

## CLINICAL CONFERENCE

### Cytomegalic Inclusion Disease

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**DR. SILVERMAN:** I shall present the history of an infant who was admitted to our premature nursery on May 9, 1956. This Puerto Rican male infant was born during the thirty-sixth week of an uneventful pregnancy. An antenatal serologic test for syphilis was negative. Delivery was spontaneous. Birth weight was 1070 gm. Physical examination on admission to the nursery revealed the liver to be 1 cm below the right costal margin and the spleen was firm, 1 cm below the left costal margin. Nothing else worthy of comment was noted and the infant was managed in a routine manner. The immediate newborn period was entirely uneventful, specifically neither petechiae nor unusual degree of icterus were noted. The ocular fundi were examined, as a matter of routine, during the third and fifth weeks of life and they were described as normal.

During the sixth week of life, when the infant weighed 2080 gm, it was suddenly noted that the abdomen was quite distended. Examination at this time disclosed marked hepatosplenomegaly, both organs were firm. Again neither icterus nor petechiae were noted. There appeared to be some difficulty in swallowing. Roentgenograms of the chest at this time were normal and of the skull revealed intracranial calcification which was displayed in a pattern that seemed to outline dilated lateral ventricles. Lumbar puncture yielded cerebrospinal fluid which was negative except for protein of 198 mg/100 ml. The urine and cerebrospinal fluid were examined for the cells characteristic of cytomegalic inclusion disease and none were found.

Funduscopy examination at this time disclosed an area of chorioretinitis in the right eye. It was presumed at this time that the infant had toxoplasmosis. Blood was obtained from the infant and his mother for the Sabin-Feldman dye test. The infant was discharged

from the nursery weighing 2450 gm and doing moderately well.

He was followed in the outpatient department and at the age of 2½ months he was seen because of vomiting and otitis media. On examination the hepatosplenomegaly was again noted, and for the first time tremors of the extremities were seen. He was treated with antibiotics with no particular improvement in the vomiting, although the otitis responded. Poor feeding and vomiting persisted and as a result he was readmitted to the hospital at the age of 3 months.

On this admission the liver and spleen were felt at the iliac crest. Chorioretinitis was now evident in both eyes. Microcephaly (head circumference 5 sigma below mean as compared with minus 3 sigma in all other measurements) seemed obvious. Laboratory data were not particularly remarkable except for a low platelet count (60,000/mm<sup>3</sup>). It should be emphasized that no petechiae were evident on examination.

At 3½ months of age, while in the hospital, the infant developed signs of a respiratory infection. Pneumonia was suspected, a roentgenogram was obtained and pneumonitis of the left lung was disclosed. Antibiotics were administered and there was slow improvement. At this time the diagnosis of cytomegalic inclusion disease was reconsidered. Urine sediment now contained typical cytomegalic cells with intranuclear inclusions. In addition, gastric washings also contained cytomegalic cells with typical inclusion bodies. No such cells were found upon examination of the saliva.

At this time the report of the Sabin-Feldman dye test for toxoplasmosis was received and it was negative. A titer of 1:256 was reported in the mother's blood. Urine was sent to Dr. Thomas Weller in Boston and he reported finding a virus which appeared to be identical with a virus obtained from two other cases of

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cytomegalic inclusion disease. We also obtained aqueous humor from which Dr. Robert P. Burns of the Institute of Ophthalmology isolated virus.

(The patient was presented.)

At present the infant is 4½ months of age and in fair health. There are additional areas of chorioretinitis in both eyes. As can be seen the head is quite small. The enlargement of the spleen and liver is still quite marked. Notice particularly that there are no petechiae and that the infant is not jaundiced.

We present this infant as an example of cytomegalic inclusion disease in a living child. There have been relatively few examples of this condition described in live infants. We wish to emphasize the point that the disease may be identified in infants who survive beyond the neonatal period.

As has been well described by Wyatt and Smith and Vellios, newborns with cytomegalic inclusion disease are usually born prematurely. They are usually noted to be ill either at, or shortly after, birth. Jaundice, purpura, hepatosplenomegaly and signs of marked involvement of the central nervous system have been the most distinctive features.

The patient being presented introduces a number of interesting considerations. First, this infant did not manifest signs in the immediate newborn period and, indeed, never exhibited jaundice or purpura. Secondly, chorioretinitis was noted, a lesion which has not previously been described in cytomegalic inclusion disease. From existing reviews of this condition one cannot judge the incidence of involvement of the eye because there are very few pathologic or ophthalmoscopic examinations reported. If this feature of cytomegalic inclusion disease occurs with any regularity, it is inevitable that it will be confused with toxoplasmosis.

In addition to the Sabin-Feldman dye test which differentiates between these two diseases, the pattern of intracranial calcification appears to be different. The calcification in cytomegalic inclusion disease outlines the ventricular system, whereas in toxoplasmosis the areas of calcification are scattered and form no distinct pattern.

The finding of inclusion-bearing, cytomegalic cells in gastric washings may prove to be a useful test. I am thinking especially of the case of an infant reported by Gallagher with pulmonary cysts following pneumonitis in the newborn period. Lobectomy was performed and

cytomegalic, inclusion-bearing cells were found in the specimen. This pulmonary syndrome in young infants is by no means rare and its pathogenesis is often not clear. It would be reasonable to propose that in obscure instances of pneumonitis or obstructive emphysema in young infants, gastric washings be examined for cytomegalic cells.

**CHAIRMAN RILEY:** Dr. Alexander, do you want to say something about this?

**DR. HATTIE ALEXANDER** (New York): The fact that we are no longer dependent on morphology, alone, for diagnosis of cytomegalic inclusion virus infection merits emphasis. Dr. Thomas Weller has reported characteristic changes produced by the virus in cells from tissue culture of human foreskin when material containing virus is seeded in the cell cultures. Antiserum, to this virus, inhibits the typical cellular reaction whether it be produced in animals or patients with the infection. Weller reports isolation of the virus from liver obtained at biopsy and urine from two different patients, in one during a 3-month period.

It is interesting that Dr. Smith of Washington University has isolated an intranuclear inclusion-forming virus from salivary gland disease which is difficult, or impossible to differentiate from the virus of cytomegalic inclusion disease. If these viruses are identical, then the sources for cytomegalic inclusion disease are very widespread.

**CHAIRMAN RILEY:** Any questions?

**DR. JOAN V. BRADY** (Urbana, Illinois): Would Dr. Silverman say something about treatment as well?

**DR. SILVERMAN:** Yes. Dr. Margileth proposed that the infants be treated with gamma globulin, cortisone and blood transfusions. No comments—we have had no experience.

**DR. MAXWELL STILLERMAN** (Great Neck, L.I., N.Y.): Is there any evidence of this disease in the mother?

**DR. SILVERMAN:** We have only performed the dye test on the mother.

It is unlikely we will find any disease in the mother, if we reason from other cases. The pregnancies have usually been completely uneventful, and if the viremia is transient, I think it is unlikely that we will recover a virus. However, antibody might be expected.

**CHAIRMAN RILEY:** Has there ever been any evidence that successive infants from the same mother are apt to be involved?

**DR. SILVERMAN:** There have been reports

that successive infants have not been involved; that is to say, infants following the diseased child have been normal. There are no reports of more than one case in a family. This leads to the prevailing opinion that there is no contraindication to further pregnancies.

**DR. J. GRAUBARTH** (New Orleans): In what percentage of specimens of gastric washings from this child would you expect the typical cell?

**DR. SILVERMAN:** As only two attempts were made, one successful, this cannot be answered.

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