Cerebral damage in neonates resulting from arteriovenous malformation of the vein of Galen

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SYNOPSIS Seven neonates with arteriovenous malformation of the vein of Galen are described. Six presented with cyanotic heart failure. Two cases had antenatal cerebral infarction, five periventricular leukomalacia, and three recent haemorrhagic infarction. Cerebral damage due to the malformation suggests that surgical correction of the arteriovenous malformation offers little to neonates, though after the neonatal period individuals can be cured by operation.

The vein of Galen, formed by the union of the two internal cerebral veins drains into the straight sinus. The malformation in which one or more arteries feed directly into the vein of Galen probably arises in the 20-40 mm fetus when arteries and veins are still simple endothelial tubes (Padget, 1956). In neonates with arteriovenous malformation of the vein of Galen, the high incidence of cerebral damage due to the malformation and the incredible multiplicity of arterial feeders into the malformation have never been emphasized. These make the clinical and therapeutic problem in neonates different from that in older infants and children. Neonates

present at or shortly after birth with cyanosis and congestive heart failure due to the magnitude of arteriovenous shunting through the malformation; infants present with seizures and hydrocephalus because the aqueduct is compressed by the aneurysm which sits on the quadrigeminal plate; older individuals present with sub-arachnoid haemorrhage (Gold *et al.*, 1964).

In three years seven cases of neonatal arteriovenous malformation of the vein of Galen have been seen at this hospital. The clinical information has been summarized in Table 1. In this paper we first present a case report (case 1) which illustrates the stereotyped histories of cases 1-6,

TABLE 1

CLINICAL DATA FROM SEVEN NEONATES WITH ARTERIOVENOUS MALFORMATION OF VEIN OF GALEN

	Case						
	1	2	3	4	5	6	7
Sex	M	M	F	M	M	M	M
Age of presentation	Birth	1 hour	3 days	Birth	Birth	Birth	6 days
Cyanosis	+	+	Intermittent	+	+	+	-
Systolic heart murmur	+	+	+	+	+	+	-
Congestive heart failure	+	+	+	+	+	+	-
Cranial bruit	+	+	+	+	NR	-	NR
Hydrocephalus	-	-	-	-	-	-	+
Neurological symptoms	Seizures and unconscious terminal	-	-	Episode of twitching of right leg	-	-	Opisthotonos seizures
Diagnosis made antemortem	+	+	+	+	+	-	-
Attempted surgical repair	+	+	-	-	-	-	-
Age at death (days)	6	5	21	2	3	2½	13

+ present. - absent. NR not recorded.

TABLE 2

PATHOLOGICAL FINDINGS IN SEVEN NEONATES WITH ARTERIOVENOUS MALFORMATION OF VEIN OF GALEN

	Case						
	1	2	3	4	5	6	7
Brain weight (% normal)	NR	48	83	140	77	100	100
Size of aneurysm (cm)	3 × 1.5	ligated	1 × 2	3 × 3.5 × 1	4 × 1.5	3 × 2.5	2 × 3 × 4
Diameter of basilar artery (cm)	0.5	0.35	0.3	0.3	—	0.3	normal
Feeding vessels	Bilat. PCA	Bilat. PCA R. PcA Bilat. ACA	Bilat. PCA R. Ch.	Bilat. PCA R. Occipital	Bilat. PCA	Bilat. PCA	L. Ch.
Thrombosis of aneurysm	—	—	—	—	—	—	+
Antenatal cortical infarction	—	+	—	—	+	—	—
Periventricular leukomalacia	+	+	—	+	+	—	+
Haemorrhagic infarction	+	—	—	—	—	+	+
Operative damage	+	—	—	—	—	—	—
Heart weight (normal 18 g)	61	NR	60	54	49	38	18

PCA posterior cerebral arteries. ACA anterior cerebral arteries. PcA posterior communicating artery. Ch choroidal. + present. — absent. NR not recorded.

followed by a report of the rather different case 7. Pathological findings for all seven cases are described briefly and are tabulated in Table 2.

CASE 1

This 4,360 g full-term male infant was admitted at 2 days of age because he was dusky while feeding, had tachypnoea, tachycardia, an irregular heart rhythm, and was becoming more cyanosed.

On admission he was dusky and irritable. His cyanosis increased when he cried. Respiration rate was 60/min; blood pressure 95 mmHg, and heart rate 160/min, regular. The heart sounds were obliterated by a loud systolic murmur which was loudest down the left sternal border in the 2nd–3rd interspace and radiated to the left axilla. His liver and spleen were enlarged. The diagnosis on admission was congenital malformation of the heart, possibly tetralogy of Fallot. He had a convulsion. Cardiac catheterization was performed (Table 3) and cineangiocardiology showed a large patent ductus arteriosus, large aortic branches, and a possible coarctation of the aorta just distal to the left subclavian artery. On the 3rd day of life, through a left thoracotomy incision, a patent ductus arteriosus was ligated; no coarctation was present. The cineangiogram and catheterization data were reviewed, and on further examination a loud cranial bruit was heard. The diagnosis of arteriovenous malformation of the vein of Galen was confirmed by a cerebral arteriogram. On the 4th day of life he had several episodes of tonic rigid hyperextended posture and twitching around the mouth. He was unconscious, without primitive responses; his pupils were dilated and reactive, his legs were rigid, arms hypertonically

tendon reflexes unobtainable, and plantar responses were upgoing. His blood sugar concentration persisted below 25 mg/100 ml. Tests of the coagulation mechanism suggested disseminated intravascular coagulation, so heparin was administered. He developed oliguria and a rising blood urea nitrogen. Frusemide (Lasix) was administered without result. Peritoneal dialysis was begun. He remained desperately ill. His congestive heart failure remained refractory to treatment (which had included adequate digitalization). On the 7th day of life he was operated on under cardiopulmonary bypass, hypothermia, and circulatory arrest. An attempt was made to clip all the vessels feeding the aneurysmally dilated vein of Galen. When the cerebral blood flow was re-started, massive bleeding occurred at the operative site and he died.

CASE 7

This 2,980 g infant was delivered normally after a

TABLE 3
RESULTS OF CARDIAC CATHETERIZATION (CASE 1)

Site	O ₂ saturation (%)	Pressure (mmHg)
Superior vena cava	62	
Right atrium	60	
Inferior vena cava	25	
Right ventricle (high)	57	90/45
Main pulmonary artery	69	95/50
Pulmonary vein	93	
Left atrium	74	
Left ventricle	77	65/14
Aorta	55	70/45

39-week normal gestation. He did well till the 3rd day when he became jaundiced (microbilirubin, 14.7 mg/100 ml. blood). On the 7th day of life he was transferred to this hospital because he had become irritable, opisthotonic, and his anterior fontanelle bulged. The sagittal suture was split. His course from then until his death on the 13th day of life was of rapid deterioration. At first he was conscious and neurologically normal. Then he had fits and developed irregular respirations: On the last day of life he was unconscious with fixed dilated pupils and Cheyne-Stokes respirations. His head circumference rose from 36 cm to 39 cm, his packed cell volume dropped from 40 to 24 per cent from his 7th to 13th day. Initially, 'congenital hydrocephalus' and sepsis were considered diagnostic possibilities. Subdural haematoma were excluded by negative taps of the subdural space. Needling of the lateral ventricles produced bloody cerebrospinal fluid, and with the drop in haematocrit reading the diagnosis of intracerebral haemorrhage was made, though the reason for the haemorrhage was not suggested.

PATHOLOGICAL FINDINGS

CASE 1 A surgical defect 7.5 × 6 cm was present in the right parietal bone. Two large tortuous arteries, corresponding in origin to the posterior cerebral arteries, encircled the midbrain and fed into the aneurysmally dilated vein of Galen. Accompanying these arteries was a leash of smaller vessels 'too numerous, fine and intertwined to dissect'. Nine Mayfield clips were found on various vessels. Blood clot (20 ml.) lay between the falx cerebri and right superior parietal lobe. Examination of the brain showed a haemorrhage 1 × 0.2 cm in the right cingulate gyrus, multiple haemorrhages in the right caudate nucleus and thalamus, and a few small, scattered haemorrhages in the left thalamus. There were a few splinter haemorrhages and small lacerations in the right superior parietal cortex under the operative defect. Microscopic examination showed that all these haemorrhages were very recent. Several scattered foci of recent periventricular leukomalacia were present around the frontal poles of the lateral ventricles.

CASE 2 Brain weight was 159 g. The vein of Galen was fed by both posterior cerebral arteries plus several smaller companion vessels, the left posterior communicating artery, and both anterior cerebral arteries. The left frontal and both parietal lobes were disproportionately small. Areas most involved were left frontal lobe, bilateral cingulate gyri, right operculum, all the left superior parietal and right superior parietal lobes, and right occipital pole. The

gyri were narrowed, the sulci widened. The cortical ribbon was replaced by a firm white astroglial tissue which extended from the leptomeninges into underlying white matter. In some places, mostly parieto-occipital, there were cavitations (Fig. 1) up to 1.0 cm under this narrow gliotic subpial band, while in others there were gritty, yellow areas of calcification in the cores of affected gyri. Microscopic sections showed greatly dilated leptomeningeal vessels over the areas of old cortical infarction. The gliosis

FIG. 1. *Case 2. Coronal section of cerebral hemispheres. Old, gliotic cavitated infarction is present in the left superior parietal region and also around the medial and inferior surfaces of the right hemisphere. The ventricles are enlarged.*

consisted of densely packed fine glial fibrils and small regular astrocyte nuclei (Fig. 2). Neurones were gone from the infarcts, though a few encrusted neurones or processes persisted at their edges. Only a few macrophages remained. There was mild neuronal loss in the lateral portion of the right thalamus, and a few small, old, calcified areas of periventricular leukomalacia adjacent to the anterior poles of the lateral ventricles.

CASE 3 Brain weight was 382 g. The vein of Galen was fed by bilateral posterior cerebral arteries plus

several smaller accompanying vessels, bilateral anterior cerebral arteries and the vessels from the right choroid plexus (Fig. 3). The brain was normal.

FIG. 2. Case 2. Old cortical infarction. The pia mater is on the left, covering a band of astroglial scar beneath which is a cavity containing foamy macrophages. H and E, $\times 192$.

CASE 4 Brain weight was 627 g. The vein of Galen was fed by three vessels arising as left posterior cerebral vessels, two on the right and one from the right choroid plexus. The only lesion in the brain was a small focus of old calcified periventricular leukomalacia adjacent to the temporal horn of the right lateral ventricle.

CASE 5 Brain weight was 288.7 g. The vein of Galen was fed by a large number of arteries mostly from the posterior cerebral arteries. The inferior surface of the right occipital lobe was covered by a meshwork of dilated vessels which drained into the vein of Galen. Old bilateral parieto-occipital infarctions, with destruction of the cortical ribbon for 2.0 cm, and yellow discolouration of underlying white matter were present. Microscopic examination showed neuronal loss and gliosis in the cortex and a widespread astrocytosis and foci of calcification in the underlying white matter. There were a number of small, dilated, thin-walled vessels with calcified walls in these areas of astrocytosis (Fig. 4). Scattered foci of periventricular leukomalacia were present.

CASE 6 Brain weight was 329 g. The aneurysm was

FIG. 3. Case 3. The arteries have been injected with barium and the right cerebral hemisphere removed. Multiple tortuous arteries are going to the dilated vein of Galen (V).

FIG. 4. Case 5. Subcortical region. Basophilic material (sometimes staining positively for calcium) deposited in walls of dilated parenchymal vessels. Similar material is present in parenchyma (arrow). *H and E*, $\times 192$.

thin-walled and distended with post mortem clot. It was fed by bilateral posterior cerebral arteries. Microscopic sections showed a small focus of organized thrombus on the wall of an adjacent vein. Lines of petechiae radiated through the centrum

semiovale bilaterally from the corners of the ventricles to the cortex in the frontoparietal region, and surrounded the posterior horns in the parietal and occipital regions.

CASE 7 Brain weight was 348 g. The vein of Galen, fed by vessels from the left choroid plexus, contained recent thrombus, and veins on the walls of the posterior horn of the left lateral ventricle were thrombosed. A dilated thrombosed vessel lay in the left central sulcus. The ventricles were filled with blood, and the haemorrhage had disrupted the basal ganglia bilaterally, the right thalamus, and extended into the adjacent centrum semiovale. The left thalamus contained streaky haemorrhages. Scattered areas of periventricular leukomalacia were present around the posterior horns. The cerebellar vermis appeared atrophic and compressed by the aneurysm, but the vermis was normal on microscopic examination. Veins in the substance of the midbrain were distended with recent thrombus.

REVIEW OF LITERATURE

Twenty-three neonatal cases of arteriovenous malformation of the vein of Galen have been described (Clément *et al.*, 1954; Pollock and Laslett, 1958; Claireaux and Newman, 1960;

FIG. 5. Case 5. (a) Lateral view of cerebral arteriogram. Note enormous dilatation of vein of Galen and straight sinus. (b) Anteroposterior view of same. Note immensity of feeding arteries.

Gagnon and Boileau, 1960; Glatt and Rowe, 1960; Hirano and Solomon, 1960; Levine *et al.*, 1962; Gomez *et al.*, 1963; Gold *et al.*, 1964; Falcone *et al.*, 1965; Stern *et al.*, 1968; Sunderland *et al.*, 1971; Holden *et al.*, 1972). Nineteen were in males and four in females. In 17 cases the diagnosis was made at necropsy; in six during life by cerebral arteriography. One child was alive at 20 months without operation (Sunderland *et al.*, 1971). Surgery was not attempted in one because of micrencephaly and frontal calcification (Falcone *et al.*, 1965). After operation two were alive (Gomez *et al.*, 1963; Holden *et al.*, 1972), one had hydrocephalus, and one died (Holden *et al.*, 1972).

Many of the reports do not describe the brain, or the descriptions are terse and uninformative, but those brains described show the same type of damage as in our series. Hirano and Solomon (1960) have described haemorrhagic infarction of the right parietal cortex and caudate nucleus, and blood filling the ventricular system. Stern *et al.* (1968) have described microcephaly, laminar cortical necrosis, and necrotic frontal foci in one case, and laminar cortical necrosis and thrombus in the lamina terminalis in another, and have suggested that the infants may show permanent neurological damage. Gomez *et al.* (1963) have described one case with a normal brain at necropsy, and three with spongy necrosis of white matter. Thus, of seven previously described cases six showed parenchymal damage. Gomez *et al.* (1963) have suggested four means by which the brain may be damaged: (1) a 'steal' phenomenon in overlying abnormal vessels; (2) ischaemia or failure of perfusion from congestive heart failure; (3) haemorrhagic infarction from thrombosis of the aneurysmally dilated vein of Galen; (4) atrophy due to compression of adjacent structures by the aneurysm. We agree with this analysis, and would add a fifth—alteration of flow caused by operation.

COMMENT

Six of the infants in our series presented with cyanosis and congestive heart failure which proved intractable to treatment. The admission diagnosis was cyanotic congenital heart disease, and investigation of the heart led to the diagnosis

of cerebral arteriovenous malformation in five cases, for the following reasons: in the face of cyanosis and intractable congestive heart failure the chest radiograph showed an enlarged *but normally-shaped* heart, there was a high oxygen saturation of blood in the superior vena cava, and an enlarged aorta and aortic branches with rapid opacification of the superior vena cava on the cineangiogram. In an infant with cyanotic congestive heart failure the presence of a cranial bruit is diagnostic of an arteriovenous malformation of the cerebral circulation, but it requires cerebral arteriograms to localize the arteriovenous malformation to the vein of Galen (Fig. 5), for other large cranial arteriovenous malformations can produce cyanosis and congestive heart failure.

Case 1 showed persistent hypoglycaemia, a complication previously noted (Claireaux and Newmann, 1960).

The seventh neonate presented with a rapidly enlarging head, due to recent thrombosis of the aneurysm and resulting intracerebral haemorrhage. Had he lived, he probably would have presented at an older age with hydrocephalus or subarachnoid haemorrhage.

Two infants (cases 1 and 2) whose pre-operative condition was desperate were operated on in the hope that the arterial feeders to the aneurysm could be clipped, for this was the only way the heart failure could be stopped and their lives saved. The operations were performed under cardiopulmonary bypass so that cerebral circulation could be stopped, but the infants bled to death during the procedure.

In neonatal cases operation is made extremely difficult because the aneurysms are fed by multiple vessels. In five of our cases a leash of vessels, often uncountable, fed the aneurysm on each side. The great cardiac enlargement, the severity of the heart failure, and the rapidity with which these infants die of heart failure all indicate the magnitude of the arterial to venous shunt, and it is not surprising that multiple arterial feeders exist. Probably the greater the number of abnormal arterial feeders, the more likely is cerebral infarction.

In only one case was the brain normal, case 3. This child's heart failure responded to treatment for several weeks before death, indicating probably that the lesser the degree of heart

failure the less likely is cerebral damage. In case 4 we saw only a single small, old, calcified microscopic focus and periventricular leukomalacia and the child might not have suffered severe neurological deficit.

The remaining five cases all showed severe parenchymal damage. Cases 2 and 5 both showed extensive gliotic infarction of cerebral hemispheres which clearly antedated birth by several weeks (this appearance has been incorrectly referred to as 'atrophy'). The leptomeningeal vessels over the infarcted areas were enlarged, and the infarction almost certainly occurred as the result of a 'steal phenomenon' occurring in the overlying vessels. That such a steal can occur in normal vessels distant from an arteriovenous malformation has been demonstrated *in vivo* (Heiss *et al.*, 1970). Cases 1, 2, 4, 5, and 7 all showed periventricular leukomalacia. It can be found in neonates dying from a number of different non-neurological diseases, and its most likely cause is a 'water-shed' infarction between ventriculofugal and ventriculopetal circulations (Van den Bergh and Vander Eecken, 1968). It is a lesion which varies in degree and may be responsible for mental retardation if severe enough (DeReuck *et al.*, 1972). Two cases showed recent haemorrhagic infarction. One of these was an operative case, and disturbance of haemodynamics by surgical interference may have caused the haemorrhagic infarction in areas remote from the operative site.

CONCLUSIONS

Arteriovenous malformation of the vein of Galen occurring in the neonatal period is difficult to operate on because of the Medusa-head of arteries feeding into the vein; the operative mortality is high. Neonates may have suffered extensive cerebral infarction *in utero* from the 'steal' of blood in dilated leptomeningeal vessels overlying the infarcted brain. Haemorrhagic infarction can also occur. These facts suggest that, even if the arteriovenous malformation can be corrected surgically, operative treatment may offer little to these neonates, though older infants, children, and adults may be cured by operation.

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