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Cerebral Infarction Secondary to Sickle Cell Disease: Arteriographic Findings

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Cerebral angiograms were performed in 14 children with sickle cell disease and clinical findings of cerebral infarction. The angiogram was normal in four patients. Ten patients had abnormalities in the carotid artery or its branches. The internal carotid artery was stenosed or occluded usually with bilateral disease. The anterior and middle cerebral arteries were involved in nine patients and branch occlusion was frequent. The posterior fossa arteries were not involved in these patients. The risk of angiography is low if appropriate precautions are taken. In these patients the indications for arteriography were to evaluate the effects of hypertransfusion therapy on cerebrovascular disease.

Cerebral arterial thrombosis is a frequent complication of sickle cell disease, occurring as frequently as 15% in some series [1], and is a major cause of morbidity and mortality [2–4]. Hypertransfusion has been proposed as a means of preventing further occlusive episodes in these patients [5].

Cerebral arteriography has been described only sporadically in sickle cell disease and the number of patients has been small [6–8]. We present our experience with cerebral arteriography in 14 patients with sickle cell disease who had clinical findings of cerebral thrombosis.

Subjects and Methods

Cerebral angiography was performed in 14 patients with clinical evidence of cerebral infarction and the electrophoretic pattern of sickle cell disease as part of a study to evaluate the role of transfusion therapy in prevention of further episodes of cerebral infarction. Age range was 4–13 years. Hemoglobin analysis revealed SS in 11 and one each with SA, SC, and S-thalassemia types.

Angiography was performed shortly after onset of symptoms using the transfemoral technique. The patients were transfused immediately prior to arteriography sufficiently so that the number of circulating sickle cells was no more than 20% of the total red blood cells. Patients were also kept well hydrated prior to and during the study. Both carotid arteries were studied in eight patients, the symptomatic carotid and vertebrobasilar system in one, only the symptomatic carotid in one, and both carotid arteries and the vertebrobasilar system in four. One patient who had inadvertently not been transfused was thought clinically to have had an episode of cerebral ischemia secondary to arteriography which resulted in a permanent hemiparesis. The exact cause of the complication, whether due to sickling, clot formation, or contrast reaction was not determined. No other complications were related to the procedure.

A program of transfusion therapy was then begun in 10 patients and repeat arteriography performed in six patients. No complications were encountered in these repeat studies.

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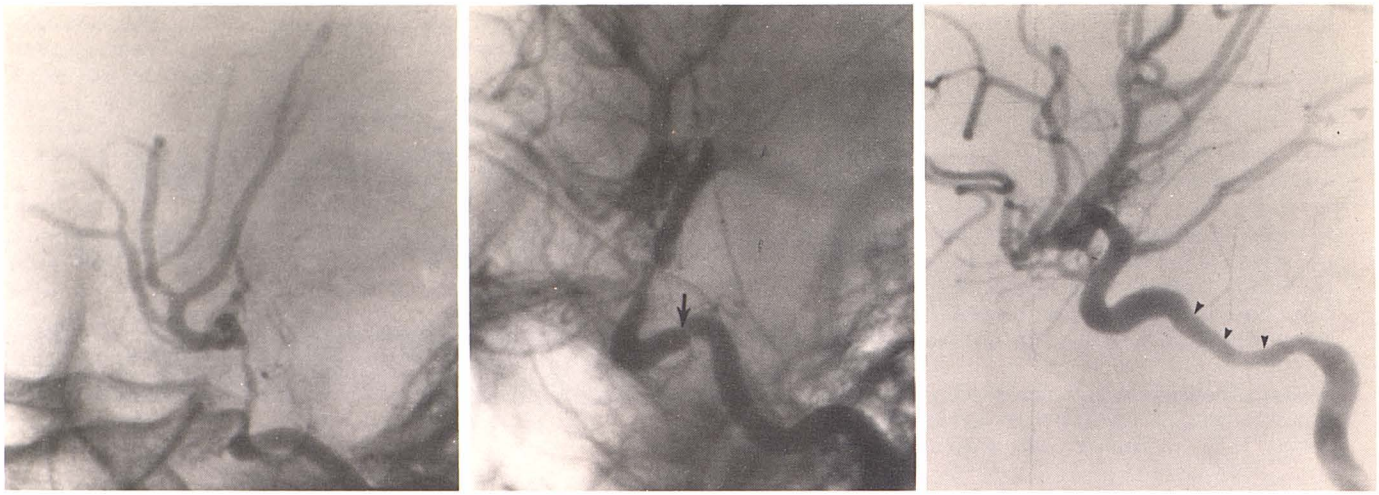
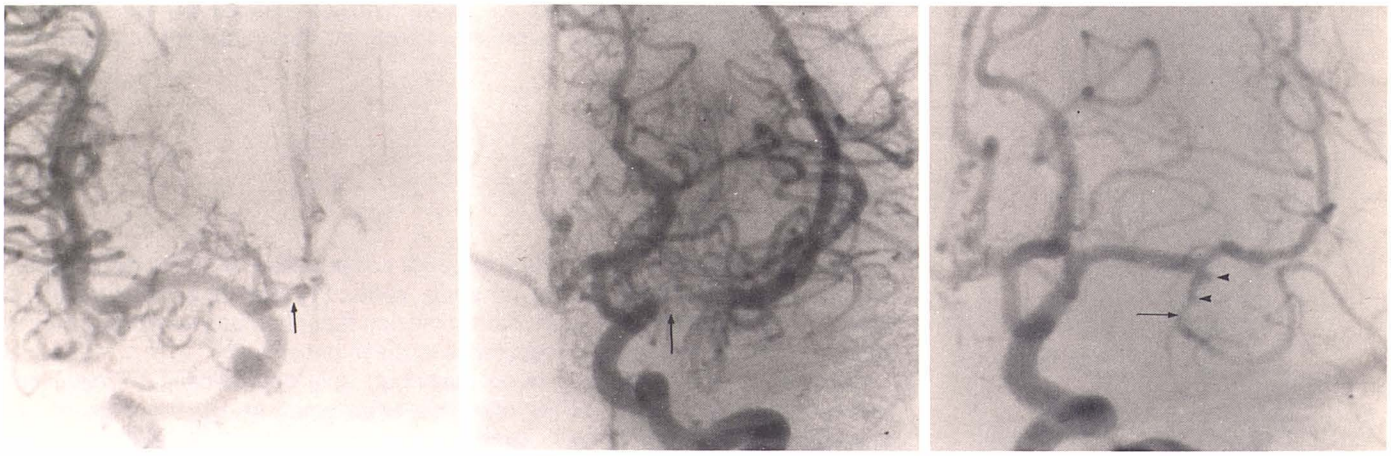


A B C

Fig. 1.—Internal carotid involvement in sickle cell disease in three patients. **A**, Severe, irregular, stenosis involves supraclinoid segment. **B**, Weblike defect in cavernous portion (*arrow*). Irregular narrowing and stenosis of supraclinoid part. Lenticulostriate arteries are enlarged and source of collateral flow. **C**, Irregular narrowing of petrous part (*arrowheads*).



A B C

Fig. 2.—Anterior and middle cerebral artery involvement in sickle cell disease. **A** and **B**, Same patient as 1**C**. **A**, Beaded appearance of anterior cerebral artery (*arrow*). Predominant flow to pericallosal artery from opposite anterior cerebral artery. **B**, Smooth-walled stenosis (*arrow*) of middle cerebral artery produces almost complete occlusion. **C**, Occlusion of two middle cerebral branches (*arrowheads*) and stenosis (*arrow*) of more inferior branch.

Results

Cerebral angiograms were normal in four patients, two with SS and one each with SA and SC hemoglobin. Three of these had both carotid arteries and the vertebrobasilar system studied. The fourth had studies of the symptomatic carotid and the vertebrobasilar system. Of the remaining 10 patients, in whom the studies were abnormal, the posterior fossa was included in one and was normal. Therefore, the posterior fossa circulation was evaluated in five of 14 patients and was normal in each.

The vascular disease resulted in decreased arterial caliber varying from a mild degree of stenosis to occlusion. Multiple deformities of the stenotic segments were seen; smooth, beaded, irregular, and tapered. No particular appearance was confined to a specific vessel.

Nine patients had abnormalities of the internal carotid arteries; bilateral in seven, unilateral in two (fig. 1). The carotid artery had more than one site of involvement in two patients. The intracranial part of the internal carotid (fig. 1A) was stenotic in 12 vessels and occluded in three. In addition, the cavernous part (fig. 1B) was stenotic in two patients and the petrous part (fig. 1C) stenotic in one patient.

The anterior cerebral artery was involved in nine patients (fig. 2A) with bilateral changes in two. In each instance the abnormality was in the proximal part of the vessel. Of the 11 vessels involved, nine were stenotic and two occluded. The occluded vessels occured in the same patient.

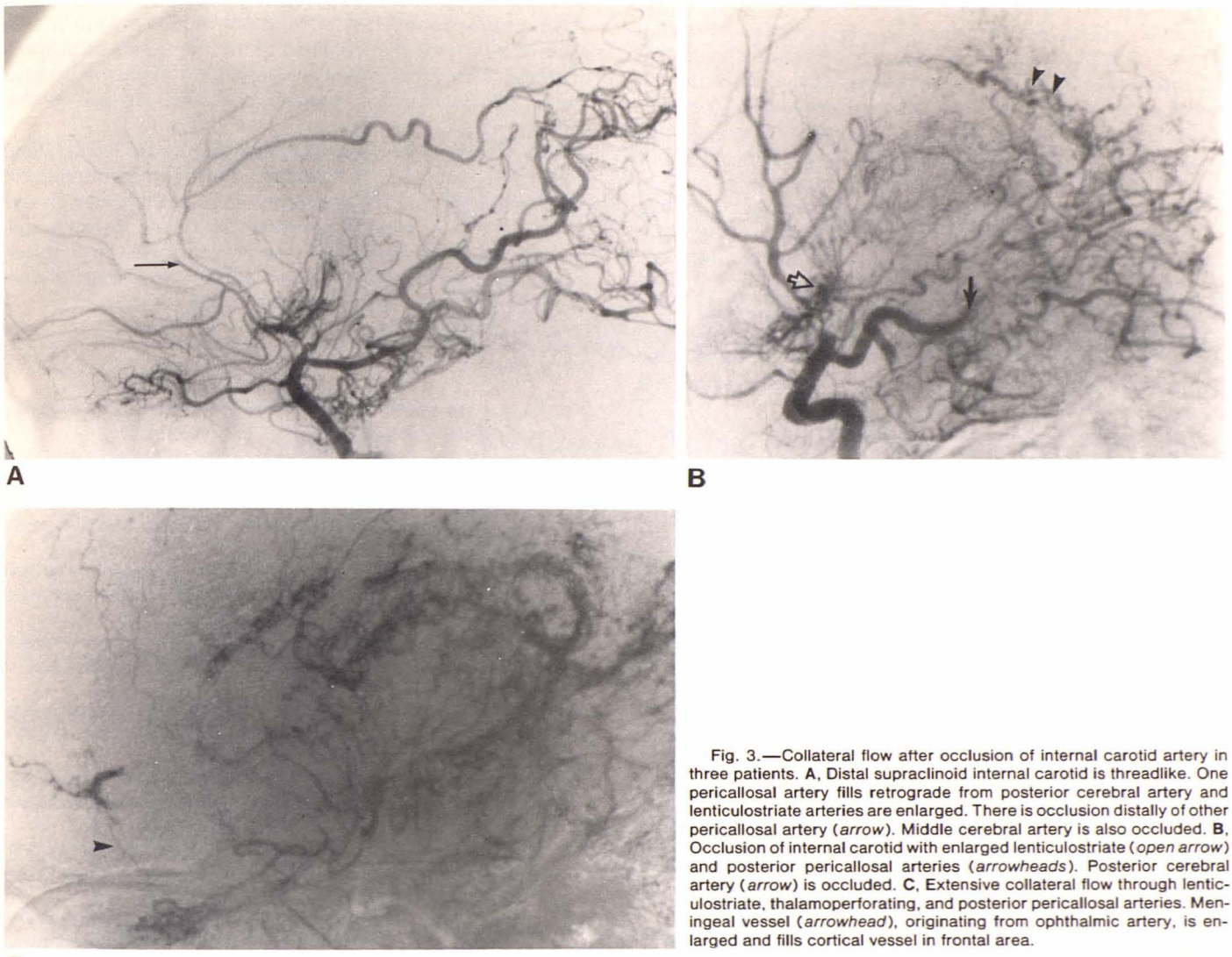


Fig. 3.—Collateral flow after occlusion of internal carotid artery in three patients. **A**, Distal supraclinoid internal carotid is threadlike. One pericallosal artery fills retrograde from posterior cerebral artery and lenticulostriate arteries are enlarged. There is occlusion distally of other pericallosal artery (*arrow*). Middle cerebral artery is also occluded. **B**, Occlusion of internal carotid with enlarged lenticulostriate (*open arrow*) and posterior pericallosal arteries (*arrowheads*). Posterior cerebral artery (*arrow*) is occluded. **C**, Extensive collateral flow through lenticulostriate, thalamoperforating, and posterior pericallosal arteries. Meningeal vessel (*arrowhead*), originating from ophthalmic artery, is enlarged and fills cortical vessel in frontal area.

The main trunk of the middle cerebral artery (fig. 2B) was abnormal in eight patients with unilateral involvement in six. Of the 10 vessels involved, six were stenotic and four occluded. One patient had bilateral occlusion and was the same patient with occlusion of both anterior cerebral arteries.

The incidence of occlusion of a branch of the anterior or middle cerebral artery is difficult to evaluate in a group of patients such as this with severe disease of the more proximal vessels. Occlusion of branches was seen frequently (figs. 2C and 3A) with the occluded segment usually having a smooth, rounded border.

Collateral circulation (fig. 3) was present in seven of the 10 patients, being absent in those with milder degrees of stenosis. The most common sources of collateral flow were through cortical and lenticulostriate pathways. External carotid-ophthalmic and transdural meningeal collaterals were also seen.

The results of transfusion therapy will be reported separately [9], but in part showed that treatment over 1 year did not prevent repeat episodes of cerebral infarction once the therapy is stopped. As stated, angiography was repeated after treatment in six patients. Of these, four patients had areas of increased stenosis. The other two had no change in findings. In the six patients, 17 vessels were abnormal and could be compared. There had been further stenosis in six (35%), no change in eight (47%), and improvement in three vessels (18%).

Discussion

Children with sickle cell disease have a reported incidence of cerebral vascular occlusive disease as high as 17%. Morbidity is high and permanent deficits occur in about 15% of those with cerebral occlusion [1]. It is estimated that

20%–60% [1, 10] of those having one episode of cerebral infarction will have a second. Also, 25% of patients having a cerebral infarction will die as a result of that or subsequent episodes [4]. Obviously, cerebral vascular occlusion is a major problem in patients afflicted with sickle cell disease.

The etiology of cerebral arterial occlusion in this entity [3] is less well studied pathologically than arterial occlusion occurring in other parts of the body, but is presumed to have the same pathogenesis. Sickling of red blood cells is thought to be initiated most often by hypoxemia, although fever and infection are other accepted factors. Capillary engorgement with sickle cells leads to coagulation and retrograde thrombosis of small vessels. Stasis in the vasa vasorum of larger vessels may lead to proliferation of the intima and media with eventual occlusion or the intimal defects may serve as a focus for clot formation within the vessel.

Hypercoagulability has been shown [7] to be present in patients with sickle cell disease and is thought due to deficiencies of factor *V* and serum plasminogen. Stasis occurring in capillaries secondary to packing by sickle cells may also contribute to the hypercoagulable state.

Embolization of fat occurs during crisis and has been shown at autopsy in areas of cerebral infarction [11]. The significance of this finding is not clear.

The intracranial part of the internal carotid artery is the most frequent site of involvement and changes are usually bilateral [8]. Involvement of the anterior and middle cerebral arteries is also frequent but, in contrast to the findings in the internal carotid, is rarely bilateral. There is no explanation for the apparent sparing of posterior fossa arteries.

The appearance of the stenotic or occluded segment varies considerably from vessel to vessel. No specific change was noted that could be considered pathognomonic of sickle cell disease; in fact, the arteriographic changes can rarely be separated radiographically from many of the other causes of acute hemiplegia of childhood [12].

Four of the 13 patients had normal angiograms despite clinical findings of cerebral ischemia. This is more frequent than previously reported [11] and may be due to a greater wilingness by our referring physicians to recommend angiogaphy, allowing us to study patients with even minimal clinical findings.

Some physicians have been loath to perform arteriography in the presence of sickle cell disease, particularly homozygous patients, because of fear that contrast medium may promote sickling [13]. We had no complications in patients adequately transfused immediately before the procedure and kept well hydrated. We believe arteriography is safe in these patients if appropriate precautions are taken. The procedure should include the distribution of both carotid arteries as a minimum because of the frequency of bilateral changes. The vertebrobasilar circulation might be omitted unless clinical findings suggest occlusive disease in that region.

However, the indications for angiography are limited if the findings do not influence treatment. Further experience with transfusion therapy [9] will clarify its role and other means of preventing or treating cerebral infarctions in sickle cell disease may be developed. At present, the arteriogram documents the degree of involvement in the cerebral vessels but would seem to have little other value.

REFERENCES

1. Portnoy BA, Herion JC. Neurological manifestations in sickle-cell disease. *Ann Intern Med* **1972**;76:643–652
2. Greer M, Southland D. Abnormal hemoglobin as a cause of neurologic disease. *Neurology* **1962**;12:114–123
3. Hughes JG, Diggs LW, Gillespie CE. The involvement of the nervous system in sickle cell anemia. *J Pediatr* **1940**;17:166–184
4. Seeler RA, Royal JE. Acute and chronic management of children with sickle cell anemia and cerebrovascular occlusive disease. *Ill Med J* **1977**;147:267–269
5. Russell MD, Goldberg HL, Reis L, et al. Transfusion therapy for cerebrovascular abnormalities in sickle cell disease. *J Pediatr* **1976**;14:382–387
6. Hilal SK, Soloman GE, Gold AP, Carter S. Primary cerebral arterial occlusive disease in children. *Radiology* **1971**;99:71–86
7. Merkel KHH, Ginsberg PL, Parker JC, Post MJD. Cerebrovascular disease in sickle cell anemia: a clinical, pathological and radiological correlation. *Stroke* **1978**;9:45–52
8. Stockman JA, Nigro MA, Mishkin MM, Oski FA. Occlusion of large cerebral vessels in sickle cell anemia. *N Engl J Med* **1972**;287:846–849
9. Williams J, Goff JR, Anderson HR Jr, Langston JW, Thompson E. Efficacy of short term transfusion for 1–2 years in patients with sickle cell disease and cerebrovascular accidents. *J Pediatr.* In press. **1980**
10. Wood DH. Cerebrovascular complications of sickle cell anemia. *Stroke* **1978**;9:73–75
11. Seeler RA, Curtis EM. Bone marrow and fat embolism in sickle cell anemia and sickle cell hemoglobin C disease. *Bull John Hopkins Hosp* **1958**;163:8–18
12. Harwood-Nash DC, Fitz CR. Acute hemiplegia of childhood. In: *Neuroradiology in infants and children.* St. Louis: Mosby, **1976**:929–955
13. Richards D, Nulsen FE. Angiographic media and the sickling phenomenon. *Surg Forum* **1971**;22:403–404