weight, mild, diffuse upper limb weakness, and severe lower limb weakness. The weakness was predominantly distal and deep tendon reflexes were absent in all four limbs. All sensation modalities were impaired in her cheeks, trunk, and limbs, predominantly distal. She complained of dysaesthesia in her left cheek, forearms, and legs. She could barely stand with support. Mild myalgia was present in the thigh muscles. Laboratory tests showed a moderate increase in serum creatine kinase (496 IU/1) and a small increase in glutamic oxaloacetic transaminase, glutamic pyruvic transaminase, and lactate dehydrogenase. On the second day in hospital, motor conduction velocity was normal in all limbs, but a low amplitude motor potential was noted in the tibial nerves. Sensory conduction velocity was normal in the median nerves, but sural nerve action potentials and F waves in the median and tibial nerves were absent. A conventional needle EMG showed that the interference pattern in limb muscles during maximal voluntary contraction was reduced but the motor unit potential was normal. There was no denervation potential at rest. Brain CT showed left frontal atrophy despite her normal intelligence. On the morning of the third day in hospital, she complained of nausea and dyspnoea with tachypnoea. Blood gas analysis showed severe metabolic acidosis (pH 7·01). Despite an intravenous infusion of 400 ml 7% sodium bicarbonate, her metabolic acidosis worsened (pH 6·97). She went into a state of shock in the evening and was given continuous haemodialysis for 52 hours. Two plasma exchanges were also given. During the next several days, her condition was critical, with multiple organ failure, including acute respiratory failure, acute renal failure, acute heart failure, and rhabdomyolysis. Even after her acute pulmonary oedema improved, she required mechanical ventilation for four months because of respiratory muscle weakness. The peak values of serum myoglobin and creatine kinase were 18 000 ng/ml and 20 800 U/l respectively at this time. Lactic acid and pyruvic acid had reached 294·4 mg/dl and 8·94 mg/dl, respectively by 10 hours after we first became aware of her acidosis. Her CSF protein and cell count were normal in three examinations carried out during the course of her illness.

Muscle biopsy from her left quadriceps femoris, taken on the seventh day in hospital, showed ragged-red fibres among necrotic fibres and scattered small angular fibres. No apparent grouping of fibre type was evident. A sural nerve biopsy three months after admission showed a severe decrease in myelinated fibres. Teased fibre preparations showed myelin ovoid formation and no demyelination.

Mitochondrial DNA analysis after amplification of the tRNA$^{Leu(UUR)}$ gene region and digestion with ApaI[1] showed 3243 A to G point mutation in blood and muscle samples from the patient, as well as in blood samples from her mother, brothers, and sisters. The percentage of mutant was about 40 in her blood and 70 in the muscle sample. She was treated with 3·0 g of sodium succinate, 150 mg of coenzyme Q, and 30 mg of idebenon per day. One month after admission motor conduction velocity of the left tibial nerve was slightly reduced (38·0 m/s) and the amplitude was reduced to 200 μV. Seven months after admission,

the motor conduction velocity had recovered to normal, with low amplitude motor potentials in the legs, but needle EMG showed polyphasic long duration motor unit potentials in her limb muscles. After 18 months, she was able to stand without support. Her reflexes were improved but the achilles tendon reflexes were still absent. Sensory disturbances also disappeared but painful dysaesthesia remained in her lower legs.

In this case, the diagnosis of MELAS was based on the history, the existence of lactic acidosis, ragged-red fibres, and mitochondrial DNA analysis. There were several new clinically important points in this patient with MELAS:

Firstly, she developed symptoms during her first and second pregnancies; therefore, gestation was possibly an aggravating factor for her.

Secondly, she had acute axonal neuropathy, which has rarely been reported with MELAS, although ophthalmoplegia plus or myoclonus epilepsy with ragged-red fibres has been reported to be associated with neuropathy.[2][3] None of the patients with MELAS reported by Markesbery[4] and Katsuragi *et al*[5] had major features of neuropathy such as sensory disturbance or muscle weakness.[4][5]

Thirdly, rhabdomyolysis has not been reported in MELAS. Our patient certainly developed rhabdomyolysis after an episode of critical acidosis, because her serum creatine kinase on that morning was 506 U/l, and it rose to 20 800 U/l the next morning. Hypotension, acidosis itself, or two days of treatment with betamethasone followed by its withdrawal might cause rhabdomyolysis.

Fourthly, she developed critical lactic acidosis, which improved with continuous haemodialysis and plasma exchange. Therefore, haemodialysis or plasma exchange should be considered in severe lactic acidosis in MELAS. Finally, this case adds a new clinical manifestation associated with the 3243 A to G mutation in mitochondrial DNA.

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1 Tanaka M, Ino H, Ohno K, *et al.* Mitochondrial DNA mutation in mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episode (MELAS). *Biochem Biophys Res Commun* 1991;174:861–8.
2 Peyronnard J-M, Charron L, Bellavance A, Marchand L. Neuropathy and mitochondrial myopathy. *Ann Neurol* 1980;7:262–8.
3 Yannikas C, McLeod JG, Pollard JD, Baverstock J. Peripheral neuropathy associated with mitochondrial myopathy. *Ann Neurol* 1986;20:249–57.
4 Markesbery WR. Lactic acidemia, mitochondrial myopathy, and basal gangria calcification. *Neurology* 1979;29:1057–61.
5 Katsuragi S, Shimoji A, Watanabe K, Miyakawa T. Pathological findings of the sural nerve in mitochondrial encephalomyopathy. *Jpn J Psychiatr Neurol* 1988;42:307–13.

Papilloedema and visual failure in a patient with nocturnal hypoventilation

A morbidly obese woman treated for polymyositis developed symptoms of raised intracranial pressure and visual failure. Invasive CSF pressure monitoring showed normal pressures during the day, but transient episodes of raised intracranial pressure during sleep. These episodes were associated with hypoxia and hypercarbia, and suggest a possible aetiological relation between increased intracranial pressure, visual failure, and nocturnal hypoventilation.

A 45 year old woman was admitted for investigation of headaches, papilloedema, and progressive visual failure. She was morbidly obese (weight 126 kg, body mass index 52·7 kg/m^2) and gave a history of recurrent deep vein thrombosis, pulmonary emboli, and polymyositis (treated with prednisolone and azathioprine). Examination showed bilateral papilloedema with visual acuities of 6/24 in the right eye, and just able to count fingers with the left. A lumbar puncture had only been successful in the sitting position; hence an accurate measurement of the CSF opening pressure had not been recorded. Biochemical and cytological analysis of the CSF was unremarkable, and CT of the head was normal. A clinical diagnosis of benign intracranial hypertension was made and a neuroophthalmological opinion sought. A left optic nerve fenestration was performed without improvement, and so detailed assessment of the intracranial pressure was requested. Access to CSF was achieved with a right frontal ventricular catheter connected to a subcutaneous reservoir. Continuous monitoring of intracranial pressure was undertaken from the reservoir (Camino optical transducer) through a fluid filled transcutaneous butterfly needle (21G). Radial arterial blood pressure, middle cerebral artery flow velocities by transcranial Doppler (Scimed), and continuous measurements of peripheral oxygen saturation by Multinex oximetry were also taken, and displayed graphically on a portable computer. The cerebral perfusion pressure (mean radial arterial blood pressure-mean intracranial pressure) and pulsatility of the middle cerebral artery flow velocity (FV) were calculated (pulsatility index PI = FV amplitude/FV mean) were calculated. Recordings were carried out during the night with the patient in her usual sleeping position (20 degrees head up) for up to 10 hours. Before sleep, baseline intracranial pressures of 5–15 mm Hg were recorded. Within one hour of sleep, cycles of high pressure waves (40–45 mm Hg) lasting 10–20 minutes were evident, occurring every 60–120 minutes and superimposed on higher background pressures of 15–25 mm Hg (fig 1). The intracranial pressure waves were accompanied by a fall in cerebral perfusion pressure to as low as 40 mm Hg, and were tightly coupled with increases of middle cerebral artery flow velocity and decreases in cerebrovascular resistance.

Respiratory function was evaluated further; arterial blood gases showed daytime hypoxia (mean PaO$_2$ = 9·1 kPa) with normocapnia (mean PCO$_2$ = 5·2 kPa). Overnight ventilation studies indicated a mean baseline arterial saturation of 88·2% and end tidal PCO$_2$ of 6·1 kPa. During the periods of raised intracranial pressure,
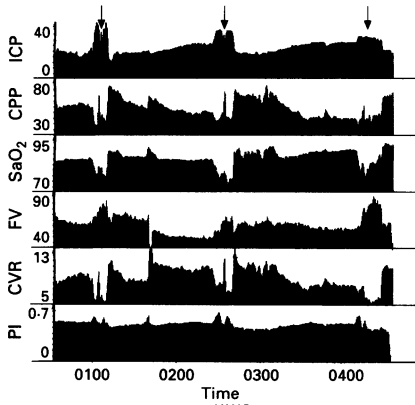
Figure 1 Recording of a four hour period of continuous signal monitoring while the patient was asleep. Three episodes of transient hypoxia are captured (arrowed) during which peripheral saturation fell to 70–75%, ICP rose to 35–40 mm Hg, and CPP fell to 40–45 mm Hg. The increase in FV and fall in calculated CVR are compatible with cerebral vasodilation. ICP = intracranial pressure (mm Hg); CPP = cerebral perfusion pressure (mm Hg); FV = middle cerebral artery flow velocity (cm/s); CVR = cerebral vascular resistance ((mm Hg/s)/cm); PI = pulsatility index of FV.

further arterial desaturation to a mean of 73% occurred with an increased end tidal PCO₂ of 7·8 kPa. These episodes were associated with hypoventilation (reduced abdominal and chest wall movements) without apnoea or airway obstruction. She was given a continuous positive airway pressure device, which provided minor symptomatic relief and improved the mean baseline arterial saturation to 97·5% but failed to abolish the high nocturnal waves of intracranial pressure. A ventriculoperitoneal shunt was therefore inserted and a further period of monitoring undertaken (fig 2). The changes in middle cerebral artery flow velocity and cerebrovascular resistance still occurred with the episodes of desaturation, but the associated increases in intracranial pressure were abolished. At six month follow up her headaches had disappeared, the papilloedema had resolved, and the acuity in the right eye had improved to 6/12.

Several possible aetiological factors for benign intracranial hypertension may have contributed to the visual deterioration in this patient including subclinical cerebral venous thrombosis.[1 2] Although the primary aetiology in our case is not known, raised intracranial pressure occurred during sleep and accompanied episodes of hypoxia and hypercapnia. These were associated with haemodynamic changes compatible with
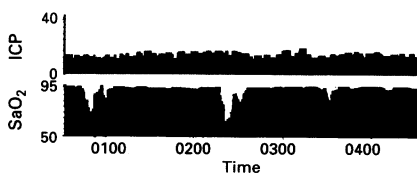

Figure 2 Nocturnal record of ICP and SaO2 after the insertion of a ventriculoperitoneal shunt. The hypoxic events still occur, but the associated increases in ICP have been abolished. ICP = intracranial pressure (mm Hg); SaO2 = peripheral oxygen saturation (%).

cerebral vasodilation. We therefore suggest that nocturnal hypoventilation producing cerebral hypoxia, hypercapnia, and a subsequent rise in intracranial pressure secondary to increased cerebral blood volume contributed to the symptoms. Chronic respiratory disease with severe hypercapnia has long been recognised as a cause of raised intracranial pressure and papilloedema[3] but there were no such features in this case, and although a significantly raised CSF pressure is required for the diagnosis of benign intracranial hypertension, the clinical and radiological features in our patient were typical of this condition.[1] Further, low baseline CSF pressures are often found in patients with chronic benign intracranial hypertension despite persisting papilloedema.[4] Two important points are raised. Firstly, abnormal CSF dynamics require continued observation over several hours as baseline CSF pressure may be normal and waves of raised intracranial pressure transient. Inadequate attention to CSF dynamics may partly explain why isolated CSF pressure estimations do not predict the development of papilloedema and visual deterioration.[5] Secondly, although nocturnal hypoventilation has not been quoted as a contributing factor in benign intracranial hypertension, a relation with raised intracranial pressure has been found. Overnight monitoring of peripheral oxygen saturation may be a useful addition to the investigation of obese patients with symptoms of raised intracranial pressure.

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1 Johnston I, Paterson A. Benign intracranial hypertension. *Brain* 1974;97:289–300.
2 Gerris F, Sorenson PS, Vorstrup S, *et al.* Intracranial pressure, conductance to cerebrospinal fluid outflow and cerebral blood flow in patients with benign intracranial hypertension (pseudotumor cerebri). *Ann Neurol* 1985;17:158–62.
3 Miller A, Bader RA, Badre ME, *et al.* The neurological syndrome due to marked hypercapnia, with papilledema. *Am J Med* 1962;33:309–12.
4 Corbett JJ. Cerebrospinal fluid pressure in normal obese subjects and patients with pseudotumor cerebri *Neurology* 1983;33: 1386–8.
5 Orcutt JC, Page NGR, Sanders MD. Factors affecting visual loss in benign intracranial hypertension. *Ophthalmology* 1984;91:1303–12.

Hemichorea reversible after operation in a boy with cavernous angioma in the head of the caudate nucleus

Hemichorea and hemiballism point to a structural lesion in the contralateral basal ganglia with a large list of possible causes, including various vascular malformations. Cavernous angiomas are congenital vascular malformations that are occult on conventional angiography (hence "cryptic" vascular malformations (CVMs) but have a characteristic, nearly diagnostic MR image.[1] The definitive diagnosis and distinction from other cryptic vascular malformations depends on histological examination. The clinical manifestations of cavernous

angiomas include epilepsy, acute signs secondary to (recurrent) bleeding, and rarely progressive neurological deficit due to expansion of a mass of thrombi within the angioma. With the availability of MRI the number of clinical reports on the subject of CVMs has increased. Recently a case was reported of cavernous angioma in the lentiform nucleus that was the first to present with a movement disorder, in this case focal dystonia. Complete resection was followed by resolution of the symptoms.[2]

We report an 11 year old boy with cavernous angioma in the caudate nucleus, presenting with contralateral hemichorea, evidence of recurrent bleeding, and the disappearance of the hemichorea after surgery.

The boy complained of involuntary movements of the right half of his body including his face, arm and leg, that had suddenly started the week before admission. He could not suppress these movements. There was no family history of neurological disease.

The neurological examination on admission showed continuous, random, jerking movements of the face and extremities on the right side of the body. Muscle strength, sensation, and reflexes were normal.

Brain MRI (figure A) showed a lesion in the head of the caudate nucleus, with the typical aspect of a cavernous angioma.

Two weeks later the boy experienced a sudden deterioration, with involuntary movements of a larger amplitude, more appropriately termed hemiballistic. Surgery was considered appropriate.

With the Leksell stereotactic frame (Elekta Co, Sweden) the shortest route to the lesion via the paramedial frontal lobe was estimated. At that spot a small burr hole was made and a silastic tube was passed to the border of the lesion with a Backlund catheter implantation set. After craniotomy the lesion was reached with the catheter as a guide. The mulberry like vascular lesion was removed completely, including two small haemorrhages.

Histology (figure B) showed a conglomerate of vascular channels of different size. The wall of these channels consisted of a single inner layer of endothelial cells and an outer layer of collagen of varying thickness. Some vascular spaces were occluded by a recent or an organised thrombus and some vessel walls were partly calcified. Iron pigment was found in and around several vessels, as evidence of prior bleeding. The surrounding brain tissue showed pronounced gliosis and deposition of iron.

In the two months after the operation the hemichorea-hemiballism disappeared completely. Control MRI (figure C) showed complete removal of the angioma.

This case is to our knowledge the first in the literature of a histologically confirmed cavernous angioma presenting with hemichorea. Hemichorea has been described in lesions of the caudate nucleus, and is thought to reflect release phenomena caused by a lesion of the striatal neurons projecting to the external globus pallidus.

The incidence of cavernous angiomas remains obscure. In a consecutive series of 11 children operated on for cerebral vascular malformations five were diagnosed to have cavernous angiomas.[3] Scott *et al*[4] state that in some paediatric institutions cavernous angiomas are the most common cerebrovascular malformations encountered. Most cavernous angiomas, however,