Abstract  Raised intracranial pressure (ICP) often complicates the course of cryptococcal meningitis. The pathogenesis of the severely raised cerebrospinal fluid (CSF) pressure commonly associated with this condition is largely unexplained, because the majority of patients have normal cranial computed tomographic (CT) findings when diagnosed. We report a case of cryptococcal meningitis in a child who had severely raised CSF pressure on admission, and in whom repeated CT scanning showed progressive enlargement of the subarachnoid space and ventricular system during the course of treatment. The normalization of these spaces after ventriculoperitoneal (VP) shunting suggests a distal CSF block as the cause of the raised ICP in this patient. The CSF pressure was monitored and treatment with oral acetazolamide and furosemide resulted in a definite, but slow and incomplete lowering of ICP. Intrathecal therapy with hyaluronidase had no beneficial effect on either ICP or the degree of visual loss.

Key words  Cryptococcal meningitis · Intracranial pressure monitoring

Introduction

Raised intracranial pressure (ICP) is a well-known complication of cryptococcal meningitis [11]. A review of the literature, however, shows that both the pathogenesis and the most appropriate treatment of the raised cerebrospinal fluid (CSF) pressure associated with this condition are still unresolved issues [3].

The purpose of this report is to demonstrate the effect of different methods of treating raised ICP in a patient with cryptococcal meningitis using repeated ICP monitoring. The serial ICP and cranial computed tomographic (CT) changes in our patient furthermore strongly suggest a distal CSF block at the level of the arachnoid villi as most likely cause of raised ICP in this condition.

Case report

A 12-year-old girl presented with a 3-week history of headache, neck stiffness, dizziness and vomiting. She had also complained of decreased vision and diplopia for 1 week before admission. Her previous medical history was negative with no disease contact or excessive exposure to animals or birds.

On admission the patient appeared chronically ill with a low-grade fever of 37.8°C. Her weight was 23 kg (below the 3rd percentile) and her height 140 cm (50th percentile). A fungal infection of two finger nails of the right hand was present. Abnormal findings on systemic examination were confined to the neurological system. Although slightly drowsy, she was fully conscious. Marked meningeal irritation was present. The pupils were equal, 5 mm in size, and reacted poorly to light both directly and indirectly. Both optic discs were very pale, the right eye blind and only finger counting possible with the left eye. Bilateral cranial nerves III, IV and VI palsies were present while cranial nerves VII, VIII, IX, X, XI and XII were affected only on the right. Clinically the patient had slurred speech and regurgitation of fluids through the nose. Examination of the motor system showed weakness of the right leg (grade III/V power) and absence of the deep and superficial reflexes bilaterally. The sensory, cerebellar and autonomic systems were intact.
Fig. 1  a CT scan on admission. Slight prominence of the sulci and lateral ventricles can be seen. No focal intracranial lesion is demonstrated. b CT scan 15 weeks after admission. The sulci, sylvian fissures and lateral ventricles are more prominent than before. No ventriculo-sulcal disproportion is present. c CT scan 19 weeks after admission (4 weeks after ventriculo-peritoneal shunt). The size of the lateral ventricles and subarachnoid space is now appropriate for age. A small post-shunting right-sided subdural effusion is present. The ventriculo-peritoneal shunt is in situ.

A CT scan of the brain on admission was initially reported as normal. However, careful re-examination showed slightly prominent cortical sulci and ventricles but no mass lesion (Fig. 1). Continuous lumbar CSF pressure monitoring over a period of 1 h by means of a method described previously [8] demonstrated a baseline CSF pressure of 80 mmHg (Fig. 2).

The CSF was clear with normal chemistry but a predominantly lymphocytic pleocytosis. An India ink stain of the CSF revealed numerous encapsulated yeast cells, typical of cryptococcal meningitis. The cryptococcal antigen titre in the CSF was 1:1024 and the cryptococcus cultured from the CSF was sensitive to both amphotericin B and flucytosine. The full blood count was normal. Investigation of the patient's immune status showed that both the total number of B and T lymphocytes as well as the lymphocyte response to stimulation with Candida antigen (9% of the expected) were decreased. These findings, however, were not considered significant by our laboratory. The patient's HIV status was negative.

Treatment was started with amphotericin B (1 mg/kg day) intravenously and flucytosine (150 mg/kg day in four divided doses) orally. Oral furosemide 0.75 mg/kg day and acetazolamide 75 mg/kg day (in three divided doses) were administered in an attempt to decrease ICP by reducing CSF production. Weekly continuous lumbar CSF pressure recording and CSF analysis were performed. The patient's ICP profile during the 3 months of hospitalization as well as the timing of and the response to the different treatment modalities are shown in Fig. 3. Within 3 weeks of the start of diuretic therapy, the patient's symptoms of raised ICP resolved completely while the lumbar CSF pressure decreased from 80 mmHg to 35 mmHg (Figs. 2, 3). A repeat CT scan done at this stage showed the subarachnoid space and the ventricular system to be slightly more prominent than before. All the neurological signs which were present on admission, except the visual disturbance, gradually resolved during the first 6 weeks of treatment. Within 1 week of admission, however, the patient became completely blind and developed marked bilateral optic atrophy.

Treatment with intrathecal hyaluronidase (1500 IU weekly) was started when the ICP reached a plateau of 30 mmHg after 4 weeks of treatment with acetazolamide and furosemide. Apart from a paradoxical increase in lumbar CSF pressure during the 1st week of therapy, no persistent change in either ICP or vision occurred during the 10 weeks of treatment with hyaluronidase (Fig. 3). A ventriculo-peritoneal shunt was considered when the secondary rise in ICP occurred after the first dose of intrathecal hyaluronidase. However, constant lumbar CSF drainage over 4 days did not lead to any improvement in vision or pupillary reflexes, and in the absence of clinical signs of raised ICP a shunt was not inserted.

In spite of her clinical improvement, the patient had persistent yeast cells in the CSF as well as a sustained high anticryptococcal CSF titre (1:128). Antifungal therapy was changed to fluconazole, which normalized the CSF findings and reduced the anticryptoccal titre to 1:64 within 8 weeks of the start of therapy.

Fifteen weeks after treatment was begun the patient again developed persistent vomiting and severe headache. A third CT scan now showed marked enlargement of the subarachnoid space and mild hydrocephalus, but no parenchymal involvement (Fig. 1). On account of the symptoms of raised ICP, together with the CSF pressure that failed to normalize and the signs of progressive hydrocephalus on CT scan, a ventriculo-peritoneal shunt was inserted. This resulted in dramatic improvement of the patient's symptoms of raised ICP but had no effect on the blindness. A post-operative CT scan showed complete resolution of the communicating hydrocephalus (Fig. 1). The patient was discharged and admitted to a school for the blind.

Discussion

Pathological studies in cryptococcal meningitis have shown that the meninges both at the base of the brain and over the cerebral convexities are diffusely involved in this disease [13]. A predominantly basal meningitis, as in tuberculous meningitis, typically results in obstruction of the basal cisterns. The CT appearance of this type of communicating hydrocephalus is panventricular dilatation and obliteration of the supratentorial subarachnoid spaces, often early during the course of the disease [10].

Diffuse involvement of the cortical meninges as in bacterial meningitis, however, often results in a distal type of