

# Symptomatic Increase in Intracranial Pressure Following Pancreatic Enzyme Replacement Therapy for Cystic Fibrosis

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**Summary.** A newly diagnosed 5-month-old infant with cystic fibrosis (CF) developed signs and symptoms of increased intracranial pressure (ICP) within days of starting pancreatic enzyme replacement therapy. Symptoms promptly resolved on two occasions after stopping enzyme replacement. At 10 months of age, enzyme replacement was well tolerated. *Pediatr Pulmonol.* 1995; 19:396-397. © 1995 Wiley-Liss, Inc.

**Key words:** Cystic fibrosis, intracranial pressure, pancreatic enzyme therapy.

## INTRODUCTION

Asymptomatic elevations of intracranial pressure (ICP) and a bulging cranial fontanelle in children with cystic fibrosis (CF) have been attributed to vitamin A deficiency.<sup>1,2</sup> They were described as a transient phenomenon following initiation of treatment for cystic fibrosis and improvement of the poor nutritional status.<sup>3-7</sup> It was also speculated that intracranial pressure elevations may be associated with severe respiratory distress,<sup>8</sup> and initiation of pancreatic enzyme replacement has been reported with asymptomatic bulging fontanelle.<sup>9</sup>

This report describes an infant with CF who developed symptomatic elevation of ICP within days of starting pancreatic replacement. Symptoms resolved on two occasions shortly after pancreatic enzymes were stopped. This case is of interest because the increase in intracranial pressure resulted in symptoms.

## CASE REPORT

A 1-year-old Caucasian male was diagnosed as having cystic fibrosis at 5 months of age secondary to failure to thrive, pneumonia and a sweat chloride of 123 mEq/L. He was homozygous for the mutation  $\Delta F508$ . He was a product of a normal pregnancy. He was delivered by normal spontaneous vaginal delivery. Birth weight was 3.60 kg and length was 50 cm. Length and weight had dropped from the 50th percentile and 75th percentile, respectively for age at birth to the tenth percentile and fifth percentile for age at diagnosis. When the diagnosis was made, treatment was started and included pancreatic enzyme replacement with Pancrease® (McNeil Pharmaceutical, Spring House, PA) in a dose of 700 IU/kg/feed (daily dose 4,200 IU/kg) and vitamin supplements. Two days after starting the above treatment, he began vomit-

ing, followed by development of a bulging fontanelle and irritability. He was afebrile. He was admitted to a local hospital. CT scan of the head was normal, aside from the bulging fontanelle. Lumbar puncture was negative, however, the opening pressure was not measured. While in the hospital, the pancreatic supplements were stopped. The patient did well and the discharge diagnosis was increased intracranial pressure of unknown etiology. Pancreatic supplements were restarted prior to discharge. One day after discharge, he returned to the local hospital with the same symptoms, i.e., vomiting, bulging fontanelle, and irritability. CT of the head was repeated and was negative, as was an MRI. Lumbar puncture showed an opening pressure of 40-42 cm H<sub>2</sub>O and a closing pressure of 10 cm H<sub>2</sub>O. The remaining LP results were negative. The patient improved during the hospitalization, while off pancreatic enzyme replacement. He was discharged home with a diagnosis of increased intracranial pressure, secondary to pancreatic enzyme supplements.

Pancreatic enzymes were withheld, and he was maintained on Pregestamil, with an accelerated growth pattern. Pancreatic supplements were restarted at 10 months of age after baby food was started and pancreatic insufficiency was apparent. He was placed on Pancrease®, at a

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dose of 400 IU/kg/meal, with a total daily dose of 2,000 IU/kg. Since that time he has had no signs or symptoms of increased ICP.

## DISCUSSION

Transient asymptomatic increased intracranial pressure shortly after initiation of treatment for cystic fibrosis has been reported repeatedly.<sup>1-9</sup> The infants improved clinically and showed spontaneous resolution of the bulging fontanelle within a few weeks without interruption of CF treatment.

Our patient demonstrated significant signs and symptoms of increased intracranial pressure within days of starting the pancreatic enzyme replacement. Although these signs and symptoms resolved within 2 to 4 days after discontinuing therapy, they recurred within 24 hr when the pancreatic enzymes were restarted. When the pancreatic insufficiency became obvious, the pancreatic enzyme supplementation (Pancrease® was used in both occasions) was restarted with no adverse effects.

The increased intracranial pressure in our patient was symptomatic and not self-limiting. To our knowledge, this has not been reported previously. The symptoms could be due to more severe CF disease, especially that the patient was found to be homozygous  $\Delta F508$ , a mutation associated with severe pancreatic insufficiency.<sup>10</sup>

The mechanism of increased intracranial pressure in cystic fibrosis patients is complex and has been attributed to vitamin A deficiency,<sup>1,2</sup> catch up brain growth,<sup>3-7</sup> and severe respiratory distress.<sup>8</sup> All of these causes seem unlikely in this case. The patient lacked xerophthalmia, corneal ulceration, anemia, and he lacked pathologic findings by skeletal X-ray. Also, the increased intracranial pressure reoccurred with resumption of pancreatic supplementation. The patient continued to grow appro-

priately and he did not have respiratory distress at the time he developed a bulging fontanelle.

The transient nature and rapidity of onset of signs and symptoms on both occasions suggest that pancreatic supplementation played a major role in the etiology of increased intracranial pressure, especially since pancreatic supplement was the only elimination from the treatment protocol after reoccurrence of symptoms.

In conclusion, this case report suggests the association of increased intracranial pressure with pancreatic enzyme replacement in a newly diagnosed CF infant.

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