Stroke in hemoglobin (SD) sickle cell disease with moyamoya: successful hydroxyurea treatment after cerebrovascular bypass surgery

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An 11-year-old boy with hemoglobin sickle disease (HbSD), bilateral stenosis of the intracranial carotid arteries, and moyamoya syndrome had recurrent ischemic strokes with aphasia and right hemiparesis. His parents (Jehovah’s Witnesses) refused blood transfusions. After bilateral extracranial-intracranial (EC-IC) bypass surgery, hydroxyurea treatment increased hemoglobin F (HbF) levels to more than 30%. During a follow-up of 28 months, flow velocities in the basal cerebral arteries remained stable, neurologic sequelae regressed, and ischemic events did not recur. This is the first report of successful hydroxyurea treatment after bypass surgery for intracranial cerebral artery obstruction with moyamoya syndrome in sickle cell disease. The patient’s religious background contributed to an ethically challenging therapeutic task. (Blood. 2001;97:2165-2167)

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Results and discussion

The patient reported here is unusual for several reasons. First, the association of SCD and moyamoya disease is rare and, to our knowledge, has never been reported in HbSD. Second, successful HU treatment after neurovascular bypass surgery has never been reported in SCD with moyamoya syndrome. Third, his religious background created an ethically challenging therapeutic task.

Acute cerebral infarction occurs in approximately 7% to 10% of children with SCD, with a peak incidence between 5 and 10 years of age. The initial mortality rate is high (20%), and the recurrence rate is nearly 70% in nontransfused patients. In HbSD, the incidence of stroke is uncertain. Risk factors include prior transient ischemic attack, abnormal TCD, low steady state Hb level, and high leukocyte count; all were present in our patient.

The standard approach in a patient with SCD who has central nervous system (CNS) abnormalities with or without vasculopathy is to initiate a chronic transfusion program and to monitor cerebral blood flow velocity with TCD. Surgical intervention is now an accepted therapy for children with moyamoya disease who have CNS infarction, but only 2 descriptions have been reported in the literature of bypass surgery for moyamoya syndrome in SCD patients. One patient underwent encephaloduroarteriosynangiosis (EDAS) that had to be repeated after 18 months; occipital arteries were used the second time. In the other report, a bilateral EC-IC bypass procedure was successful; neurologic symptoms improved, but follow-up time was not reported.

This patient’s parents refused blood transfusions because of their religious beliefs. In view of the vital risk posed by the child’s last stroke episode, we obtained a single judicial permission for an emergency exchange transfusion. After EC-IC bypass surgery and in the absence of clear vital emergency, our ethics committee recommended that we follow the will of the parents, and we started HU therapy. This decision took into account the possible negative impact of enforced chronic transfusion treatment on the child’s psychosocial development.

Recent therapeutic approaches to SCD have focused on the use of HU to stimulate HbF production. It reduces the frequency of
pain crisis, chest crisis, and hospital admission for pain crisis in children with SCD.17-19 No consistent hematopoietic or developmental abnormalities have been observed in a 3-year follow-up of treated children.9 In another study, recurrence occurred in 20% of children who received HU instead of chronic transfusions.22 Therefore, the efficacy of HU in preventing ischemic strokes is still open to question. In comparison with data shown previously,18,20,21 an unusually high increase in HbF to 36% during HU treatment was seen in our patient. In agreement with recent data on chest syndrome in SCD,23 high (greater than 30%) HbF levels may be sufficient in specific situations to prevent the progression of CNS vasculopathy. In addition, EC-IC bypass surgery is a valuable therapy in severe CNS vasculopathy. Longer follow-up times and comparative studies are needed for an examination of the efficacy of HU to prevent the progression of CNS disease in SCD.

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References

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