Major Cerebral Arterial and Venous Disease in Osteopetrosis

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SUMMARY Two patients with osteopetrosis were studied in whom severe stenosis of one or both internal carotid arteries was demonstrated. One patient had autosomal dominant osteopetrosis and the other patient had the autosomal recessive form of the disease. In one patient, probable occlusion of one internal jugular vein and retrograde thrombosis of the contributing dural venous sinuses was present. Venous drainage of parts of the brain occurred through dilated emissary and scalp veins. It appears that major extracranial vessels may be impinged upon by dysplastic bone in osteopetrosis, although this is the first report of such an occurrence. A posterior fossa aneurysm was present in one case, and may have been related to abnormal intracranial hemodynamics.

OSTEOPETROSIS is a rare metabolic bone disease characterized clinically by pathological fractures, bone marrow failure and neurological deficits. Cranial nerve palsies and blindness with optic atrophy are the commonest neurological manifestations of the disorder.

Cerebrovascular complications so far described include intracerebral hemorrhage, subdural hematoma, cerebral venous thrombosis, and subarachnoid hemorrhage. On occasion, dilated scalp veins of uncertain significance have been observed in affected infants. There are no reported cases of severe intrapetrous stenosis of the internal carotid arteries, or of occlusion of major veins or dural sinuses.

Case 1
K.K., a 31-year-old right-handed woman, experienced a sudden severe headache without loss of consciousness or neurological deficit. Angiography subsequently revealed a ruptured aneurysm at the superior cerebellar/basilar artery junction.

The patient had osteopetrosis as had her father. Her mother was unaffected and she did not know the condition of her sibling from whom she had been separated since childhood. She had no children. She had suffered over 30 pathological fractures; four fractures of the left hip occurred in an 18 month period, necessitating internal fixation. Several rib fractures had occurred during sexual activity. Poor vision had been present since birth and was nonprogressive. She had always been mildly anemic. No anosmia, diplopia, deafness, facial paresis, or facial numbness had been experienced.

On examination, she was 4’10” tall and scaphocephalic. Blood pressure was 100/70 and a soft systolic ejection murmur was present. There was no hepatosplenomegaly or lymphadenopathy. The right hip was externally rotated and both hips were limited in range of motion. All pulses were present including those of the carotid, supraclavicular, superficial temporal and facial arteries. No cervical bruits were present.

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References
Visual acuity was 20/200 in the right eye; she could detect hand motions at one foot in the left eye. There was bilateral optic atrophy. Visual fields and pupillary reactions were normal, and a minimal left exotropia was present. The remaining cranial nerves were normal. Sensory and motor examination was unremarkable, as were cerebellar functions, deep tendon reflexes and the plantar responses.

Hemoglobin was 9.9 g/dl with normal granulocyte and platelet cell lines; iron studies were normal. Calcium and phosphorus were normal, although alkaline phosphatase was minimally elevated.

In addition to the aneurysm, carotid angiography demonstrated severe stenosis of both internal carotid arteries within the carotid canals and probable occlusion in the carotid canal, with collateral flow from the external carotid arteries via the ophthalmic arteries (fig. 2 and 3). The entire intracranial circulation filled with injection of the left vertebral artery (fig. 4). A superior cerebellar artery aneurysm was present. High resolution computerized tomography of the base of the skull failed to demonstrate the carotid canals, although other bony canals were well seen.

A left subtemporal craniectomy was performed, during which the temporal squama was found to be one-half inch thick, and the aneurysm obliterated with a Sugita clip. The post-operative course was uneventful.

Case 2

G.E was one of two monozygotic twins born in 1972 to normal parents at 34 weeks gestation, and weighed four pounds, four ounces at birth. Both twins suffered from the autosomal recessive form of osteopetrosis. In her eleventh month, a left facial palsy developed. By fifteen months, she had bilateral abducens palsies, bilateral proptosis and was developmentally delayed. Pancytopenia with hepatosplenomegaly was present.

Concern over an expanding head, neurological deficits and the presence of a large dilated scalp vein prompted angiography. The left internal carotid artery was severely stenosed within the petrous bone with evidence of increased flow in the external carotid system (fig. 5 and 6). The jugular system could not be demonstrated with carotid injection. Injection of a large emissary vein showed initial reflux into the superior sagittal sinus but with a subsequently abnormal pattern of flow (fig. 7). The superior sagittal sinus did not drain posteriorly into the transverse sinuses but instead contrast was carried out into a network of dilated scalp veins. These then coalesced into a massively dilated scalp vein which eventually drained into the external jugular vein. There was a small amount of reflux up the internal jugular vein. It was concluded that the left internal carotid artery was severely stenosed within the carotid canal, and at least one internal jugular vein was occluded within the jugular foramen with probable thrombosis of the transverse sinuses and posterior third of the posterior sagittal sinus.

Severe proptosis with exposure keratitis and failing vision was treated with orbital decompression and subsequent tarsorrhaphy. By age two the patient and her twin both had bilateral facial palsies, optic atrophy and severe hematological problems including thrombocytopenia. Both had shunted hydrocephalus which was stable. Just before her third birthday, she suffered a
probable subarachnoid hemorrhage with minimal neurological deficit. Two weeks later she died of a respiratory arrest.

Discussion

Osteopetrosis (Albers-Schonberg's disease, marble bones) is a rare bone disorder first described in a 26-year-old man with generalized skeletal sclerosis and multiple pathological fractures. Osteoclasts are abundant but dysfunctional, resulting in disorganized bone structure and failure of remodeling. Two forms of the disease occur clinically. The autosomal recessive form is seen in infancy, in which myelophthisic anemia usually proves fatal. Extramedullary hematopoiesis and peripheral leukoerythroblastosis occurs but is insufficient to prevent death in the first few years of life. The less severe autosomal dominant variety is asymptomatic in 50% of cases and in others results in variable degrees of pancytopenia, pathological fractures, bone pain and osteomyelitis. Serum calcium and alkaline phosphatase are usually normal. Treatment is supportive, with splenectomy in older patients if indicated. Recent experience with bone marrow transplantation and with calcitriol has been encouraging.

Neurological manifestations of osteopetrosis are common. Deposition of mineralized osteoid occurs in cranial nerve foramina and cerebrospinal fluid flow pathways, in a manner analogous to the ablation of marrow cavities. In the infantile, autosomal recessive type, hydrocephalus and developmental delay may be seen. In both forms of the disease, cranial nerve palsies are common. Compression of cranial nerves...
1–8 has been reported, but not nerves 9–12. This is surprising but may reflect natural selection operating against those unable to protect their airway, i.e. those with lower cranial nerve involvement. Combined frontal and parietal bossing is said to be characteristic. Features suggestive of intra-axial involvement, of uncertain significance, include vertical nystagmus, neuroaxonal dystrophy, EEG abnormalities, neuronal storage disease, and signs of pyramidal dysfunction not explained by stenosis of the foramen magnum or spinal canal.

Blindness, with optic atrophy and pendular nystagmus, is frequently seen but poorly understood. Narrowing of the optic foramina has frequently been observed and surgical unroofing of the optic canal has been advocated. There are, however, several cases in which other mechanisms appear to be operative. These have included primary retinal degeneration and optic atrophy secondary to chronic papilledema.

The two patients described in this report present several features which are unique in the literature concerning neurological complications of osteopetrosis. Severe stenosis of the carotid arteries within the carotid canals was present in both cases, and was bilateral in one. There were no ischemic deficits present, but the resultant abnormal intracranial hemodynamics may...
have been a factor in the development of a posterior fossa aneurysm. In view of the intrapetrous location of the stenoses, the failure to demonstrate the carotid canals with CT and the generally accepted tendency of osteopetrotic bone to impinge upon skull foramina, this latter mechanism was probably responsible for the carotid stenosis in these patients. The child with abnormal patterns of venous flow had non-filling of the transverse sinuses and internal jugular veins on both carotid and venous angiography, with well-developed extracranial venous collateral pathways. It is probable that bony overgrowth intruded upon the internal jugular veins in the jugular foramina. Dilated scalp veins are a recognized clinical sign of superior sagittal sinus thrombosis in other conditions.

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