Problems in Management of Subarachnoid Hemorrhage in Sickle Cell Anemia

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The purpose of this paper is to report problems of diagnosis and management in a case of subarachnoid hemorrhage from intracranial aneurysm in a patient with known sickle cell anemia. In addition, the results of an in vitro experiment dealing with one of these problems, the effect of contrast media on the sickling phenomenon, are presented.

Sickle cell anemia is an hereditary and familial form of chronic hemolytic anemia peculiar to negroes, and occurring in 0.3 to 1.3 per cent of various groups of negroes examined. The incidence of the sickle cell trait varies somewhat among negroes in different parts of the United States (from 8.5 to 13.4 per cent).\(^1\) Though not sex linked the abnormality is somewhat more common in females.\(^5\)

Clinically this form of anemia is characterized by rheumatoid manifestations, leg ulcers, and acute attacks of pain. It is distinguished morphologically by the presence of peculiar sickle-shaped and oat-shaped red corpuscles, as well as signs of excess blood destruction and active blood formation.\(^4\)

Neurological manifestations consisting of drowsiness, headache, nuchal rigidity, stupor or coma, hemiplegia, aphasia, convulsions, irritability, nystagmus, pupillary changes, blindness, cranial nerve palsies and paresthesias of the extremities are frequent.\(^5\) The lesions in the central nervous system are most often due to thromboses precipitated by the sickling phenomenon,\(^1\) but subarachnoid hemorrhage may also occur.\(^3\) Depending upon the type of central nervous system lesion resulting from the sickling phenomenon, the cerebrospinal fluid may be normal or under increased pressure, with xanthochromia, sickled erythrocytes, and elevated protein.

Seventeen different inherited variants of normal hemoglobin have been recognized. The most common one, hemoglobin S, is present in sickle cell anemia. The basis of the sickle cell phenomenon is the very low solubility of hemoglobin S in the deoxygenated form. It has been shown\(^3\) that the low arterial oxygen saturation in sickle cell anemia is due to two factors: (1) an increased alveolar arterial oxygen tension gradient; (2) an abnormal oxyhemoglobin dissociation curve. The high viscosity of blood with low oxygen saturation has been demonstrated to be an important factor in the production of the thromboses commonly seen in this disease. Thrombotic processes in the lower leg which result in chronic skin ulcers may be explained by the concurrence of sickling and low temperature causing excessively high blood viscosity.\(^9\) Lowering of the blood pH has also been shown to contribute to the formation of sickle cells.\(^4\)

Case Report

The patient was a 36-year-old negro school teacher and housewife, admitted on December 27, 1962, 24 hours after a subarachnoid hemorrhage verified by lumbar puncture at another hospital.

Past Medical History. Sickle cell anemia was first diagnosed in 1949, and the patient had been hospitalized on numerous occasions since that time for evaluation and blood transfusion. She had experienced repeated episodes of venous thrombosis of the arms and severe chronic pyelonephritis. Previous surgery included cholecystectomy and appendectomy. She had been married for 6 years and had had no children.

Examination. The blood pressure was 130/75; pulse, 76; temperature, 100.4°. Positive physical findings included scleral icterus, slight nuchal rigidity, and a Grade II harsh systolic murmur over the precordium. She was right handed.

A positive sickle cell preparation was obtained

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using the sodium bisulfite technique. The reticulocyte count was 40.8 per cent; hematocrit, 22 per cent; hemoglobin, 7.4 gm.; and the white cell count was 16,000/mm³ with a normal differential. The platelet count was adequate. Serum electrolytes were normal and the blood urea nitrogen was 8 mg. per cent. The cerebrospinal fluid was xanthochromic and the cell count was 1,725 white blood cells and 125,000 red blood cells/mm³. The cerebrospinal fluid sugar was 104 mg. per cent, and the spinal fluid protein was 80 mg. per cent.

Course. The morning after admission, the patient became semicomatose and was found to have a left hemiplegia and left hemianopia. Reflexes were normal and sensation was intact. A carotid arteriogram demonstrated a right middle cerebral artery aneurysm. An emergency right frontal craniotomy was performed and the aneurysm was clipped. The postoperative course was uneventful and at the time of discharge on January 9, 1963, the patient was neurologically intact with the exception of a resolving left hemiparesis and left homonymous hemianopia.

Follow up has continued over a period of 2 years; during this time the patient has remained neurologically intact and has continued to teach school without difficulty.

Comment

A review of the literature revealed an almost identical case reported in 1942 in which subarachnoid hemorrhage was assumed to be due to sickle cell anemia with hemolytic crisis. At autopsy, four days following the onset of symptoms, a ruptured left middle cerebral artery aneurysm was found.

The diagnosis of subarachnoid hemorrhage in the present case was made on the basis of the history and confirmed by spinal puncture. Establishing the correct etiology of the hemorrhage presented a diagnostic problem, since bleeding secondary to the sickling phenomenon or to rupture of an intracranial aneurysm were equally good possibilities. Differentiation between these two disease processes required cerebral arteriography, but this was not done initially because of the unknown effect of contrast media on the sickling phenomenon. Evidence of a second hemorrhage, and deterioration of the patient's neurological status, justified the possible additional risk of carotid arteriography, which demonstrated an aneurysm of the right middle cerebral artery (Fig. 1). The patient received a total of 16 cc. of Hypaque 50 per cent in 2 separate injections of 8 cc. each. Injections were made into the right common carotid artery. The arteriogram was well tolerated and there was no evidence of clinical change to suggest further sickling.

In view of the evidence of a second subarachnoid hemorrhage within 36 hours, it was decided to clip the aneurysm through an immediate direct approach by right frontal craniotomy.

Problems of Management. Preparation for operation posed such problems as selection of the proper anesthetic agent, the use of urea, and the use of hypothermia. Because of the increased sickling which occurs with hypoxia and with lowering of the blood pH due to build-up of CO₂, adequate oxygenation during anesthesia was vital. A gaseous mixture of nitrous oxide and oxygen was used with careful maintenance of the oxygen volume at 30 per cent. Controlled hyperventilation was also used. Prior to clipping the aneurysm, the systolic blood pressure was dropped briefly to 70 mm. Hg with Arfonad.

Urea was not used to facilitate operative exposure because its effect on the sickling phenomenon was not known. Because of the hypertonicity of urea it was thought that additional sickling might occur with its use. A rapid review of the literature prior to operation yielded no information which fully answered this question. Recent investigative work has shown that urea does not produce sickling when mixed with sickle cell blood in vitro, probably because urea crosses the red cell membrane freely and exerts no noticeable osmotic effects.

Use of hypothermia to reduce the oxygen requirement of brain tissue during clipping of the aneurysm was considered. It also received consideration because of its effect in shifting the oxygen dissociation curve of hemoglobin and thereby reducing the percentage of sickle forms. However, because of evidence indicating a marked net increase in the viscosity of the blood with lowered body temperature, hypothermia was not used.