adversely affects neonatal outcome as assessed by the one-minute Apgar score and perinatal mortality. Five- and 10-minute Apgar scores were not evaluated as too few infants in either group had Apgar scores under 7 at five or 10 minutes to allow meaningful comparison.

No differences were found in either the interval between full dilatation and delivery of the first twin or the forceps rate for poor maternal effort in the two groups. This was probably related to our practice of waiting for the presenting part to become visible before encouraging the patient to push.

It has already been shown that the use of an epidural block in labour in singleton breech presentations does not increase the incidence of breech extraction.^{5 6} Our study has shown that neither does it increase the incidence of breech extractions when either twin presents by the breech.

We conclude therefore that epidural block is safe in labour in twin pregnancy. It affords better pain relief and allows prompt

intervention should intrauterine manipulations be necessary to effect delivery of the second twin.

We thank the consultant obstetricians who allowed us to study patients under their care and Mr C R West, who kindly helped with the statistical analysis.

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Respiratory arrest in familial hemiplegic migraine: a clinical and neuropathological study

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Summary

We describe a fatal case of familial hemiplegic migraine. A transient respiratory arrest in this patient led to a persistent "vegetative state," culminating in death four months later. Neuropathological findings included deep microinfarcts in the basal ganglia and a remarkable sparing of brain-stem nuclei associated with the function of respiration.

Introduction

Known complications of migraine include persisting hemiparesis, facial weakness, ophthalmoplegic and visual field defects. Deaths have been attributed to migraine,^{2 3} but terminal anoxia in some cases makes pathological interpretation difficult. We describe a patient who suffered respiratory arrest during an attack of hemiplegic migraine, which led to a "persistent vegetative state." By familial hemiplegic migraine, we refer to the condition defined by the World Federation of Neurologists Research Group as "a rare condition, which may exhibit a dominant inheritance, characterised by episodic migrainous attacks associated with hemiplegia outlasting the headache."¹

Case report

A 41-year-old, right-handed housewife presented at Hull Royal Infirmary as an emergency admission in October 1976. She was a

member (IIc) of a family with hemiplegic migraine (fig 1). All the affected members shown in the pedigree suffered from hemiplegic migraine, with paresis lasting from two hours up to seven days in various attacks we have observed. In 1972 she had described attacks of severe right or left frontal headache, accompanied after five minutes by numbness and weakness of limbs of either side, which had occurred since the age of 9. The face, arm, and leg were affected, with variable dysphasia and sickness, but no visual disturbance. Attacks lasted up to one hour. She had had no such attack since 1962.

FIG 1—Family pedigree of patient, showing members affected by familial hemiplegic migraine. Age in years shown beneath each member of family.

Thirty-six hours before admission she awoke with severe right temporal headache, and some minutes later was unable to use her left arm. She had not taken oral contraceptives. On admission she was drowsy, but would talk coherently, and was orientated when roused. She was feverish (38.5°C), irritable, and photophobic; her neck was stiff. She had a moderate left hemiparesis, and the fundi were normal. In view of the previous episodes and family history we diagnosed hemiplegic migraine.

The next day she developed alternating left- and right-sided epileptic attacks, on occasions becoming generalised, lasting two minutes, and recurring frequently. She remained unconscious

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between fits, which were controlled by intravenous phenytoin and diazepam. As she recovered a dense right hemiplegia became apparent. Lumbar puncture was performed, producing clear cerebrospinal fluid (CSF), pressure 160 mm; white cells $0.29 \times 10^9/l$ (94% polymorphonuclear cells); protein 0.41 g/l (41 mg/100 ml); no organisms seen; culture sterile. Electroencephalography (EEG) showed diffuse delta activity at 10–25 μV . Similar EEG patterns were found two, 10, and 36 days later.

We performed a tracheostomy because of inadequate irregular ventilation, and gave oxygen, dexamethasone, and dextran 40. Over the next seven days she gradually regained consciousness and moved all limbs spontaneously, but she was dysphasic, and failed to obey simple commands. Nine days after admission she suddenly stopped breathing. She became cyanosed with fixed dilated pupils, but there was no evidence of circulatory arrest. We estimated the apnoeic interval at four minutes. Twenty minutes after resuscitation she could breathe spontaneously; the pupils were normal. Respiration again became irregular, and mechanical ventilation was begun. Bilateral carotid angiography showed nothing abnormal, and repeat lumbar puncture produced cell-free fluid. After three days adequate independent respiration returned, but she remained in stupor. The subsequent picture was of a post-anoxic encephalopathy with no improvement.

Three months later she was in a "persistent vegetative state", totally dependent on nursing care and unable to communicate. She developed a salmonella infection, complicated by hypostatic pneumonia, and died four months after the episode of respiratory arrest.

Necropsy findings

MACROSCOPIC APPEARANCES

Brain—Weight (after fixation) 980 g. Serial coronal section showed bilaterally distributed lesions in the basal ganglia (fig 2). These took the form of 0.3-cm diameter cysts in the dorsal globus pallidus, with a smaller, more laterally placed lesion in the medial putamen on the left. There was granular necrosis of the head and body of the caudate nucleus, which extended into the tail at the level of the thalamus.

FIG 2—Cystic infarcts in head of left caudate nucleus (L) and putamen, and granular infarct in head of right caudate nucleus (R). Floor of left lateral ventricle is indented.

Elsewhere through the hemispheres white matter-vessels were prominent, but no large white or grey matter infarctions were seen. The substantia nigra was normally pigmented, and the thalamus showed no macroscopic lesion. The brain stem and cerebellum were normal externally, and section showed only congestion of stem vessels. No focal ischaemic lesions were visible within the cerebellar hemispheres, although there was a patchy greyness of the granular layer.

Histology—Blocks were taken from representative areas and embedded in paraffin. Routine stains were used.

Cerebral cortex—There was no laminar necrosis, but both parietal and occipital cortex showed small sulcal infarcts, characterised by loss of most neurons and an abundant gliosis with swollen astrocytes. The

parietal lesion involved all cortical laminae in the depths of the sulcus, but in the occipital lesion the fifth and sixth laminae were spared. A capillary close to the parietal infarct contained a formed, granular thrombus.

Basal ganglia—There were many small, irregular, coalescent infarcts in the basal ganglia, of varying age, one traversing the internal capsule. They were present in the head and body of the caudate nucleus (fig 3), putamen, globus pallidus, and thalamus. The oldest showed central rarefaction, a peripheral zone of massed foam cells, and an outer zone of proliferated, swollen astrocytes. Capillaries were prominent in the peripheral zone. Others showed no rarefaction, but various combinations of neuron loss, capillary prominence, foam cells, astrocytosis, and demyelination. Small arteries were mostly normal, but some within or near the infarcts were thick-walled, with or without subintimal fibrous hyperplasia, some loss of muscle nuclei, and a variable reaction of the elastica (fig 4). This consisted of fragmentation and reduplication of the internal elastic lamina throughout the media, or sometimes complete loss. Arteries in the pallidum showed siderosis, including those within infarcts. Occasionally there was fibrous adventitial thickening. No thrombi were found.

Midbrain, pons, and medulla—The brain stem including pons and medulla showed no external signs of infarction. Four transverse sections were taken through the pons and medulla, and stained with haematoxylin and eosin, haematoxylin van Gieson, reticulin, and Luxol fast blue. No evidence of ischaemia or infarction was apparent.

FIG 3—Stained section showing softening in head of caudate nucleus, with cavitation. Walls of blood vessels are thickened. (Haematoxylin and eosin. $\times 40$.)

FIG 4—Stained section showing softening of elastica in head of caudate nucleus and reduplication of elastic lamina in vessel walls. (Elastic van Gieson's. $\times 100$.)

Cerebellum—There was widespread loss of Purkinje's cells, with proliferation of Bergmann's glia and gliosis of the dentate nucleus.

Examination of the heart, aorta, carotid, and vertebral vessels at the base of the brain showed no occlusive atherosclerotic lesions, nor were there any vascular stenoses.

Discussion

The diagnosis of migraine was confirmed by previous serial clinical examination of the patient and all the members of her remarkable family. Other possible lesions were excluded by angiography, EEG, and CSF examinations. CSF pleocytosis is well recognised in migrainous cerebral infarction,⁴ and the pathological findings rule out an incidental encephalitis.

The only similar example of respiratory arrest in migraine is a girl who required mechanical ventilation for several hours before dying of "intense ischaemia confined to territories supplied by the carotid and supratentorial basilar vessels."² The clinical possibility of basilar artery migraine⁵ causing an infarct of the "respiratory centre" in the medulla was not confirmed pathologically. Thus, the reason why she stopped breathing is not clear.

Interpretation of the pathological findings in our patient was not obscured by the anoxic changes secondary to respiratory arrest, which have made interpretation of other cases so difficult. Before respiration was impaired the clinical features (for example, epilepsy, dysphasia, and preservation of oculovestibular reflexes) strongly suggested bilateral hemisphere ischaemia; secondary pontomedullary ischaemia cannot, however, be excluded. Until further cases have been recorded in detail, the possible explanations are either primary hemisphere ischaemia and oedema with secondary brain-stem failure, or primary brain-stem failure due to basilar artery migraine. It is curious, however, that an ischaemic insult of this clinical severity may leave no pathological trace of damage in the appropriate site.

Since this patient had had attacks of hemiplegic migraine from the age of 9, which presumably resulted in vascular spasm and humoral changes affecting the microcirculation,⁶ then it is reasonable to suppose that temporary ischaemia of vulnerable structures, including the internal capsules and the neighbouring basal ganglia, might ensue. It was in just such areas that microinfarcts of differing ages were found at necropsy. When she was admitted to hospital the spasm may have been so prolonged as to produce foci of total and subtotal infarction. The lesions produced were microinfarcts, rather larger than the infarcts of the état lacunaire which is so closely associated with hypertension, but consisting of tiny perivascular infarcts only. Interestingly, some small arteries in the affected areas in this relatively young patient had thickened walls with reduplicated elastic laminae. This may have been a reaction to repeated spasm. Siderosis of arteries occurred only in areas where vascular infiltration by iron salts is common, such as the globus pallidus, and is not likely to be relevant. Fatal cases of migraine are obviously very rare. So far as we know, however, micro-

infarcts with focal medial and intimal changes in deep structures have not been previously described.

As the patient developed respiratory arrest, resulting in a persistent vegetative state in the middle of her illness, lesions due solely to cerebral anoxia should be identified at necropsy. Clearly a single anoxic episode could not have caused the infarcts of widely differing ages in the basal ganglia and internal capsules. Nevertheless, such an episode may have caused the loss of Purkinje's cells in the cerebellum and the cortical sulcal infarcts, although cortical hypoxia usually takes the form of laminar necrosis. Thus we feel that these deep microinfarcts may be associated with migraine per se rather than a sequel to a diffuse anoxic brain injury.

Restriction of cerebral blood flow may be so severe as to reach critical levels of oxygen supply.⁷ In such instances reflex increase in flow in response to inhaled CO₂ is abolished, and a lactic acidosis in the CSF indicates local tissue acidosis resulting from ischaemia.

Clinical evidence of infarction with survival is well established in migraine,⁸ but a recent paper⁹ identified three infarcts on computerised axial tomography in a series of 53 patients with exceptionally severe or complicated migraine; mild generalised atrophy was common, but focal atrophy, a recognised sequel to infarction, was shown in eight of this series.

Thus there is abundant precedent for migrainous vasospasm, with occasional instances of ensuing infarction or atrophy. But respiratory arrest and deaths are mercifully rare. This case provides no good explanation. It does suggest that deep basal microinfarcts may correspond to previous attacks of migrainous hemiplegia, and that respiratory arrest may occur without pathological evidence of a primary ischaemic infarct in the medulla. A possible explanation is medullary failure secondary to massive hemisphere oedema, which was reversed by steroids, leaving no gross pathological changes in cortex or white matter at death four months later.

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