all patients with systemic malignancy, of which 16% are to the cerebellum.¹ In contrast to other tumours, parenchymatous brain metastases resulting from prostate cancer are uncommon, occurring in only 1.5–1.9% of patients.^{2,3} Neurological disorders experienced by patients with malignancy are not, however, exclusively the result of metastatic invasion. Paraneoplastic neurological and muscular manifestations may develop, even before the underlying cancer is evident. To date, no case of either paraneoplastic cerebellar degeneration (PCD) nor opsoclonus myoclonus associated with prostatic carcinoma has been described.

Case 1

A 67 year old male was diagnosed as having carcinoma of the prostate in 1989. This was poorly differentiated and involved 95% of prostatic chip-pings examined histologically after transurethral resection. Initial investigations revealed a prostate specific antigen (PSA) level of 47 ng/ml (normal range 0–4 ng/ml) and the clinical stage of the tumour as T3 NX M0.⁴ Cyproterone acetate was commenced at this time.

Three months later, the patient developed a rapidly progressive cerebellar deficit associated with truncal ataxia, pseudobulbar palsy, diplopia and transient migratory paresis of the right inferior

rectus muscle and rotatory nystagmus. Despite extensive investigation: (cranial) computed tomography (CT), magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) examination and oligo-clonal band analysis, VDRL, electroencephalography (EEG) and visually evoked potentials (VEP), no cause was found to account for the physical findings. Temporary discontinuation of cyproterone acetate did not improve the physical signs. During this period, the PSA declined to 2 ng/ml. Over the next 8 months, despite PSA levels remaining < 1.5 ng/ml whilst the cerebellar deficit stabilized, the ophthalmic defect progressed associated with bizarre eye movements. A diagnosis of paraneoplastic cerebellar degeneration, secondary to carcinoma of the prostate, was made. The eye movements were attributed to an associated opsoclonus myoclonus.

Case 2

In 1984, carcinoma of the prostate was diagnosed in a 71 year old man presenting with chronic retention of urine. The tumour was initially staged as T4 NX M1.⁴ His serum prostatic acid phosphatase level was determined to be 5.0 IU/ml at diagnosis (normal range 0–1 IU/ml). In the days following admission, the patient developed progressive leg weakness, headaches, poor concentration and lack of co-ordination of his left arm. His clinical condition rapidly progressed to semi-consciousness, associated with an up-going left-sided plantar reflex. An urgent cranial CT scan revealed

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an isolated cerebellar space occupying lesion, for which the patient underwent a posterior fossa craniotomy and excision of the tumour. Histological examination revealed this to be an adenocarcinoma with a positive reaction to PSA immunohistochemistry, a metastatic deposit originating from a primary prostatic carcinoma.

Postoperatively, his mental picture improved markedly and he subsequently underwent transurethral resection of the prostate and bilateral subcapsular orchidectomy, at which time confirmation of the prostatic primary tumour was obtained. Over a period of review of 7 years, the patient has remained well with no residual neurological deficit, no rise in serum acid phosphatase levels (and later PSA levels), nor evidence of new intracranial lesions on MRI. Areas of increased uptake, observed on the isotope bone scans at the time of diagnosis, resolved completely during this period, with no abnormality detectable on the most recent isotope examination.

Discussion

Cerebellar metastases usually arise from lung, breast, gastrointestinal and cutaneous primaries.⁵ Cerebellar deposits of prostatic origin are extremely rare, an extensive literature search revealing only five previous case reports.^{2,3,6-8} The mechanism by which the intracranial contents are invaded by tumour is controversial, this possibly being one of retrograde infiltration of the valveless vertebral veins of Bateson and Virchow-Robin spaces which, during Valsalva manoeuvre, allow pelvic blood to reach the base of the skull and subsequent dural veins.¹ Cerebellar metastases generally carry a poor prognosis, possibly because they are often a manifestation of disseminated malignancy. Indeed, this feature has led some authors to suggest that they are part of a multi-step cascade process, occurring secondary to bone and pulmonary involvement.³ Cerebellar deposits are usually solitary, in contrast to supratentorial deposits, this feature making them amenable to surgical resection. Gilman *et al.*⁵ proposed that, wherever possible, surgical intervention should be undertaken for solitary lesions, subsequent reports supporting this proposal^{3,9} with occasional reports of prolonged survival in patients with otherwise favourable parameters.⁵

The first patient developed a cerebellar deficit of non-metastatic, paraneoplastic, origin. Previously described paraneoplastic phenomena relating to prostate cancer are listed in Table I. Possibly the best known non-metastatic, neurological complication of malignancy is paraneoplastic cerebellar degeneration (PCD), albeit affecting less than 1% of patients with cancer.¹⁰ Previous reports have described this syndrome in adults associated with

Table I Previously described paraneoplastic manifestations of prostatic malignancy

Endocrine
Cushing's syndrome
Inappropriate antidiuretic hormone production
Hypercalcaemia without associated bone metastases
Hypophosphataemia
Haematological
Anaemia
Non-bacterial thrombotic endocarditis
Disseminated intravascular coagulation
Hypercoagulability
Thrombophlebitis
Neurological
Necrotizing myelopathy
Carcinomatous neuromyopathy
Cutaneous and muscular
Dermatomyositis
Migratory paraneoplastic erythema
Non-specific
Cachexia and anorexia

(Based on Matzkin, H. & Braf, Z.¹⁶)

small cell lung tumours,¹¹ carcinomas of the breast,¹² uterus and ovary¹³ or with Hodgkin's lymphoma,¹⁴ and in children, with neuroblastoma.¹⁵ This is the first case report describing this complication in relation to prostate cancer. Matzkin and Braf¹⁶ fail to discover any similar syndrome in an extensive literature review. The classical syndrome consists of truncal and appendicular ataxia, often associated with dysarthria and mild global symptoms associated with mild cerebellar atrophy. Pathologically, there occurs diffuse loss of Purkinje cells, sometimes accompanied by a proliferation of Bergman astrocytes and loss of granule cells. A proportion have more widespread clinical and pathological abnormalities. Anti-neuronal antibodies have been identified in the serum and cerebrospinal fluid of some patients with PCD, suggesting an autoimmune aetiology.

The term opsoclonus myoclonus describes bizarre, rhythmic, multidirectional, high-amplitude conjugate saccadic eye movements, exacerbated by attempts at visual pursuit. In adults, fewer than 20 cases of opsoclonus myoclonus have been reported¹⁷ – none of which was associated with prostate cancer. Only occasionally do patients with otherwise classical PCD develop opsoclonus. This group of patients differs from those with classical PCD by a more rapid onset of symptoms, a predominance of truncal over appendicular ataxia, absence of dysarthria and in some cases the presence of severe encephalopathy. Pathologically there is a relative preservation of cellular Purkinje cells,¹⁴ in contrast with other paraneoplastic syndromes and possibly explaining why remission has

been reported in some cases.¹⁴ Whilst the documented eye movements of the second patient were not exacerbated by visual pursuit movements, they were otherwise typical of opsoclonus.

It is perhaps a paradox that the second patient with disseminated carcinoma obtained symptom relief and possibly even cure from his disease following resection of the metastasis and subsequent androgen deprivation, whilst the neuro-

logical deficit of the first man, with a reduced tumour burden, continued to progress despite biochemical evidence of response of his primary tumour to hormonal manipulation.

These two cases serve to illustrate the unpredictability of the course of prostate cancer and also allow further insight into the complex immunological aspects of cancer biology which interact with host defences, modulating the final outcome.

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