Retinal Hemorrhages in Meningococcal Septicemia

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Purpose: Meningococcal septicemia is associated with coagulopathy and hemorrhagic tendency. We carried out this study to determine the incidence of retinal hemorrhages in meningococcal septicemia. ***Methods:*** This was a prospective study involving all children admitted to the Sheffield Children's Hospital, Sheffield, England, with a diagnosis of meningococcal septicemia. Confirmation of meningococcal infection was by blood culture or DNA analysis using polymerase chain reaction. The children underwent ocular examination including dilated fundus examination by direct and indirect ophthalmoscopy. Details of their coagulation status were also obtained. ***Results:*** Twelve children (mean age, 4.5 years) with a confirmed diagnosis of meningococcal septicemia were included. All children had coagulopathy. Retinal hemorrhages were found in 5 children (42%). The disease was fatal in 3 children. Group C meningococcus was responsible for the infection in all those with retinal hemorrhages and those with fatal outcome. ***Conclusions:*** Retinal hemorrhage is a common feature in meningococcal septicemia. Ophthalmic evaluation should be part of the assessment of children with meningococcal septicemia. Future studies on meningococcal disease should include retinal hemorrhage as another parameter in the assessment. This should help us to understand the role of retinal hemorrhage in the prognosis of this serious disease. (J AAPOS 2002;6:221-3)

Meningococcal septicemia is a potentially fatal condition. This condition is associated with disseminated intravascular coagulation and hemorrhages in various parts of the body. Retinal involvement has been reported in patients with nonmeningococcal septicemia and retinal hemorrhages were found in 14% of the patients studied.[1] Cases of retinal hemorrhage in meningococcal meningitis have been reported.[2,3] However, to our knowledge, retinal involvement in meningococcal septicemia has not been studied. We carried out this study to assess the incidence of retinal hemorrhages in meningococcal septicemia at the Sheffield Children's Hospital, Western Bank, Sheffield, England.

METHODS

This was a prospective study involving all the children who were admitted to the pediatric intensive care unit with a diagnosis of meningococcal septicemia. They underwent ophthalmic examination after initial evaluation and initiation of treatment by the pediatric team. The examination included anterior segment and fundus examination with dilated pupils. Both direct and indirect ophthalmoscopy were carried out. This study included all those children who were confirmed to have septicemia due to meningococcal infection. The diagnosis was confirmed by blood culture and/or DNA analysis using polymerase chain reaction. All children had coagulation studies including prothrombin time, activated partial thromboplastin time, and platelet count. Surviving children who had ocular involvement were recalled for an orthoptic and ophthalmic evaluation.

RESULTS

Twelve children who had confirmed meningococcal septicemia were included in the study. The mean age of the children studied was 4.5 years. Group C meningococcus was responsible for the infection in 10 (83%) of these children and group B was responsible in the remaining 2 children (17%). All children had features of disseminated intravascular coagulation with low platelet count and abnormally raised prothrombin time and activated partial thromboplastin time. The mean platelet count was 70.09 $\times 10^9$/L (range, 12-108 $\times 10^9$/L), the mean prothrombin time was 24.91 seconds (range, 18-36.8 seconds), and the mean activated partial thromboplastin time was 70.53 seconds (range, 37.3-250 seconds). Normal ranges for the platelet count are 150 to 370 $\times 10^9$/L, for prothrombin time are 10.3 to 14.5 seconds, and for activated partial thromboplastin time are 24.6 to 36.9 seconds.

Retinal involvement with retinal hemorrhage was found in 5 (42%) of these children. The disease was fatal in 3 children (25%), of whom 2 had retinal hemorrhages. The 2 children who had meningococcal group B infection did not have any retinal involvement. All fatalities occurred in children with group C infection.

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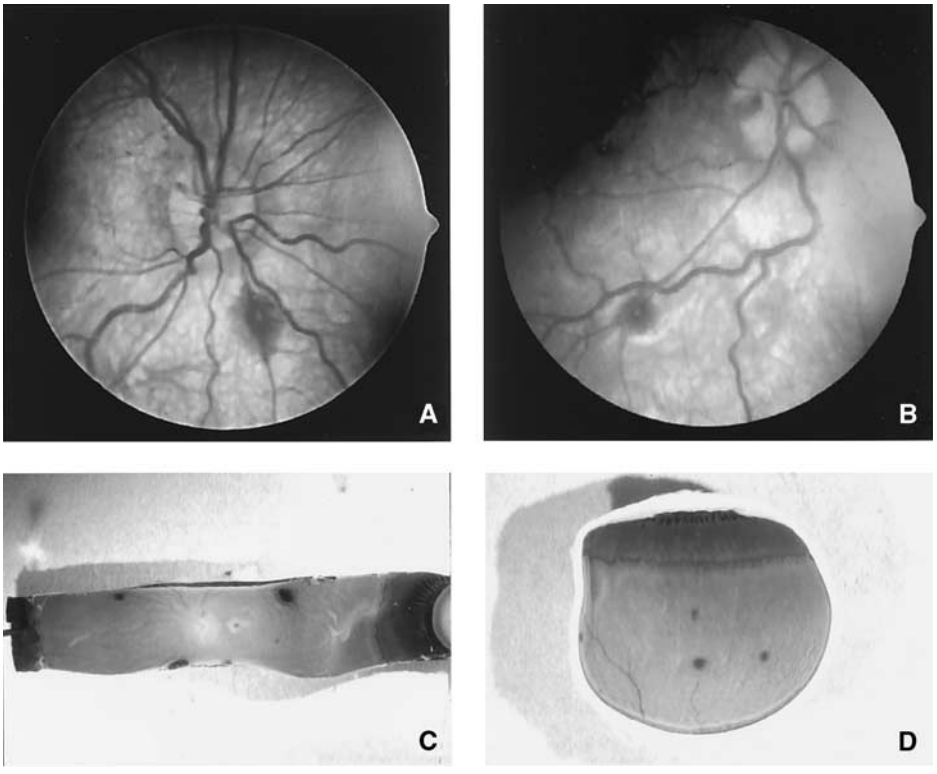

FIG 1. (A, B) Fundus photographs showing retinal and disc hemorrhages. **(C, D)** Postmortem macroscopic appearance of retinal hemorrhages.

We statistically analyzed the difference in the incidence of retinal hemorrhages and severity of coagulopathy in the different groups. There was no statistically significant difference in the incidence of retinal hemorrhage between the survivors and the nonsurvivors and between the children with group B and group C infection. Although the coagulopathy was more severe in group C disease and in those children with retinal hemorrhages, the difference did not reach statistical significance. However, when we compared the coagulopathy between the survivors and the nonsurvivors, the platelet count was statistically significantly low in patients with fatal disease ($P = .01$, Student t test).

The retinal hemorrhages (Figure 1, *A* and *B*) were seen predominantly posterior to the equator. They were scattered and numbered less than 20 in each fundus. The hemorrhages were flame-shaped, dot-and-blot hemorrhages. Some of these were white centered hemorrhages. Macular hemorrhage was found in 2 eyes. In all cases the retinal hemorrhages were bilateral. No other retinal lesions like cotton wool spots were seen on ophthalmoscopy. Subconjunctival hemorrhage was seen in 2 children, 1 of whom also had retinal hemorrhages. In addition to the retinal hemorrhages, disc hemorrhage was seen in 1 child. The macroscopic appearance of the retinal hemorrhages examined postmortem is shown in Figure 1, *C* and *D*. In the absence of wide field fundus photographs these figures show the distribution of the hemorrhages in the fundus.

Orthoptic and ophthalmic evaluation was carried out 9 to 12 months after recovery of the 4 surviving children with ocular involvement. Their visual acuity ranged from 6/6 to 6/4. No manifest strabismus was seen. Fundus examination was normal in all of them.

DISCUSSION

Meningococcal septicemia is a serious form of invasive meningococcal disease. The disease is associated with significant morbidity and mortality. Disseminated intravascular coagulation and multi-organ failure may be associated. Group B and group C meningococcal infection is responsible for most cases of invasive meningococcal disease (meningitis and septicemia) in the western world. Group B disease predominates although group C disease is seen with increasing frequency in Europe, North America, and Australia. Group C disease is also associated with higher mortality.[4-8] In the present study we found that the most common infective agent was group C meningococcus, which caused 83% of the meningococcal septicemia.

Meyers[1] studied the incidence of fundus lesions in septicemia in 69 adults. He found 18 patients with retinal lesions of which 12 had cotton wool spots and 10 (14%) had retinal hemorrhages. These lesions were predominantly found in the posterior pole. None of these patients had meningococcal disease. We are not aware of any study on retinal findings in meningococcal septicemia. Meningococcal septicemia is associated with petechial hemorrhages in the skin and is also associated with hemorrhage into internal organs. Disseminated intravascular coagulation and purpuric rash are its known features. Vascular occlusion secondary to vasculitis can lead to gangrene and

loss of extremities. In this study, 1 child had this complication, leading to loss of digits.

In this study, coagulopathy was seen in all children. However, only 5 had retinal hemorrhages. The coagulopathy was more severe in children with retinal hemorrhages and in those with group C disease, although the difference was not statistically significant. Two children who had group B disease had no retinal involvement although they had abnormal coagulation. In comparison 5 of 10 children with group C disease had retinal hemorrhages. However, the difference in the incidence of retinal hemorrhages between the 2 groups was not statistically significant. Vasculitis is a known feature of meningococcal septicemia. Whether the presence of vasculitis in addition to the coagulopathy increases the incidence of retinal hemorrhages is unclear.

These hemorrhages were predominantly in the posterior pole extending up to the equator. The total number of hemorrhages in each fundus was less than 20. This contrasts with the findings in nonaccidental injury, where the hemorrhages are in the posterior pole and in the periphery, implicating the vitreous base in the pathogenesis.[9] Various studies[10-12] have looked at the clinical and laboratory findings in patients with meningococcal disease to use them as prognostic factors. This study shows that retinal hemorrhage is common in meningococcal septicemia. The clinical relevance of this association may only be known if future studies looking at the prognostic factors include retinal hemorrhage as a clinical parameter. These studies may help us to understand the significance of retinal hemorrhage in meningococcal septicemia. Ophthalmic assessment should be a part of assessment of children with septicemia, especially those caused by meningococcal disease.

This study shows that retinal hemorrhage is a common feature in meningococcal septicemia. Future studies on prognostic factors should include retinal hemorrhage as one of the clinical factors in their assessment to find the clinical relevance of this association.

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