Lower urinary tract dysfunction in children with central nervous system tumours

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Abstract

The findings in 10 children with neuro-pathic vesicourethral dysfunction after the onset of a central nervous system tumour are presented. Eight had a spinal tumour and two a brainstem tumour. Bladder dysfunction occurred late in most children except in those with neoplastic infiltration of the conus and cauda equina. Moreover, tumour recurrence was often heralded by loss of bladder control before other neurological signs became obvious. Videourodynamics (VUD) showed various combinations of "filling" and "voiding" dysfunction in tumours extending from the pons to the cauda equina, whereas an isolated "filling" dysfunction was evident in the patient with a suprapontine tumour. Urinary incontinence and recurrent urine infection can be immensely distressing to children and their families, particularly when they have had to cope with the stress of diagnosis and treatment of the underlying tumour. Different management strategies, based on VUD findings, are discussed highlighting the impact these have on the children's quality of life.

(Arch Dis Child 1998;79:344-347)

Keywords: urinary tract dysfunction; central nervous system tumours; oncology; videourodynamics

Tumours along the neural axis can interrupt the pathways modulating the storage or voiding mechanisms of the bladder and urethra. As a result, various degrees of bladder dysfunction can occur in children with central nervous system (CNS) tumours. This may range from transient loss of control, resolving after surgical treatment of the tumour, to persistent dysfunction.¹⁻³ The psychological impact and physical distress caused by bladder symptoms may be immensely stressful, even devastating, to children and families. We have reviewed children referred to us with chronic neuro-pathic vesicourethral dysfunction secondary to a CNS tumour. We discuss the results and management of investigations highlighting the impact of a CNS tumour on the quality of life for these children.

Methods

We identified 10 children with bladder disturbance after discovery of a CNS tumour from within a population referred for neurourological evaluation to Guy's Hospital, London between 1980 and 1996. No child had urinary symptoms before tumour diagnosis. We reviewed medical notes, radiological investiga-

tions, and tumour histology. We recorded urinary symptoms and the time interval between first symptoms of the illness and onset of urinary dysfunction. The site and extent of the tumour was identified by magnetic resonance imaging (MRI) in all but one child who had an extradural tumour identified by myelography. If more than one MRI had been done we analysed the one closest in time to the onset of lower urinary tract dysfunction. All children had an ultrasound scan of the urinary tract before and after micturition when they presented with bladder dysfunction. In addition, seven children had a videourodynamics (VUD) study and one child had a micturating cystourethrogram performed after tumour surgery. Advanced disease in two children precluded VUD studies.

The VUD study consists of a filling and voiding cystometrogram and a micturating cystourethrogram. These are recorded on videotape and viewed simultaneously so that events occurring in the bladder and urethra can be correlated with pressure changes. We did these studies using a standard technique and slow filling rates. Seven VUD variables were evaluated and correlated with the level of the tumours: four during the filling phase (bladder capacity, detrusor hyperreflexia, bladder compliance, and state of bladder neck) and three during the voiding phase (voiding pressures, state of distal sphincter, and completeness of bladder emptying). We sought vesicoureteric reflux throughout the study. The terminology used to describe the urodynamic findings is that recommended by the International Continence Society.⁴ All children had a renal biochemical profile, urine cultures, and other renal investigations if indicated.

Results

There were five boys and five girls with a mean age at diagnosis of 4.8 years (9 months to 10 years). Two children presented with a brain tumour, one arising within the brainstem at the level of the pons and another within the cerebellum with secondary midbrain extension. Eight children presented with a spinal cord tumour, six of which were intramedullary and two were extradural. Three had an astrocytoma of the spinal cord, two an astrocytoma of the brain, and there was one each of spinal ependymoma, ganglioglioma, rhabdoid tumour, ganglioneuroblastoma, and neuroblastoma. All tumours were debulked, four children requiring repeated debulking procedures. Postoperatively, five children had radiotherapy, one received chemotherapy, and one had radiotherapy and chemotherapy. In all, urinary

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Accepted 24 April 1998

Table 1 Urinary symptoms, site, and histology of the tumours

Case	Age at diagnosis (years)	Urinary symptoms	Time from initial symptoms to bladder dysfunction (years)	Site of tumour (cord segments)	Histological diagnosis
1	5	Dribbling stream, urge incontinence, nocturnal enuresis, recurrent UTI	1.2	Brainstem (pons)	Pilocytic astrocytoma (grade 1)
2	8	Frequency, urgency, diurnal enuresis	2.3	Cerebellar + midbrain recurrence	Pilocytic astrocytoma (grade 1)
3*	10	Dribbling stream, stress incontinence, recurrent UTI	1.2	Cervicomedullary (medulla–C6)	Astrocytoma (grade 2)
4*	10	Nocturia, urgency, hesitancy	1	Cervical to upper thoracic (C1–T5)	Ependymoma (grade 2)
5	2.5	Urge incontinence, frequency, nocturia	4.6	Cervicothoracic (C7–T3)	Ganglioneuroblastoma
6*	0.8	Dribbling, retention	0 (at presentation)	Cervicothoracic (diffuse)	Rhabdoid tumour
7	6	Urge incontinence, frequency, nocturnal enuresis	6.7	Lower thoracic (T9–T12)	Fibrillary astrocytoma (grade 2)
8	1	Retention, recurrent UTI	0.8	Lower thoracic to conus (T5–conus)	Ganglioglioma (grade 1)
9	1.4	Dribbling, retention	0.4	Conus and cauda equina	Neuroblastoma
10	2.5	Delay in getting dry	0 (at presentation)	Conus	Fibrillary astrocytoma (grade 2)

*Died.

UTI, urinary tract infection.

dysfunction persisted after initial or further debulking surgery. Table 1 summarises the urinary symptoms, the site, and the histology of the tumour.

Most patients developed bladder dysfunction late after the first neurological symptom. Urinary symptoms in the two children with brain tumours occurred 2.3 years (case 2) and 14 months (case 1) after the initial symptoms. Similarly, bladder dysfunction occurred several months to years after the first presenting symptom in the children with spinal cord tumours. There were two exceptions to this: one child with a cervicothoracic rhabdoid tumour and another with an astrocytoma of the conus medullaris whose urinary symptoms were part of the presenting symptom complex. In four patients (cases 2, 3, 4, 5) change in bladder habit was an important early indicator of tumour recurrence or advancing disease. Their urinary symptoms occurred one to six months before radiological or clinical evidence of tumour recurrence.

We were able to classify urinary symptoms in nine children into two groups—irritative (frequency, nocturia, urgency, urge incontinence) and obstructive (hesitancy, poor stream, terminal dribbling, retention). Three children presented with irritative symptoms, four with obstructive symptoms, and two with both. No child with irritative symptoms had recurrent urinary tract infections, whereas all the children with urinary tract infections had obstructive symptoms.

Table 2 shows VUD findings in seven children, the micturating cystourethrogram findings in one, and the ultrasound scan findings in the other two in relation to tumour level.

VUD findings showed that both children with brain stem lesions had a filling dysfunction with detrusor hyperreflexia and an open bladder neck seen during the filling phase of the study. However, the voiding mechanism was undisturbed in the child with a lesion at midbrain level, whereas detrusor sphincter dyssynergia occurred during voiding in the child with a lesion at the level of the dorsal pons.

Voiding dysfunction in the form of a fixed unrelaxing distal sphincter and detrusor sphincter dyssynergia together with evidence of a filling abnormality were present in the spinal tumours involving the sacral segments. An isolated filling dysfunction in the form of detrusor hyperreflexia and an open bladder neck anomaly was associated with tumours at the cervicothoracic, lower thoracic, and conus region. A micturating cystourethrogram confirmed a fixed distal sphincter in the child with a cervicothoracic lesion, and significant residual urine volume was seen on an ultrasound scan in the two children with advanced disease: one presenting with a cervicomedullary tumour and another with a cervicothoracic tumour. No child had vesicoureteric reflux and all had normal upper tracts on ultrasound and a normal renal biochemical profile.

Table 2 Urodynamic findings

Site of tumour (cord segments)	Case	Capacity	Detrusor hyperreflexia	Bladder compliance	Bladder neck	Voiding pressure	Distal sphincter	VUR	Voiding
Upper brainstem (midbrain)	2	D	+	N	Open	I	N	Nil	Complete
Lower brainstem (pons)	1	I	+	N	Open	I	DSD	Nil	Incomplete
Cervicothoracic	5	D	+	N	Open	N	N	Nil	Complete
Lower thoracic	7	D	+	N	Closed	N	N	Nil	Complete
Lower thoracic to conus	8	I	+	N	Closed	N	DSD	Nil	Incomplete
Conus+cauda equina	9	D	–	D	Open		Fixed	Nil	Incomplete
Conus	10	N	+	N	Open	N	N	Nil	Complete
Micturating cystourethrography									
Cervicothoracic	4	I			Open		Fixed	Nil	Incomplete

No urodynamics in case 3 (cervicomedullary) and case 6 (cervicothoracic) tumours. An ultrasound scan taken before and after micturition showed large incompletely emptying bladders in both cases.

DS, distal sphincter; DSD, detrusor sphincter dyssynergia; VUR, vesicoureteric reflux, D, decreased; I, increased; N, normal; +, present; –, absent.

Table 3 Treatment and duration of bladder dysfunction

Case	Treatment regimen	Duration (years)
1	CIC, oxybutinin, and antibiotics	3.5
2	Oxybutinin	1.5
3	CIC and antibiotics	0.6*
4	CIC	3*
5	Oxybutinin	0.3
6	CIC and oxybutinin	0.6*
7	Nil (regular voiding)	3
8	CIC and antibiotics	1.7
9	CIC, ephedrine, and antibiotics	16
10	None	0.25

*Died. CIC, clean intermittent catheterisation.

These findings confirm that various combinations of storage and voiding dysfunction can occur with tumours along the neural axis from the pons to the cauda equina. An isolated storage dysfunction was seen, however, in the child with the suprapontine lesion.

Management

All children were treated conservatively, and table 3 shows the treatment regimen and duration of treatment. Selective treatment was based on results of VUD studies and consisted of a combination of clean intermittent catheterisation, oxybutinin, ephedrine, and prophylactic antibiotics. The six children with voiding difficulties and significant residual urine volumes were started on clean intermittent catheterisation alone or together with prophylactic antibiotics in those with recurrent urinary tract infections. Children with detrusor hyperreflexia on VUD were treated with oxybutinin, whereas one child with mild bladder neck incompetence was treated with ephedrine. All achieved continence. The children have been followed up for a mean of three years (3 months to 16 years). Two children died within eight months of onset of the bladder dysfunction, but treating their bladder symptoms helped ease the discomfort and the inconvenience associated with urine infections and incontinence. Medication was unnecessary in two cases (7 and 10) as incontinence was acceptable in one child because of young age and a regular voiding regimen achieved continence in the other.

Discussion

CNS tumours are a rare cause of bladder dysfunction in children, as reflected in one series by Blavias in which spinal and brain tumours accounted for 0.06% of 336 patients with neurological conditions investigated for vesico-urethral dysfunction.⁵

We have shown that various combinations of storage and voiding dysfunction can occur with tumours along the neural axis from the pons to the cauda equina. This is what we would expect given the complexity of central neural control of micturition, which requires coordinated actions of the autonomic and somatic nervous system.⁶ An area in the dorsal tegmentum of the pons is thought to act on a spino-bulbo-spinal pathway and "switch" between the storage and the voiding phases of micturition.⁷ The central function of the pons in the normal micturition reflex was first recognised by

Barrington in animal studies in 1925.⁸ This was later supported by electrophysiological studies in which stimulation of bladder afferents produced field potentials in the pontine micturition centre⁹ and by positron emission tomography of the human brain during micturition, which showed an increased metabolic activity in the pontine area.¹⁰ Neural pathways that modulate bladder function traverse the length of the spinal cord between the pons and the sacral spinal cord. Interruption of these pathways may result in detrusor hyperreflexia and/or loss of the coordinated action of the detrusor and the external striated urethral sphincter known as detrusor sphincter dyssynergia (DSD).

Few clinical reports in adults and children with pontine tumours document voiding dysfunction.¹¹ Ueki reported urinary symptoms in 22 patients with pontine tumours,¹² and Renier and Gabreels in 1980 observed urinary retention and difficulty in voiding in 71% of children with pontine tumours.¹³ One of our patients had a brainstem astrocytoma arising at the level of the left facial colliculus and developed DSD. The contribution of suprapontine centres to neuropathic bladder dysfunction is poorly defined with the exception of the frontal lobes.¹⁴ Our patient with midbrain involvement secondary to a recurrence of a cerebellar astrocytoma showed a storage dysfunction in the form of hyperreflexia, with no dyssynergia. This may imply that the micturition centre modulating filling extends to the midbrain or that this area in the brain mediates the inhibitory influences from higher centres. This child had an internuclear ophthalmoplegia presumably owing to the proximity of the median longitudinal fasciculus to the area involved in micturition.

INCIDENCE OF BLADDER DYSFUNCTION IN SPINAL AND BRAIN TUMOURS

Urinary dysfunction is a frequent symptom in children with spinal tumours. Dincer *et al* in a retrospective review reported urinary dysfunction in 40.8% of children with spinal tumours.¹⁵ Bladder dysfunction is, however, rare in children with brain tumours and this is reflected in the few clinical reviews reporting this association. In a series of 462 patients with brain tumours, Ueki reports an incidence of 18% of patients with bladder dysfunction with the highest incidence seen in those with pontine tumours.¹²

ONSET AND DEGREE OF BLADDER DYSFUNCTION IN SPINAL TUMOURS

The location, size, underlying histology, and any delay in diagnosis of a spinal cord tumour combine to determine the clinical course of bladder dysfunction—that is, the time of onset and severity. Bladder dysfunction is often a late finding unless there is neoplastic infiltration of the conus medullaris.^{2 16 17} In our series, urinary symptoms presented late in children with tumours of the cervical and thoracic spinal cord, whereas urinary symptoms were the first to appear in one child with a conus and cauda equina tumour. The biological behaviour of the

tumour, its invasiveness, and response to treatment will largely determine whether bladder dysfunction is transient, resolving after treatment of the underlying tumour, or persistent. We compared our six children with an intramedullary spinal cord tumour and chronic bladder dysfunction with seven children with operated intramedullary spinal cord tumours and normal bladder function presenting over the same time interval. The main feature differentiating the two groups was tumour histology. In the children with normal bladder function most tumours were of low grade malignancy with predominantly cystic components.

OUTCOME

Advances in microsurgical techniques, radiotherapy, and, possibly, chemotherapy have improved survival in children with CNS tumours. Because of this the goals of treatment have broadened to include an improved quality of life; urological complications then become important determinants of the quality of life.

A VUD study remains the definitive and most informative investigation in children with neuropathic vesicourethral dysfunction.¹⁸ The simultaneous pressure measurements superimposed on the fluoroscopic appearance of the bladder and urethra provide valuable information on the behaviour of the bladder and urethra during filling and voiding.¹⁹ We were able to diagnose two types of voiding dysfunction in terms of distal sphincter behaviour: DSD and a fixed distal sphincter. The diagnosis of poor compliance, open bladder neck during filling, hyperreflexia, high pressure voiding, and vesicoureteric reflux can be made quickly and easily with this method.²⁰ Correct interpretation of the urodynamic findings is essential for rational treatment, and these findings may also have prognostic significance. In their study on VUD evaluation of neuropathic vesicourethral dysfunction in children, Mundy *et al*¹⁹ showed that DSD was the main determinant of voiding efficiency and the most important cause for renal impairment; the state of the bladder neck during filling was the main determinant of bladder capacity; and poor compliance was the main ominous prognostic factor for continence. An ultrasound scan before and after micturition is a useful screening test that reliably identifies cases with significant residual volumes, thickening of the bladder wall, and upper renal tract dilatation—all indicators of altered lower urinary tract function.

The diagnosis and treatment of CNS tumours are distressing in themselves, additional incontinence and recurrent urinary tract infections are also distressing and can be demoralising for children and families. Clean intermittent catheterisation is an effective method of bladder emptying and can be used

alone or in combination with anticholinergic and α adrenergic agents to achieve satisfactory continence.

CONCLUSIONS

Urinary symptoms, although frequent in children with spinal cord tumours, are often underplayed. Our series shows that although bladder dysfunction occurs late in the course of most spinal cord tumours, loss of bladder control in established cases can be the earliest indication of tumour recurrence. Bladder dysfunction causes significant morbidity in surviving children. In these cases it is important to assess fully bladder and urethral dysfunction. VUD remains the definitive and most informative investigation in children with neuropathic vesicourethral dysfunction. However, if this is not possible because of the medical condition of the child, useful information can be obtained from an ultrasound scan before and after micturition.

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