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BRIEF COMMUNICATION

Akiko Arimoto
Hiroshi Yoshioka
Minako Kihara
Tomohito Yagi
Tadashi Sawada

Tuberculous meningitis with hydrocephalus

Contribution of PCR assay of CSF before VP shunting

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A. Arimoto (✉) · H. Yoshioka · T. Yagi
T. Sawada
Department of Pediatrics,
Kyoto Prefectural University of Medicine,
465 Kajii-Cho, Kawaramachi,
Hirokoji, Kamigyo-ku,
Kyoto, 602-8566 Japan
Tel.: +81-75-251-5571
Fax: +81-75-252-1399

M. Kihara
Kyoto Shakaihoken General Hospital,
Kyoto, Japan

Abstract A 10-month-old infant with tuberculous (Tb) meningitis accompanying hydrocephalus was successfully treated with a VP shunt operation soon after a PCR assay of CSF was found to be negative for *Mycobacterium tuberculosis*. PCR assay of CSF is helpful for determination of the timing for VP shunting in Tb meningitis.

Key words Tb meningitis · Hydrocephalus · VP shunt · PCR assay

Introduction

The incidence of tuberculous (Tb) meningitis is low, but even today its prognosis remains poor. Many patients have such complications as hydrocephalus, basal exudate, infarction and tuberculoma.

Cases with noncommunicating hydrocephalus usually require ventricular drainage or a ventriculoperitoneal shunt (VP shunt) in addition to the antituberculosis treatment. It would be preferable for infants with Tb meningitis and concomitant noncommunicating hydrocephalus to receive a permanent shunt as early as possible, because temporary ventricular drainage limits their body movements and could inhibit their normal development. However, a VP shunt operation can bring about intraperitoneal dissemination of *Mycobacterium tuberculosis* when it is done before the CSF becomes negative for *M. tuberculosis*. With the traditional culture examination it is many days before one can be sure that the CSF is negative for the mycobacterium, so that the best timing for the VP shunt operation may be missed. Here we report a case of miliary Tb and Tb meningitis in a 10-month-old Japanese infant, in whom a VP shunt operation was performed soon after confirmation that CSF was negative for *M. tuberculosis* was yielded by a polymerase chain reaction (PCR) assay and in whom the operation had a satisfactory outcome.

Clinical history and management

A 7-month-old Japanese infant girl became febrile in December 1992 in the United States. Her pediatrician prescribed antibiotics, but the fever did not respond for 3 weeks. Culture of an exudate from her left ear revealed acid-fast bacilli. She was admitted to hospital: a chest radiogram showed a miliary pattern in both lung fields, and brain computed tomography (CT) revealed mild dilatation of the lateral ventricles. Examination of cerebrospinal fluid (CSF) revealed pleocytosis (100/mm^3) with lymphocytosis, a low glucose level (31 mg/dl) and a high protein level (130 mg/dl). Tuberculin skin tests of the patient, her father and her mother were all strongly positive, and her father was found to have active pulmonary tuberculosis. *M. tuberculosis* was isolated from the patient's gastric aspirate, ear drainage and CSF. A diagnosis of Tb meningitis and miliary tuberculosis was recorded, and treatment with isoniazide (INH), rifampicin (RFP), ethambutol (EB) and pyrazinamide (PZA) was initiated. Since the pulmonary infiltration was resolving, she was discharged from the hospital in January 1993. Two months later, however, the patient was losing ground, with poor weight gain and poor motor development. When she was readmitted to the hospital, CSF examination revealed meningeal inflammation (cell count 500/mm^3, glucose

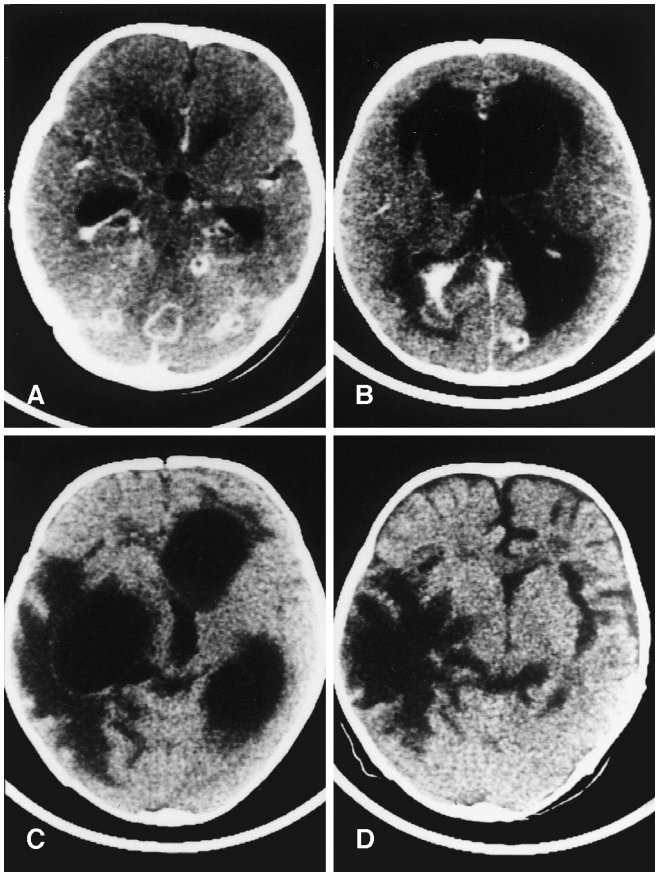

Fig. 1 A–D Serial changes on CT. **A** Enhanced CT on 9 April 1993. Note hydrocephalic changes and multiple ring-enhancement lesions in occipital lobe and ventricular wall. **B** Enhanced CT on 12 May 1993. Tuberculoma adjacent to the lateral ventricle seems to interrupt CSF flow, thus causing marked hydrocephalus and periventricular edema. **C** CT on 7 June 1993. Periventricular edema increased after extraction of the drainage. **D** CT on 8 July 1993. Following VP shunt operation, ventricular dilatation improved, but periventricular edema persisted

16 mg/dl, protein 500 mg/dl). The family then returned to Japan, and the patient was admitted to our hospital for further treatment on 22 March 1993.

On admission the infant was alert, but irritable. Her body temperature was 37.2 °C, pulse rate 140/min, and respiration 36/min. Blood pressure was 80/0 mmHg. Body weight was 6530 g, head circumference was 43.0 cm. The anterior fontanel was 1.5×1.5 cm and flat. The breath sounds were rough, and no crackles were audible. The heart, abdomen, and extremities were normal. Deep tendon reflexes and muscle tone were normal. Kernig and Brudzinski signs were absent. Optic fundi were normal. A granulomatous lesion was noted in the left middle ear.

White blood cell counts were 21,800/mm^3, the erythrocyte sedimentation rate was 14 mm/h, and the C-reactive protein level was 1.4 mg/dl. CSF showed lymphocytosis (1,021/mm^3, mononuclear cells 76%), lowered glucose (14 mg/dl), and elevated protein (329 mg/dl). There was no auditory brain stem response (ABR) below 90 db on the left side. A brain CT scan obtained on 9 April showed hydrocephalic changes and multiple ring-enhancement lesions in the occipital lobes and on the ventricular walls (Fig. 1A). CT also showed that the left middle ear contained no air and was filled with a content having the density of soft tissue. Brain MRI showed multiple round lesions of white matter intensity in the cerebellum and occipital lobes on T1-weighted images. T2-weighted images revealed hypointense lesions surrounded by a hyperintense ring and lesions that were heterogeneous in intensity (Fig. 2A).

She was treated with INH, RFP, PZA and streptomycin (SM). Dexamethasone and 10% glycerol were also administered intravenously (Fig. 3). Since CT scans revealed progression of hydrocephalus (Fig. 1B) and disturbed conciousness, appetite loss and nausea were noted, a right ventricle drainage operation was performed on 19 May. However, the drainage tube was obstructed, and it was removed on 26 May. CT scans on 7 June demonstrated marked dilatation of both lateral ventricles and right periventricular edema (Fig. 1C). A drainage operation was performed on both sides, and the hydrocephalic condition was greatly improved. On 29 June, however, the drainage tubes were removed to avoid infection. Dilatation was again observed in both lateral ventricles on CT scans of 5 July. At that time a PCR assay for *M. tuberculosis* in the CSF was performed, and soon after it was ascertained that CSF was negative for *M. tuberculosis*, a left VP shunt operation was performed. CT scans on 8 July showed a great improvement of ventricular dilatation and the periventricular edema (Fig. 1D). On 5 August tuberculomas were hardly discernible on T1-weighted MRI (Fig. 2B), but after

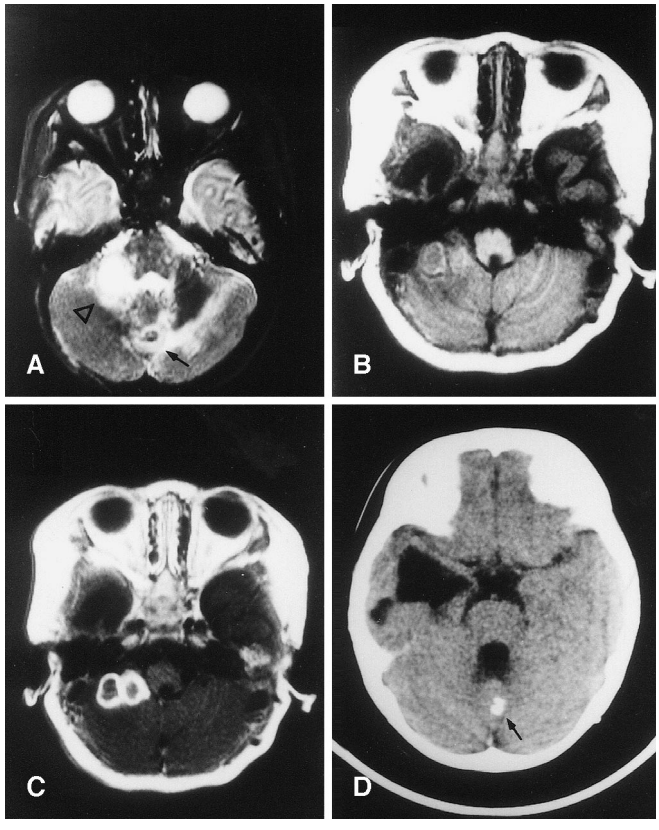

Fig. 2 **A** MRI (TR2500/TE90) on 8 April 1993. Note tuberculomas with central low intensity (*arrow*) or with central high intensity (*arrowhead*). **B** MRI (TRI501/TE15) on 5 August 1993. **C** Gd-DTPA-enhanced MRI (TR501/TE15) on 5 August 1993. Tuberculomas are ring enhanced. **D** CT on 25 August 1994, 16 months after therapy: a calcified tuberculoma (*arrow*) and a cystic lesion in the right temporal lobe remained

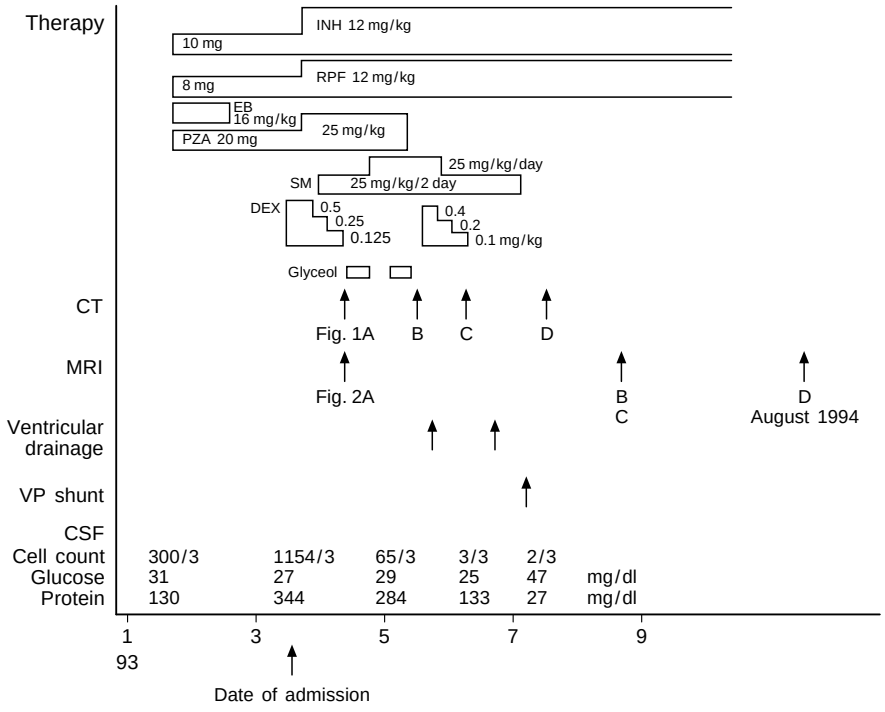

Fig. 3 Clinical course of the case

Gd-DTPA injection several tuberculomas were visible with ring or nodular enhancement (Fig. 2C). When the girl was discharged in September, 1993, only a few calcified tuberculomas were visible on CT scans (Fig 2D). Her general condition was fine, and her development quotient (DQ) had improved from 44 to 81.

Discussion

Hydrocephalus almost always appears if a patient with Tb meningitis survives longer than 4–6 weeks [2]. In this case, mild ventricular dilatation was seen at the onset of the disease. Four months later CT showed marked hydrocephalus, brain edema and tuberculomas with surrounding edema. Ventricular drainage operations were performed twice. The first time, the tube had to be removed because it was obstructed. The second time, the infant could not bear to lie still in bed for days on end; when she rolled over or sat up, the drainage pressure could not be adequately controlled and the risk of infection through the tube was increased. Therefore, placement of a permanent shunt, rather than temporary drainage, was desirable as early as possible, not only to avoid infection but also to avoid holding back her motor and social development. However, a VP shunt operation should not be performed until the CSF is completely free of *M. tuberculosis*: if it is done too early it can result in peritoneal dissemination of *M. tuberculosis* [1].

Recently, the PCR assay has been used for diagnosis of Tb infection [3–5, 9, 11]. Several papers have reported an advantage of the PCR assay performed in CSF samples for the diagnosis of Tb meningitis [6–8, 10, 12]. Those reports suggest that the PCR assay enables a rapid diagnosis of Tb meningitis and has a higher sensitivity and specificity than such traditional methods as culture and microscopy. However, there are few previous reports describing use of the PCR assay to evaluate the efficacy of therapy [13] or to determine the timing of the VP shunt placement for correction of hydrocephalus in Tb meningitis. In the present case, as soon as we ascertained that the CSF was negative for the mycobacterium by PCR assay, we proceeded to performance of the VP shunt operation. We had to wait only a few days for the result of the assay, and could then release the patient from the terrible stress and risk of drainage tube infection. Furthermore, early removal of the drainage tube was also important to allow the patient to catch up on her development. Therefore, our experience suggests that the PCR assay of CSF for *M. tuberculosis* is very useful not only for early diagnosis of Tb meningitis but also for optimal timing of a VP shunt operation.

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