AJNR Am J Neuroradiol 19:1437–1440, September 1998

Spontaneous Labyrinthine Hemorrhage in Sickle Cell Disease

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Summary: We report the clinical and MR imaging findings in two African-American patients with manifestations of sickle cell disease affecting the inner ear. Both suffered sudden-onset sensorineural hearing loss and vestibular symptoms, and both had high labyrinthine signal on T1-weighted MR images attributed to labyrinthine hemorrhage. Follow-up studies of the first patient revealed a decrease in abnormal vestibular signal. Careful attention to the labyrinth on T1-weighted MR images can reveal vestibulocochlear clinical findings in sickle cell patients, with important implications for management and prognosis.

Sickle cell disease is a common inherited blood disorder among people of African descent. The clinically important variants include homozygous hemoglobin SS (sickle cell anemia) and the compound heterozygous variants sickle B thalassemia, sickle C (SC), and sickle D (SD) diseases. Abnormal hemoglobin produces sickling of red blood cells under low oxygen tension, leading to capillary occlusion. Affected individuals suffer constitutional manifestations, anemia, and ultimately organ damage due to micro- and macroinfarcts. In the CNS, findings may include seizure, infarct, hemiplegia, visual disturbance, or coma, attributed to cerebral thrombosis (1). An association with sensorineural hearing loss (SNHL) is well documented (2). Patients with hemoglobin SS also have an increased frequency of subarachnoid hemorrhage (3). Exchange transfusion is beneficial to children suffering a major neurologic complication (1).

We present the clinical and MR imaging findings of two men with sickle SC variant who had signs and symptoms referable to presumed hemorrhage in the inner ear. Recognition of the imaging appearance of labyrinthine hemorrhage can affect both management and, to a limited degree, prognosis.

Case Reports

Case 1

A 23-year-old previously healthy African-American man experienced sudden left-sided hearing loss, ipsilateral tinnitus, and mild imbalance while dehydrated during strenuous exertion in hot weather. Three days later he sought treatment for acute right-sided elbow pain, unrelated to trauma. Two days before otologic evaluation, steroids were prescribed without symptom improvement. He reported no symptoms of recent or current viral infection. Head and neck examination was noncontributory. Audiometric testing showed profound left-sided SNHL. A fistula test was negative. Screening bloodwork for autoimmune disorder; syphilis; and Lyme, renal, and thyroid diseases was negative. CT findings on a scan of the temporal bones were unremarkable. Hemoglobin analysis showed the SC variant of sickle cell disease.

MR imaging 2 weeks after symptom onset revealed high signal intensity on noncontrast and contrast-enhanced T1-weighted images (obtained with parameters of 422/30/4 [TR/TE/excitations], 3.0-mm-thick sections, and a 0.3-mm intersection gap) of the left cochlea, vestibule, and semicircular canals (Fig 1A and B). MR imaging 11 weeks later (503/20/4; with 2.5-mm-thick sections and a 0.5-mm gap) showed persistently high, although somewhat diminished, signal in the same areas (Fig 1C). No contrast enhancement occurred at either time. Ophthalmologic examination disclosed extensive retinal neovascularization, requiring laser photocoagulation. The episode was consistent with a sickling crisis, with elbow symptoms resolving over several days. Follow-up examinations over 21 months have shown no recovery of left-sided hearing. Retinopathy has been stable, and no further sickling crises have occurred.

Case 2

A 21-year-old African-American man with previously diagnosed sickle cell disease (hemoglobin SC variant) was admitted to the hospital with visual loss compatible with bilateral retinal artery branch occlusions. He had no history of trauma or drug use, but had suffered one prior vasoocclusive crisis at age 13, which involved chest pain. One day after his admission he reported a feeling of light-headedness and dizziness on standing, as well as a left-sided decrease in hearing. Neurologic examination was unremarkable, as was high-resolution CT of the temporal bones. The patient was treated with exchange transfusion and his visual loss did not progress, with no further symptoms supervening. Audiographic findings obtained 24 days after admission, by which time he reported some left-sided hearing improvement, were normal on the right but showed a mild degree of low-frequency hearing loss on the left. A subsequent audiogram at 3 months showed no change. Four weeks after the onset of symptoms, a T1-weighted MR imaging study (522/20/2) showed high signal from the cochlea, vestibule, and semicircular canals on the left, without change after administration of contrast material (Fig 2C).

Received August 12, 1997; accepted after revision November 25.

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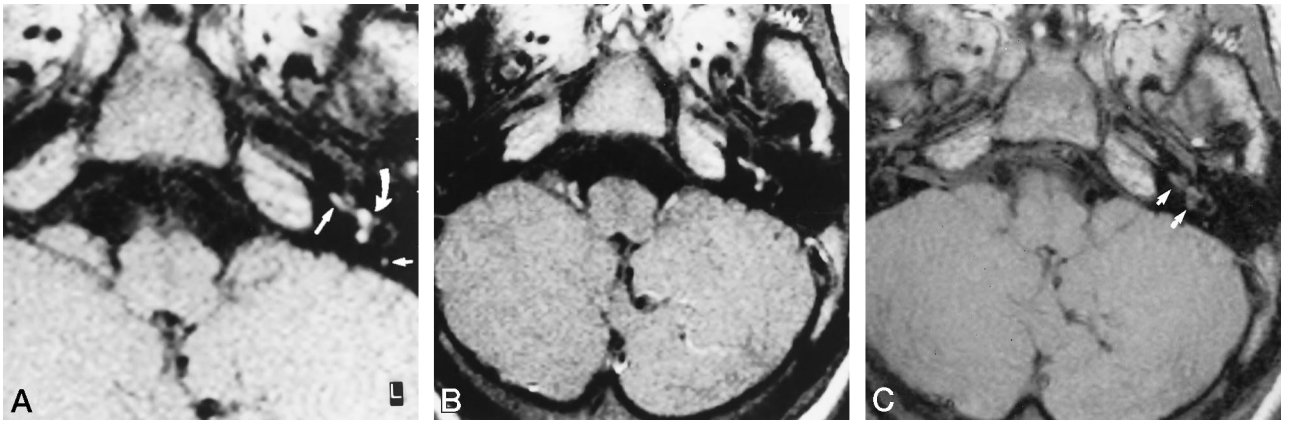

FIG 1. Case 1.

A and *B*, Axial T1-weighted images (422/30/4) before (*A*) and after (*B*) contrast administration show high signal interpreted as spontaneous hemorrhage in the vestibule (*curved arrow*), cochlea (*long arrow*), and posterior crus of the posterior semicircular canal (*short arrow*) on the left. No change is evident after contrast administration.

C, Follow-up T1-weighted image (503/20/4) 11 weeks later shows a lesser degree of abnormally intense signal relative to CSF in the same areas (*arrows*). Despite divergent window settings, when using the petrous apex marrow signal for comparison, the relative signal clearly goes from isointense to less intense on the follow-up study. An incidental developmental venous anomaly is present deep in the left cerebellar hemisphere.

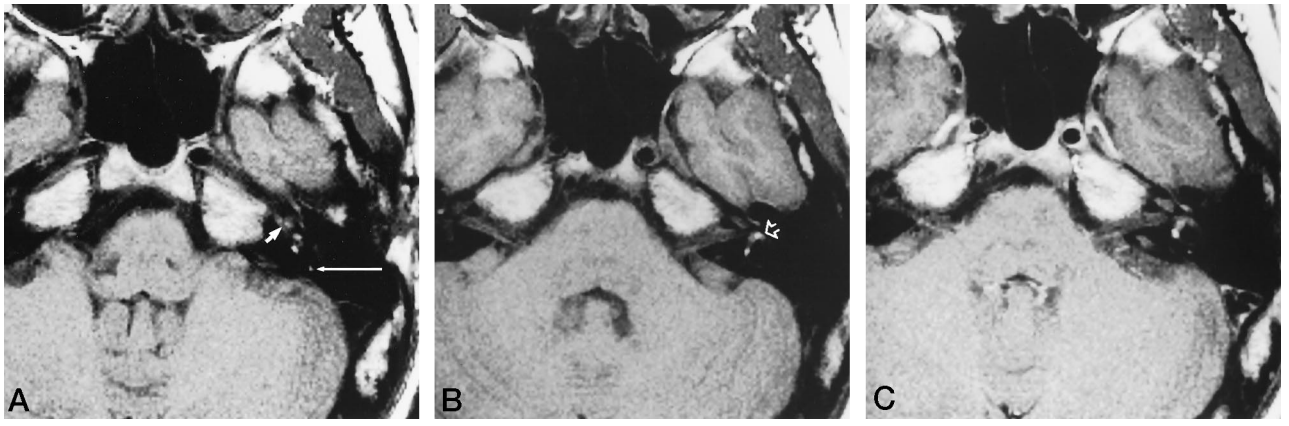

FIG 2. Case 2.

A–C, Axial T1-weighted images (522/20/2) before (*A* and *B*) and after (*C*) contrast administration show increased signal attributed to hemorrhage in the cochlea (*short arrow*), vestibule (*open arrow*), and posterior crus (*long arrow*) on the left. No contrast enhancement has occurred.

Discussion

We attribute our patients' inner ear symptoms to a sickling crisis. Strenuous exertion, dehydration, and hot weather can precipitate a vasoocclusive crisis in patients with sickle cell disease. SNHL is a well-recognized complication of sickle cell disease, with at least four cases reported in the literature (4–7). In the histopathologic study by Morgenstein and Manace (8), expansile and diffusely hyperplastic petrosal marrow accompanied degeneration of the organ of Corti, consistent with ischemia. Between 12% and 22% of patients with sickle cell disease tested show hearing loss (9, 10). Reversible SNHL has also been ascribed to sickling crises (11, 12). In a study of 75 adults with sickle cell disease, Crawford et al (13) determined that 69% of patients with the SC hemoglobin variant, as against only 36% of those with hemoglobin SS, had suffered hearing loss. The reasons for this counterintuitive discrepancy are unknown. Clinically, patients with sickle cell anemia suffer a much more serious natural history with a much greater frequency of end-organ damage than do patients with the sickle SC variant (1).

The high signal intensity seen in our patients' otic labyrinth after sudden-onset SNHL is consistent with either hemorrhage or proteinaceous exudate. This finding has been reported in two cases of idiopathic SNHL (14). The alternative explanations for this finding include fat or slow-moving spins within a vascular structure. A small cholesteatoma of the adjacent middle ear is a consideration as well, but in our cases had been ruled out on high-resolution temporal bone CT scans. Fat is an extremely unlikely cause of high signal in the labyrinth, although theoretically possible with transverse temporal bone fracture traversing the otic capsule and an egress of bone marrow contents. There are no large vessels coursing in this area in a person with normal CT findings, and the contents of the semicircular canals do not circulate in a patient lying still for an MR examination.

Discerning the difference between high protein exudate and hemorrhage is difficult. In principle, MR spectroscopy of larger collections could make this determination; however, in the case of the small and complex shape of the otic labyrinth and the supervening susceptibility effects of the adjacent temporal bone and middle ear, this becomes impossible. The interval decrease in abnormally high signal intensity at short-term follow-up MR imaging does not help in differentiating between these alternatives, as this characteristic is consistent with either hemorrhage into or another highly proteinaceous transformation of the endolymph and perilymph, in either case representing resorption or partial clearance of the process. Long-term follow-up detection of hemosiderin would also help, but in the special situation of the otic capsule within the temporal bone, this is, practically speaking, impossible. The common underlying condition of our two cases argues in favor of the process being hemorrhagic in nature. However, histologic proof of hemorrhage was not obtained in either case.

Spontaneous hemorrhagic sudden hearing loss is exceptional in the absence of coagulopathy. Isolated case reports or small case series have documented its occurrence in the setting of leukemia with leukostasis syndrome and thrombocytopenia (15, 16), in cases of aplastic anemia (17), and in patients with diffuse metastatic breast carcinoma to the surrounding temporal bone (18). Vascular causes of sudden hearing loss include thromboembolism, vasospasm, hemorrhage, and vascular occlusion. In our two patients, occlusion of labyrinthine vasculature due to intravascular sickling was the presumptive causative event. The bleeding may have been immediate or delayed, and may have resulted from altered capillary hemodynamics or reperfusion of an injured vascular bed.

The clinical significance of labyrinthine bright signal on unenhanced T1-weighted MR images in idiopathic sudden hearing loss was not discussed in the report by Weissman et al (14). The long-term prognosis for hearing recovery after cochlear hemorrhage is imperfectly understood, because a series of cases with well-documented follow-up has not to our knowledge been reported. In the single cases reported, recovery has been uniformly poor (15–18); however, many of these patients harbored neoplasms and did not survive for long after the labyrinthine hemorrhage. Simple hemorrhage into the perilymphatic space in small amounts is reportedly well tolerated (16); massive hemorrhage, however, has not been followed up long enough in reported cases and series. Further, in principle, hemorrhage by itself may have a different outcome from hemorrhagic transformation of an ischemic process. Although our second patient reported partial subjective left-sided hearing recovery after 4 weeks, neither our first patient nor the two patients described by Weissman et al recovered hearing at 2 years' follow-up (Hirsch BE, personal communication). Longer-term follow-up would be helpful, but our second patient has been lost to follow-up. A more accurate estimate of the long-term hearing prognosis associated with these imaging findings awaits study of a greater number of cases.

Hemorrhagic sudden hearing loss in a patient with sickle cell disease indicates a sickling crisis of the labyrinthine capillary bed, either in the distribution of the anteroinferior cerebellar artery or a branch of the basilar artery, which should be considered equivalent to other intracranial sickling events. For an evolving infarct or transient ischemic attack, appropriate therapies include emergent admission and exchange transfusion. The need to perform noncontrast, thin-section, T1-weighted MR imaging before contrast-enhanced imaging has been emphasized previously (14); in the circumstance of our two cases, in which differentiation of hemorrhage from enhancement was important, this approach is mandatory. Without venturing into the debate over the most appropriate screening sequences for vestibular schwannomas (19–22), clearly a screening examination consisting of either a high-resolution T2-weighted sequence or a contrast-enhanced T1-weighted sequence will not by itself accurately diagnose hemorrhage (except perhaps for the T2 characteristics evident during the transient interval when vestibulocochlear deoxyhemoglobin is present). The best approach would be to weigh the pretest prevalence of sickle cell disease and its variants in the population screened to decide whether detection of hemorrhage would warrant the lengthier imaging protocol.

Neither of our patients was imaged sufficiently early in the course to affect management decisions. The acute care of one patient was directed toward management of coincidental retinal problems. The imaging appearance of hyperacute and acute hemorrhage in the otic capsule might be expected to evolve in analogous fashion to that in the brain, but published data are scarce on this subject. It is likely that as blood passes through the stage of intracellular deoxyhemoglobin, its signal on T2-weighted images would be hypointense and consequently less visible (or perhaps invisible) within the temporal bone, transiently mimicking fibrous obliteration of the labyrinth. Clinical indications and appropriate choice of MR imaging protocol in the right clinical setting may confirm such an appearance in an African-American patient with hearing loss temporally closer to symptom onset.

Conclusion

High labyrinthine signal on noncontrast, thin-section, T1-weighted MR images may be taken to represent hemorrhage related to a vasoocclusive crisis in African-American patients with the sickle cell SC variant. A heightened awareness of the evolving appearance of hemorrhage within the membranous labyrinth on multiple imaging sequences could lead to a better understanding of the clinical, prognostic, and therapeutic implications of this finding.

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