INTRAVENTRICULAR HAEMORRHAGE OF THE NEWBORN A PATHOLOGICAL ANALYSIS OF 49 CASES

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INTRODUCTION

Intraventricular haemorrhage has been frequently recorded in the literature as a common finding in autopsies on the newborn. Weyhe (1889) recorded a frequency of 2.2 per cent in 959 autopsies. Kowitz (1914) found a frequency of 6.0 per cent in 2114 autopsies. Browne (1921) discovered the condition in 8.5 per cent of 200 autopsies. The lesion occurred in 8.7 per cent of Grove's (1959) series of 445 autopsied infants. Rohrbach (1953), Arey (1960) and many other investigators have noted its frequency as a post-mortem finding in the newborn. It is stated to constitute 16 to 70 per cent of all cases of fatal intracranial haemorrhage (Ward, 1954).

This paper is a pathological analysis of 49 consecutive cases of intraventricular haemorrhage of the newborn encountered among autopsies performed at the Kandang Kerbau Hospital, Singapore. Such a project has not hitherto been undertaken in Singapore.

MATERIAL AND METHODS

The present analysis is based on autopsies performed over a period of six months, extending from 12 June, 1962 to 11 December, 1962, inclusive. During this period, there were 19,765 consecutive deliveries at the Kandang Kerbau Hospital. There were 345 neonatal deaths and 199 stillbirths. The neonatal mortality rate was 17.5 per thousand total births, and the stillbirth rate 10.1 per thousand total births, the total mortality (neonatal deaths plus stillbirths) being therefore 27.6 per thousand total births. It may be noted that these figures are relatively low, and compare favourably with those of other countries.

Autopsy was performed on 274 of the 345 neonatal deaths and on 102 of the 199 stillbirths (97 of the stillbirths were macerated and therefore not subjected to post-mortem examination). The autopsy rate, after disregarding all macerated stillbirths, was very high, being 84.1 per cent. This autopsy series is therefore representative of the stillbirths and neonatal deaths in the hospital, except for Malay infants, on whom post-mortem examination was never performed. In addition, autopsy was performed on 18 neonates delivered outside the hospital, who were admitted soon after birth and subsequently died. The total number of autopsies performed was therefore 394, composed of 102 stillbirths and 292 neonatal deaths. Two hundred and seventy (or 68.5 per cent) of the infants were premature, i.e., 5 lb. or less in birth weight. Except for 13 who were Indian, all the babies were Chinese.

The bodies were kept in refrigeration at 40-45°F for 24 to 48 hours prior to autopsy. In all cases, a full post-mortem examination was done. A special method of fixing the intracranial contents was adopted as follows: Except for 5 cases in which the bodies were claimed by relatives, the heads from all the bodies were decapitated at autopsy. They were then perfused for several hours with 10 per cent formal-saline through both internal carotid arteries, after which they were immersed completely in the fixative for about two weeks before dissection. Treatment by perfusion is the most effective method of fixing the brain of the newborn. It also allows haemorrhagic blood to harden in situ, so that its amount, location, extent and origin can be accurately determined.

THE PRESENT SERIES

Incidence

In this series, intraventricular haemorrhage was found in 49 infants. This figure constitutes a frequency of 12.4 per cent in 394 autopsies. In 18 infants, intraventricular haemorrhage was the only form of intracranial haemorrhage present, while among the rest, there was associated subdural haemorrhage in 5, subarachnoid haemorrhage in 23 and intracerebral haemorrhage in 11 (intracerebral haemorrhage in this context refers to grossly recognisable haemorrhages into the brain substance, including those subependymal haemorrhages which did not rupture into the cerebral ventricles).

Survival Rate

All but 5 of the 49 affected infants were liveborn. The majority of the livebirths, however, died within a few days of birth. Thirty-

five (79.5 per cent) died within 4 days, and all except 2 were dead within 7 days. The 2 infants who survived unusually long died on the tenth and the eighteenth day respectively.

Birth Weight

The 394 autopsied infants in this series were divided into 4 birth weight groups as follows: 1-3 lb., 3-5 lb., 5-7 lb. and above 7 lb. An infant weighing exactly 3 lb. was placed in the 1-3 lb. group; similarly one weighing exactly 5 lb. was placed in the 3-5 lb. group, and so on. None of the infants in this series weighed 1 lb. or less.

It was found that the disease was virtually confined to premature infants. Forty-four (89.8 per cent) of the 49 infants were premature. The percentage of infants in each weight group showing intraventricular haemorrhage was analysed, as shown in Fig. 1. It may be noted that the smaller the infants, the higher was the frequency of intraventricular haemorrhage. The 1-3 lb. group showed the highest frequency (28.3 per cent), followed by the 3-5 lb. group (10.1 per cent). Among infants weighing above 5 lb., intraventricular haemorrhage was infrequently found.

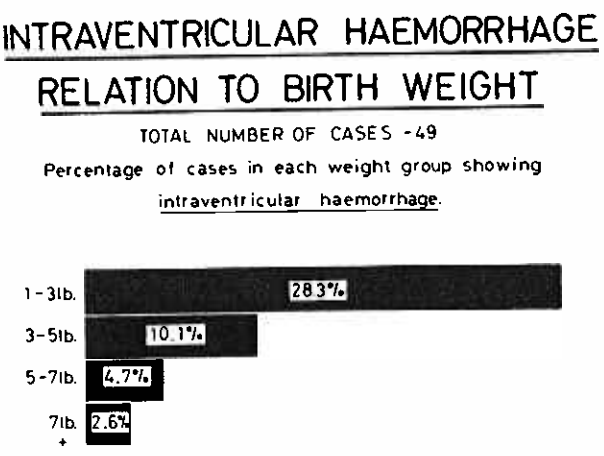

Fig. 1

Pathological Anatomy

There are two sources of intraventricular haemorrhage: (a) subependymal haemorrhage, resulting from rupture of the terminal vein or its ramifications; such a haemorrhage very often extends into the lateral ventricles, resulting in profuse intraventricular bleeding (Rydberg, 1932, and Hemsath, 1934); and (b) haemorrhage from the choroid plexuses (Cruickshank, 1930; Litchfield and Girvan, 1934, and Craig, 1938).

The terminal vein runs just beneath the ependymal lining of the lateral ventricles between the caudate nucleus and the thalamus, receiving numerous branches from these structures (Fig. 2). The veins of the choroid plexus of each lateral ventricle unite to form a single tortuous vessel called the choroid vein which courses in the plexus to the interventricular foramen and there joins the terminal vein to form the internal cerebral vein of the corresponding side. The two internal cerebral veins then run backwards parallel to each other, and, below the splenium of the corpus callosum, unite to form the vein of Galen or great cerebral vein.

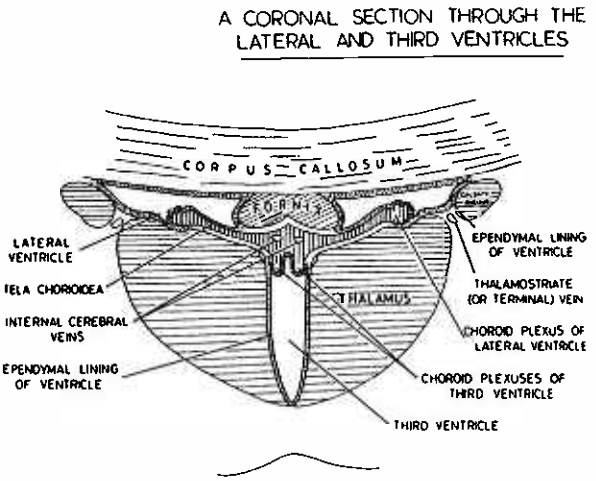

Fig. 2

(Adapted from Gray's Anatomy, twenty-ninth edition).

Among the 49 affected infants, a rupture in the wall of either lateral ventricle could be detected in only 9 instances. These ruptures were invariably situated on the floor of the ventricle in the groove between the caudate nucleus and the thalamus, along which courses the terminal vein. These cases of intraventricular haemorrhage were undoubtedly of subependymal origin. It is possible that bleeding might have arisen from the choroid plexuses as well, but there was no way of ascertaining this. In 6 instances, the ependymal rupture was on the right side, in 2 on the left, and in 1 it was bilateral.

In those cases where the ependymal lining was seen to be smooth and intact throughout, the bleeding was assumed to have arisen from the choroid plexuses. Where the bleeding was limited, a blood clot was often seen enmeshed in a choroid plexus. In many instances of massive bleeding in which the ventricles were distended with blood under tension, the origin of the haemorrhage could not be accurately determined.

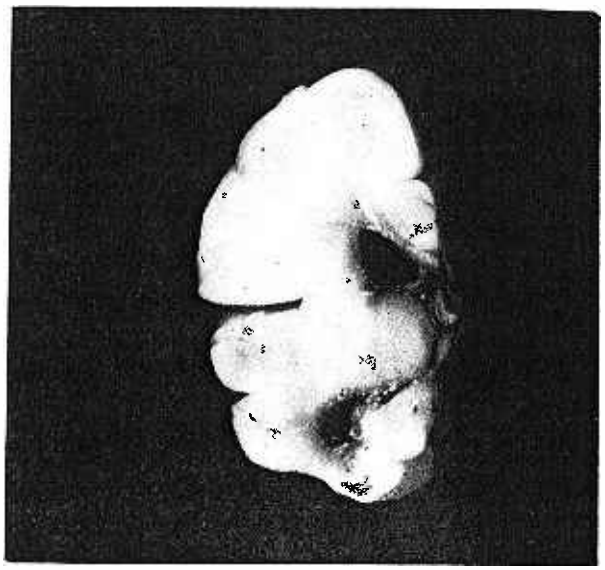

Fig. 3. Coronal section through the left cerebral hemisphere, showing the lateral ventricle filled with blood (Case A1449/62).

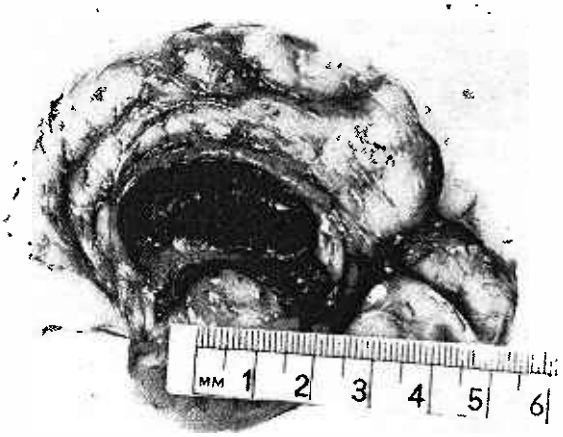

Fig. 4. Median section of the forebrain. The right lateral and the third ventricles are seen to be distended with blood (Case A1250/62).

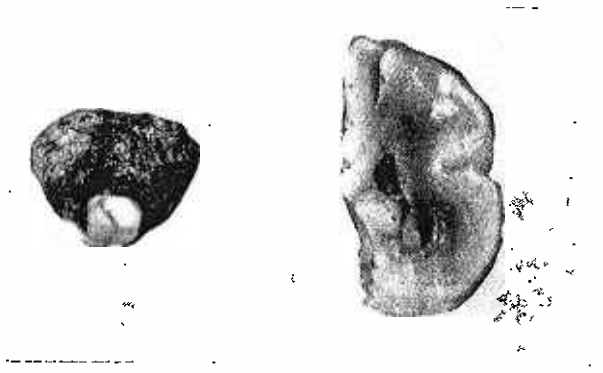

Fig. 5. Large blood clot in the cerebello-medullary cistern (left). from extension of an intraventricular haemorrhage of subependymal origin (right) (Case A1693/62).

In 17 infants, the haemorrhage was massive, blood clots being present in the entire ventricular system, and invariably in the subarachnoid cisterns at the base of the brain (Fig. 3, 4 and 5). In a few instances, the blood clot had formed a complete cast of the ventricular chambers.

Bleeding was less extensive in the remaining 32 infants, blood clots being confined to only portions of the ventricular system, usually the lateral ventricles. In 9 instances, clots were present at the base of the brain.

Intraventricular haemorrhage is probably rapidly fatal in most cases. Sometimes, there is a "silent" period during which the infant appears quite normal, followed by a sudden change for the worse and rapid death. This is probably due to the fact that a subependymal haemorrhage has initially occurred, but rupture through the ependyma has been delayed for some hours or days (MacGregor, 1946, and Arey and Dent, 1953).

In this series, there were 6 instances of grossly recognisable, petechial, subependymal haemorrhage which did not extend into the ventricles (Fig. 6). The lesion was confined to the left side in 3 cases, and was bilateral in the other 3. The haemorrhagic foci varied from less than 1/10 inch to 2/10 inch in diameter. All the affected infants were below 4 lb. in birth weight and 5 of the 6 were below 3 lb. All the infants were liveborn.

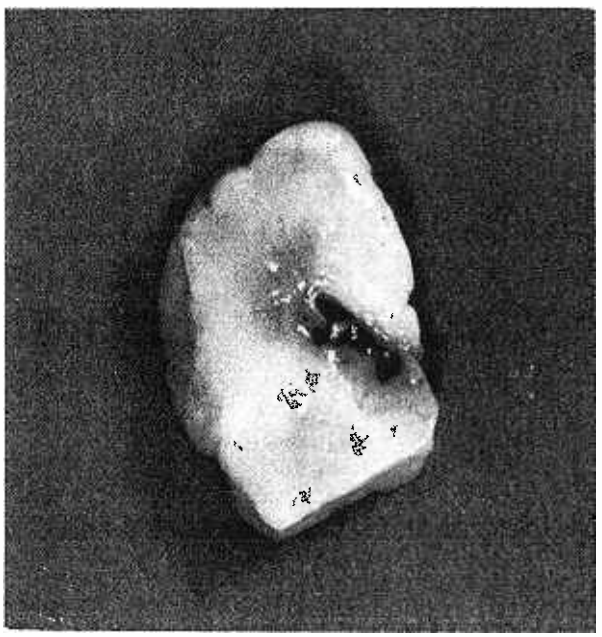

Fig. 6. Coronal section through the left cerebral hemisphere, showing a localised subependymal haemorrhage in the floor of the lateral ventricle (Case A1563/62).

Most probably, these subependymal haemorrhages per se are relatively innocuous. This view is supported by the finding of old blood pigments in the subependymal region in older infants dying of other causes (Arey and Dent, 1953).

Obstetric History

In analysing the antecedent obstetric history of the 49 infants with intraventricular haemorrhage, it was found that premature labour occurred in 34 cases, twin pregnancy in 5, triplet pregnancy in 1, antepartum haemorrhage in 9, caesarean section in 2, breech delivery in 7, internal version in 1 and low forceps in 2. From these figures, the outstanding factor associated with intraventricular haemorrhage was prematurity of the infant as a result of premature labour or of multiple pregnancy. Antepartum haemorrhage in 9 instances and caesarean section (in the face of foetal distress) in 2 were indicative of foetal anoxia. Anoxia might have been present also to some degree in the 7 breech deliveries and in the case of internal version. An obstetric history consistent with foetal anoxia was therefore frequently obtained.

DISCUSSION

The aetiology of intraventricular haemorrhage is still not finally established. Nevertheless, there is general agreement that certain factors are of definite importance in its pathogenesis.

Most investigators have come to the conclusion that it is not due to mechanical trauma at birth, although Arey and Dent (1950 and 1953) did not exclude the possibility that trauma plays a part. There is general agreement that anoxia is the factor of prime importance (Morison, 1949; Potter and Adair, 1949; Gruenwald, 1951; Balf, 1952; Haller et al, 1956, and Mitchell et al, 1959).

The fact that the condition is virtually confined to premature infants points to prematurity as being a very important predisposing cause. There are several factors incident to prematurity which explain this great liability to intraventricular haemorrhage. To begin with, premature infants are much more susceptible to the effects of anoxia. The engorged blood vessels of asphyxiated infants are definitely more prone to rupture than the less distended ones of normal infants (Ehrenfest, 1929, and Arey and Dent, 1953). This applies particularly to poorly supported vessels such as the veins of the choroid plexuses and the terminal veins lying superficially in the walls of the lateral ventricles.

In premature infants, the structure of the subependymal tissue of the ventricular wall predisposes to haemorrhage (Rückensteiner and Zoellner, 1929; Hemsath, 1934, and Gruenwald, 1951). Hemšath (1934) referred to it as the "developmental factor". He pointed out that subependymal haemorrhages are found always in the region of the stria terminalis thalami. This region is made up of aggregates of embryonal neuroglial tissue which is highly cellular and deficient in glial fibres (MacGregor, 1960). These cellular aggregates are referred to as medulloblasts by Tuthill (1938) and as undifferentiated neuroectodermal elements by Schwarz et al (1932). They are normal in the stria terminalis thalami, and are especially prominent in premature infants (Arey, 1952). Being embryonal tissue, they offer extremely poor support to the vessels. Undifferentiated subependymal tissue is also found in much smaller amounts in areas other than the region of the stria terminalis, but these areas unlike the stria terminalis are poorly vascularised and therefore are not generally a seat of haemorrhage (Gruenwald, 1951).

Prematurity is associated with a generalised thinness and fragility of vessel walls. This is particularly true of veins in the subependymal tissue. Gruenwald (1951) has shown by histological studies that subependymal veins have a much thinner wall than those in other parts of the brain, a feature which explains why subependymal vessels rupture more easily than other cerebral vessels. Gruenwald (1951) and Arey and Dent (1953) have also pointed out that the terminal and choroid veins are exposed to back pressure of severe degrees from the vein of Galen, of which they are tributaries.

An additional factor which may play a part in the pathogenesis of intraventricular haemorrhage is the "lower pressure principle" (Schwartz, 1927, 1956, 1958, 1961 and 1961a). Following rupture of the membranes, the presenting part of the foetus is exposed to atmospheric pressure while the rest of the body is under high intra-uterine pressure. This pressure difference produces a "suction effect" (Ehrenfest, 1929) on the presenting part. When the head is presenting, this negative pressure brings an increased flow of blood to the cerebral vessels which then become engorged and may rupture. Schwartz (1956) stressed that all the branches of the Galenic system of

veins, including the intracerebral ramifications, especially the terminal and choroid veins, may be involved by the lower pressure effect. Gruenwald (1951), however, has justly pointed out that the lower pressure effect cannot be the principal cause of subependymal haemorrhage, because it does not explain the occurrence of such haemorrhage in breech deliveries, when the negative pressure does not act on the head. He, however, agreed that the pressure difference may increase the severity of the haemorrhage in cephalic presentations, and may play a part in converting a relatively harmless, localised, subependymal lesion into a fatal intraventricular haemorrhage.

In short, it appears that intraventricular haemorrhage is the result of the interaction of a number of factors. Prematurity is the underlying predisposing condition. In premature infants, the vessels, especially the subependymal and choroid vessels, are thin-walled and fragile and easily rupture. Moreover, the subependymal vessels lie in a soft, fragile, embryonic brain tissue which offers them very little support; the veins of the choroid plexuses have virtually no support. Under such conditions, these vessels rupture very easily when they become engorged as a result of anoxia to which premature infants are particularly prone. The pressure difference as described by Schwartz (1927 and 1956) may, by increasing the severity of a haemorrhage, play a part in converting a relatively innocuous, localised, subependymal haemorrhage into a fatal intraventricular haemorrhage. Mechanical trauma does not appear to play a role, as borne out by the lack of association between intraventricular haemorrhage and evidence of traumatism.

SUMMARY

A pathological analysis was made of 49 consecutive cases of intraventricular haemorrhage of the newborn encountered at the Kandang Kerbau Hospital, Singapore, from 12 June, 1962 to 11 December, 1962.

The frequency of intraventricular haemorrhage of the newborn was 12.4 per cent in 394 autopsies on stillbirths and neonatal deaths.

The vast majority of the affected infants (44 out of 49) were liveborn, but practically all of them died within a few days of birth.

The disease is virtually confined to premature babies, 89.8 per cent of the affected infants being 5 lb. or less in birth weight. It was found also that the smaller the infants, the higher was the frequency of intraventricular haemorrhage.

In analysing the obstetric records of the affected infants, a clinical history consistent with foetal anoxia (especially maternal antepartum haemorrhage) was frequently obtained.

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