Eur J Pediatr (1982) 139 : 158–159

Unilateral Hydrocephalus Due to Obstruction of the Foramen of Monro: Another Complication of Intrauterine Mumps Infection?

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Abstract. Unilateral hydrocephalus due to foramen of Monro-obstruction was diagnosed in a newborn who presented with macrocephaly at birth. The mother had mumps in the second trimester of pregnancy and immunological studies indicated possible intrauterine infection of the baby with mumps virus. His condition deteriorated rapidly, and he developed myoclonic seizures. The possible relationship of intrauterine mumps infection to neonatal neurological complications is discussed.

Key words: Hydrocephalus – Mumps – Intrauterine infection

Introduction

The cause of congenital aqueduct stenosis is usually obscure. An experimental model for its induction has been developed by fetal inoculation with mumps virus [7]. Another cause of congenital hydrocephalus, obstruction of the foramen of Monro, is exceedingly uncommon, and has not previously been related to mumps. The following case may well illustrate this association.

Case Report

A 2900 g male infant was the product of 38 weeks gestation and a normal vaginal delivery. The mother had mumps during the fifth month of pregnancy. Macrocephaly was noted immediately after birth. The OFC was 38 cm, and a CT brain scan showed enlargement of the right lateral ventricle, which was interpreted as due to an obstructive lesion at the foramen of Monro. The baby was transferred to our hospital for further studies at the age of three weeks. Physical examination on admission revealed a full term, alert and irritable neonate. The head configuration was scaphocephalic and the OFC was 40.5 cm. The anterior fontanelle was full but soft and measured 6×6 cm. The posterior fontanelle measured 4×4 cm and a third fontanelle was also palpable. He had prominent head lag. The rooting, sucking, grasping and Moro reflexes were easily elicited; however, stepping and placing reactions were lacking. There was a right gaze preference and he did not follow persistently.

Muscle tone was moderately increased, more so on the left. The deep tendon reflexes were brisk and symmetrical. Frequent episodes of myoclonic convulsions were observed.

Complete blood count, routine blood chemistry and urinalysis were normal. Spinal fluid was clear and colorless, with an opening pressure of 240 mm H_2O. Protein concentration was 74 mg/dl and glucose 52 mg/dl (blood glucose 100 mg/dl). The cell count was 2/mm^3. EEG showed a right frontal spike focus. Isotope brain scan using ^{99m}Tc was normal. Computerized tomography of the brain showed moderate dilation of the right lateral ventricle, enlargement of the right hemisphere with resultant displacement of the left hemisphere (Fig. 1). Since there was evidence of increasing size of the right lateral ventricle, a ventriculoperitoneal shunt was installed on the 28th day of life. At surgery the cerebral cortex appeared edematous, ischemic, and hard on palpation. A right frontal brain biopsy was obtained and showed glial reaction with microscopic calcifications around blood vessels.

Immunologic-Virologic Studies

The antibody and cell-mediated immune responses were studied in the patient, and in his mother.

An effort to isolate mumps virus from the patient's CSF, pharyngeal washings, urine, feces and buffycoat yielded no positive results. A search for possible intrauterine infection with rubella, herpes simplex, cytomegalovirus, toxoplasmosis and syphilis was unrewarding.

Mumps complement fixation tests were performed with mumps V and S antigens which were prepared according to Henle [3]. Neutralizing antibodies to mumps virus were measured as described by Buynak [2]. Sera were heat-inactivated at 56°C for 30 min and absorbed with an equal volume of 10% sheep red blood cells. All serologic tests in the infant were done at the age of 4 months. Only traces of complement fixing (CF) antibodies to S antigen were found in the infant whereas the CF antibody titer to V antigen was 1:20–1:40. The neutralizing antibody titers (NT) in serum and CSF were 1:64 and 1:2, respectively.

No attempt was made to determine mumps specific IgM antibodies.

Maternal serologic tests revealed CF antibody titers of 1:20 to mumps S and of 1:80 to V antigens. The neutralizing antibody titer to mumps virus was 1:250.

The cellular immune response of the patient was studied by delayed hypersensitivity and lymphoproliferative assays. Delayed hypersensitivity was studied by the mumps skin test [8] performed at the age of 10 weeks after the serologic and the other immunologic tests had been done. The skin test with live attenuated mumps virus (Merck, Sharpe and Dohme, NY, USA) showed an erythema of 12 mm and an induration of 10 mm, 48 h after testing. The lymphocyte mitotic response to mumps antigen and to phytohemag-

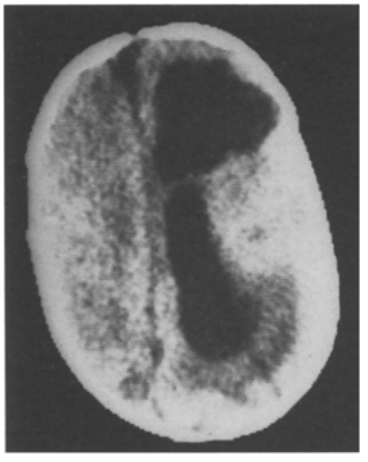

Fig. 1. CT of brain demonstrating severe dilatation of the anterior and occipital horns of the right lateral ventricle, and midline shift to the left

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0340-6199/82/0139/0158/$ 01.00

Table 1. Cell-mediated immune function in the mother, infant and appropriate controls

Stimulation	Mother	Controls[a]		Patient	Controls[a]	
		1	2		1	2
Index						
PHA	560	600	485	220	360	480
Mumps	18	20	1.2	16	3.6	1.9

[a] Normal, age-matched healthy controls

glutinin (PHA) was studied when the patient was 8 weeks old. Lymphocytes were separated from heparinized blood by centrifugation through a Ficol-Hypaque gradient. Cell were washed and resuspended in medium RPMI 1640 supplemented with 100 units/ml of penicillin, 50 μg/ml of streptomycin, 300 μg/ml of glutamine and 10% fetal calf serum. Aliquots of 5×10^5–1×10^6 lymphogytes were incubated in microtiter wells (Nunc Ltd) with 0.1 ml mumps antigen (Flow Labs Inc.) or 10 μg phytohemagglutinin (Sigma Inc.). Cultures were run for 96 h at 37°C in 5% CO_2. Twenty-four hours before harvesting lymphocytes, 1 μci of tritiated thymidine was added to each well. Stimulation indices were calculated as the ratio of counts/min of test cultures to corresponding controls. In both, mother and child, the mitotic response to PHA was normal (Table 1). No spontaneous blastogenesis was found, while stimulation of peripheral blood lymphocytes with mumps antigen revealed significantly high stimulation indices.

Discussion

Mumps infection in infants during the perinatal period occurs infrequently and is usually benign. A long term prospective study in New York City on the fetal effects of various maternal infections provided substantial information on the fetal death rate in pregnancies complicated by different virus infections at various periods of gestation [11]. In mumps and rubella an increased fetal wastage was observed when maternal disease occurred in the early stages of gestation. The nature of the lethal effects of mumps in early gestation are not well understood. Abortions usually occurred shortly after onset of maternal parotitis.

In our case mumps virus was not isolated from the CSF. However, the clinical history of maternal mumps during pregnancy, the serological evidence of recent mumps infection in the mother, a positive mumps skin test in the infant and the positive blastogenic transformation after stimulation with mumps virus both in the mother and infant, all serve as strong evidence for a causal relationship between intrauterine mumps infection, mumps ependymitis and congenital hydrocephalus due to obstruction of the foramen of Monro. The titer of neutralizing antibodies in the cerebrospinal fluid may reflect a passive transfer from the serum through an immature blood brain barrier.

Johnson showed that mumps virus infection in newborn hamsters was associated with aqueductal stenosis [7]. Subsequently, St. Geme et al. [12] have demonstrated that maternal mumps viremia can result in placental and fetal infection. Intracerebral inoculation of rhesus monkey fetuses with wild mumps virus can cause viral dissemination and the virus can be isolated from many fetal tissues. Congenital hydrocephalus was induced in some of the delivered rhesus monkeys [9].

A possible role for mumps virus in the pathogenesis of aqueductal stenosis in human being was demonstrated by several authors [1, 6, 14]. Herndon and Johnson [4] found ependymal cells in the CSF of patients with meningoencephalitis. Some of these cells contained cytoplasmic inclusions suggestive of mumps nucleocapsids. The affinity of the mumps virus for ependymal cells was also observed on experimental animals [7].

A case of maternal mumps in the fourth months of pregnancy resulting in hydrocephalic twins is cited by Hollowach-Thurston in her comprehensive review [5]. One of the twins was stillborn, and the other was spastic and severely retarded.

Thompson et al. [13] demonstrated in 7 out of 23 infants with congenital CNS anomalies and increased cell mediated immune response (lymphocyte blastogenesis) to mumps virus antigen, implying that intrauterine exposure to mumps virus had occurred in some infants with congenital anomalies.

We therefore suggest that maternal mumps should be regarded as a potentially harmful event to the fetus at any time during pregnancy. However, the exact incidence of congenital hydrocephalus due to intrauterine mumps infection can only be determined by more large-scale prospective studies.

Acknowledgement. This work was supported by ICRF

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Received May 4, 1981/
Accepted May 13, 1982