Micturitional disturbance in herpetic brainstem encephalitis; contribution of the pontine micturition centre

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Abstract
Micturitional disturbance is rarely mentioned in human herpetic brainstem encephalitis although the pontine tegmentum, called the pontine micturition centre, seems to regulate the lower urinary tract in experimental animals. The case of a 45 year old man, who developed subacute coma and hiccup-like dysrhythmic breathing, and needed assisted ventilation is reported. Examination of CSF showed mononuclear pleocytosis and antibody against herpes simplex virus type 1, but the opening pressure was 90 cm H2O. Brain CT showed brain swelling, predominantly in the posterior fossa, and bilateral subdural effusion. Herpetic brainstem encephalitis was diagnosed, and he received 900 mg/day vidarabine. On regaining consciousness, he had left trochlear nerve palsy, left corectopia, ageusia, and urinary retention. Brain MRI showed right side dominant, bilateral pontine segmental lesions extending slightly to the midbrain and medulla. After two weeks he was able to urinate but showed nocturnal urinary frequency, urinary incontinence, and voiding difficulty. Urodynamic studies showed a residual urine volume of 350 ml and detrusor hyporeflexia on voiding. Micturitional disturbance gradually disappeared together with the neurological signs. The bilateral pontine tegmental lesions in this patient are similar to those in previous findings on brainstem strokes, evidence of the presence of a pontine micturition centre in humans.

Case report
A 45 year old, previously healthy man developed band-like headaches around the bilateral occipitotemporal area which responded partially to analgesia but continued for five weeks, changing to a persistent throbbing headache in the bilateral frontal area. A week after onset he was admitted to our hospital. On admission his body temperature was normal, and he was alert and responded well, although his neck was stiff and the Kernig sign was positive. The ocular fundi, pupils, extraocular muscles, and other cranial nerves were intact, and coordination of the limbs was normal. Tendon reflexes were active and symmetric with no extensor planter responses. Sensations to pin prick and position were normal. The second day after admission he gradually became somnolent. On the fourth day he was comatose and had no oculocephalic reflex, hiccup-like dysrhythmic breathing, and a fever of 38.5°C. An indwelling urinary catheter was used to monitor urinary volume, and he was placed on assisted ventilation. Periperal blood analysis showed normal findings. An EEG showed diffuse slowing, without periodic synchronous discharge. Brain CT detected diffuse brain swelling, particularly in the posterior fossa, and bilateral subdural effusion with nstive. Examination of CSF showed a low opening pressure of 90 cm H2O, mild mononuclear pleocytosis of 10 /mm3, and increased...
total protein of 93 mg/dl. Antibody values against HSV-1 in the CSF and the serum respectively were 0.583 and 1.864 in the IgG enzyme immunoassay and 1:32 and 1:256 in the complement fixation test. The antibody index was 8.5 (albumin 60 mg/dl in CSF and 4100 mg/dl in serum). Herpetic encephalitis, predominantly in the brainstem, was diagnosed.

Aciclovir (1200 mg/day) was started, but was without benefit. On treatment with 900 mg vidarabine/day, 24 mg dexamethasone/day, and 900 ml mannitol/day, he gradually regained normal consciousness on the 32nd day. Brain oedema and subdural effusion had disappeared on the follow up brain CT. A CSF examination gave a normal opening pressure of 150 cm H2O, no pleocytosis, and mildly increased total protein of 44 g/dl. At this time, after removal of the urinary catheter, he had left trochlear nerve palsy, left corectopia, ageusia, and urinary retention, and needed clean, intermittent catheterisation. Brain MRI showed right side dominant, bilateral pontine segmental lesions extending slightly to the midbrain and medulla (fig 1), but no apparent cerebral lesion. He gradually became able to urinate and to walk to the toilet. On the 44th day, as he still had nocturnal frequency, urinary incontinence and voiding difficulty, urodynamic studies were made.

The methods and definitions used for the urodynamic studies conformed to the standards proposed by the International Continence Society. Neither urinary tract infection nor organic obstructive urological disease were present. 

![MRI](image1.png)

Figure 1  MRI (A Axial plane R–L, B sagittal plane; T2 weighted image, TR 2500, TE100). Abnormally high signal intensities present in the right side dominant, bilateral pontine tegmentum, and extend slightly to the midbrain and medulla.

![Urodynamic Study](image2.png)

Figure 2  Results of urodynamic studies. Simultaneous recordings of intravesical pressure (Pves) and external urethral sphincter EMG. Bladder volume at first desire to void (FDV) was 200 ml and at maximum desire to void (MDV) 500 ml. There is no detrusor hyperreflexia. During voluntary micturition (VOID), the detrusor pressure rise was insufficient, evidence of hypocontractile bladder on voiding. EMG activity has disappeared, and there is no detrusor-sphincter dyssynergia (DSD).
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found by digital examination of the prostate and cystourethrography. He had a residual urine volume of 350 ml. Water cystometry showed a bladder volume of 200 ml at first desire to void, and 500 ml at maximum desire to void, without detrusor hyperreflexia. External sphincter EMG showed normal anal and bulbocavernous reflexes, with no detrusor-sphincter dysynergia or uninhibited sphincter relaxation. During voluntary micturition the detrusor pressure rise was insufficient, indicative of a hypocontractile bladder (fig 2). His urinary symptoms gradually improved without medication and had disappeared almost completely up to the 60th day with no abnormal uroflowgram or residual urine. A month later left trochlear palsy disappeared, but ageusia has persisted for the past two years.

Discussion
Herpetic brainstem encephalitis was diagnosed because the main clinical features of our patient had acute deterioration of consciousness with absence of the oculocephalic reflex, hiccup-like dysrhythmic breathing, left trochlear palsy, left corectopia after-wards, suggestive of brainstem tegmental lesion. Ageusia reflects a lesion of the central gustatory pathway, which travels in the medial part of the medial lemniscus or of the reticular formation.13 14 MRI showed right sided dominant, bilateral pontine tegmental lesions that extended slightly to the midbrain and medulla. These lesions explain the neurological findings and contributed to his micturitional disturbance. Holman14 stated that voiding difficulty could be a sign of posterior fossa tumours. Ueki20 later showed that of the posterior fossa tumours urinary incontinence and voiding difficulty are common in pontine tumour. Betts et al21 and Manente et al22 found voiding difficulty or retention in a patient with a tumour of the dorsal pons. Previously, we showed that micturitional disturbance is common when the pons is affected in brainstem strokes. The lesions detected by MRI were concentrated in the pontine reticular nucleus and the reticular formation adjacent to the medial parabrachial nucleus and locus coeruleus (fig 3). This region, called the pontine micturition centre in experimental animals,1-3 regulates lower urinary tract function by way of the spinobulbos-pinal reflex. The lesions in the patient reported here are similar to those in our previous findings and support the presence of a pontine micturition centre in humans.

1 Barrington FJF. The relation of lesions of the hind-brain to micturition. Brain 1921;44:23–53.

Figure 3 Suspected pontine micturition centre in humans. The dotted circle (pontine micturition centre) includes the pontine reticular nucleus, the reticular formation adjacent to the medial parabrachial nucleus, and the locus coeruleus. (Cited from Sakakibara et al.)
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