

# Severe retinal hemorrhages in infants with aggressive, fatal *Streptococcus pneumoniae* meningitis

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**Retinal hemorrhages in children occasionally accompany bacterial meningitis, usually due to *hemophilus* or meningococcal organisms. The hemorrhages may be intraretinal, usually in the posterior pole of the eye and few in number, or, more uncommonly, subhyaloid or vitreous. Pathogenesis may include vasculitis, disseminated intravascular coagulation, or intracranial hypertension. We report 2 cases of bilateral severe retinal hemorrhages in fatal *Streptococcus pneumoniae* meningitis.**

## Case 1

A 16-day-old girl born at term by spontaneous vaginal delivery following uncomplicated pregnancy was well and breastfeeding. After 3 days of decreasing feeding, intermittent fever, and irritability, she was admitted to a community hospital for observation. Initial urinalysis, blood and urine cultures, blood count, and serum electrolytes were normal. On the third day she became acutely ill over a period of approximately 2 hours with a bulging fontanel, pallor, and lethargy. A lumbar puncture was performed and intravenous ceftriaxone was given. Seizures and apnea developed and she was intubated. Intravenous ampicillin, fresh frozen plasma, and red blood cell transfusion were given prior to the child's transfer to the Hospital for Sick Children in Toronto, Canada.

On arrival, the baby was afebrile and hypotensive, with dilated fixed pupils. Head circumference was 50th percentile. Hemoglobin was 9.4 g/dL, platelets 100,000, and white cell count 3.1 with normal differential. Electrolytes were normal. Coagulation studies were not done. Neurological assessment showed no evidence of cerebral activity. Physical examination was otherwise normal. Lumbar puncture results from the community hospital revealed cloudy fluid with 901 white blood cells, 7 red blood cells, protein 3.66 g/L, and glucose 11 mg%, with Gram-positive cocci. The blood culture and spinal fluid cultures

were subsequently positive for *S. pneumoniae* sensitive to all antibiotics.

Ophthalmology consultation revealed predominantly intraretinal hemorrhages too numerous to count throughout the retina bilaterally in a radiating pattern from the optic nerve to the ora serrata consistent with central retinal vein occlusion (Figure 1A). Retinal veins were dilated but often obscured by the massive hemorrhaging. The macula in each eye was flat and appeared completely avascular with no cherry-red spot, suggesting central retinal artery occlusion combined with infarction of the choroidal circulation (Figure 1B). Retinal arteries were extremely attenuated. There was no papilledema.

The child died within 24 hours. Autopsy revealed grossly purulent cerebrospinal fluid, including around the optic nerves. The ocular pathology slides and report were not made available for this study.

## Case 2

A boy born at 38 weeks following a normal pregnancy was diagnosed with cystic fibrosis and primary immune neutropenia at 4 months old following *Pseudomonas aeruginosa* sepsis. At 13 months of age, after 3 days of upper respiratory symptoms, fever, and 1 day of vomiting, he presented stuporous with a respiratory rate of 14/min, tachycardia, and delayed capillary refill. There was flexor upper limb reaction to painful stimuli and bilateral, unreactive to light, fixed dilated pupils. The computed tomographic scan of head, neck, chest, and abdomen was normal. Myocardio-pathy, pulmonary edema, metabolic acidosis, and neutropenia (3300/mm<sup>3</sup>) ensued. Electrolytes (including sodium 134.8 mm/L) were normal. Hemoglobin was 13.7 g/dL, prothrombin 46 (normal range, 70-120), and activated partial thromboplastin time 30 (normal range, 23-36). Platelet count was normal.

On the same day a pediatric ophthalmologist (JPL) performed indirect ophthalmoscopy and found bilateral edematous (right greater than left) optic disks, numerous right eye nerve fiber layer hemorrhages, and left eye dot intraretinal hemorrhages. Hemorrhages extended from the optic disk to the ora serrata bilaterally. In the right eye a large subinternal limiting membrane macular hemorrhage was present without retinal folds.

Lumbar puncture showed opening pressure of 76 cm H<sub>2</sub>O, grossly purulent cerebrospinal fluid, total proteins of 1.380 g/L, and glucose of 4 mg%. Culture was positive for *S. pneumoniae*. The patient died 12 hours after presentation. Autopsy was not performed.

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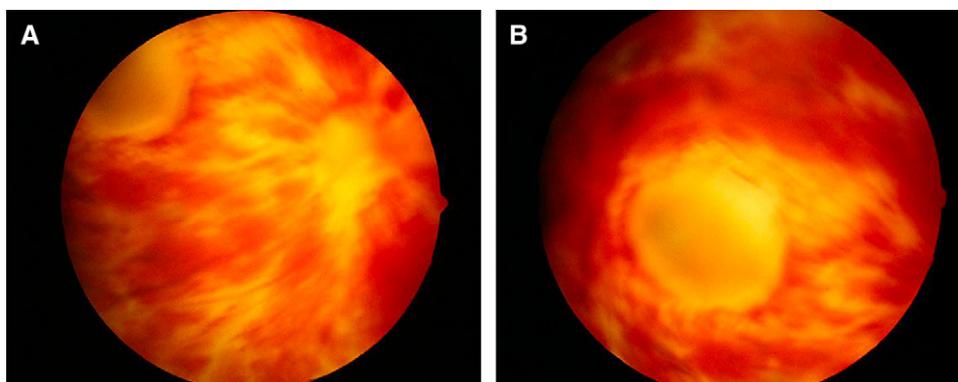
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**FIG 1.** Fundus photographs obtained from Case 1 after admission. A, Severe radiating pattern of intraretinal hemorrhage consistent with central retinal vein obstruction in right eye. Optic nerve is to the right and nonperfused macula on the upper left. Note attenuated and nonperfused (not visible) retinal arteries. A single engorged retinal vein is seen running through the bottom half of the image. B, Nonperfused macula of right eye without cherry-red spot, consistent with combined central retinal artery occlusion and infarction of choroidal circulation.

## Discussion

Dinakaran and colleagues<sup>1</sup> found retinal hemorrhages in 5 (42%) of 12 children with meningococcal septicemia and disseminated intravascular coagulation, but the authors did not mention the number of children who had meningitis. Hemorrhages were less than 20, intraretinal, and posterior to the equator. Subhyaloid retinal hemorrhages have also been reported in children with *hemophilus* meningitis.<sup>2</sup> Fraser and colleagues<sup>3</sup> described large unilateral subretinal and vitreous hemorrhage in a 12-year-old girl with meningococcal meningitis and normal clotting studies. To the best of our knowledge, ours is the first report of retinal hemorrhages in *S. pneumoniae* meningitis and the first report of extensive retinal hemorrhages in meningitis of any kind.

Our cases had fulminant fatal pneumococcal meningitis. In Case 1 the child clinically had a combined central retinal vein and artery occlusion with choroidal infarction. It appears this resulted from arrest of the circulation from the purulent cerebrospinal fluid. Central retinal vein obstruction in meningitis has been reported.<sup>4</sup> Unlike the typical central retinal vein obstruction pattern of retinal hemorrhage in Case 1, children with severe hemorrhagic retinopathy due to abusive head injury have a more random distribution of hemorrhages at all levels.<sup>6</sup>

Case 2 also had grossly purulent cerebrospinal fluid but a hemorrhage pattern not consistent with vein or artery occlusion. Papilledema, hypercoagulability, and sepsis may have contributed. The pathogenesis of the subinternal limiting membrane blood remains unclear, although we suspect that peripheral and macular intraretinal vessels may have necrosed from the infection.

The extensive retinal hemorrhages, in particular, the macular schisis-like lesion in Case 2, are reminiscent of abusive head injury.<sup>5,6</sup> Such patients can also present with no history of trauma and a sudden change in mental status. Evaluation for meningitis may be an important part of the evaluation of patients with extensive retinal hemorrhages,

particularly when there is underlying predisposition to infection and no evidence of intracranial trauma.

*S. pneumoniae* is the most common cause of community-acquired pneumonia, meningitis, and bacteremia in children and adults. Invasive pneumococcal disease primarily affects young children, older adults, and individuals with comorbidities or impaired immune systems. Case fatality rates range from 10% to 30% in adults but are much lower (<3%) in children.<sup>7</sup> Most patients with pneumococcal meningitis present nonacutely after hours or days of developing signs and symptoms that may be nonspecific. Pneumococcal meningitis carries a greater risk of death and significant neurological disability than other causes of bacterial meningitis.<sup>8</sup>

## Literature Search

MEDLINE was searched for the period from 1960 to the present for the following terms: *retinal hemorrhages/haemorrhages, meningitis, bacterial, pneumococcus, and sepsis.*

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