Review Article:

Ventricular Dilation Following Intraventricular Hemorrhage in the Premature Infant

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SUMMARY: Periventricular/intraventricular hemorrhage occurs commonly in the premature newborn. Recent studies indicate an incidence of 35-45%. Following PVH/IVH, the likelihood of developing hydrocephalus is related to the severity of the hemorrhagic lesion. Ventricular dilation may be due to an obliterative arachnoiditis affecting principally the posterior fossa or, less commonly, due to obstruction of flow of cerebrospinal fluid within the ventricular system by clots or other debris. With moderate to severe hemorrhagic lesions, ventricular dilation may occur at the time of PVH/IVH. More commonly, progressive dilation begins one to three weeks following PVH/IVH. The classical clinical signs of hydrocephalus, ie. bulging of anterior fontanelle and inappropriate increase in head circumference, may not appear for days to weeks following onset of ventricular dilation. The precise significance of such normal-pressure hydrocephalus in the genesis of brain injury in the newborn is unknown. Following diagnosis of PVH/IVH, close surveillance of ventricular size with ultrasound scans is indicated. When there is slowly progressive ventricular dilation with normal intracranial pressure, the choice of therapy is made difficult because of frequent spontaneous arrest in such cases. Several modes of therapy have been reported including drugs to decrease the formation of cerebrospinal fluid and the use of serial lumbar punctures. When ventricular dilation is rapid with intracranial hypertension, ventricular drainage is indicated.

Periventricular/intraventricular hemorrhage (PVH/IVH) in the newborn is responsible for a large proportion of the morbidity and mortality in the modern neonatal intensive care unit (Volpe, 1981; Hill and Volpe, 1981c). The increasing importance of PVH/IVH is due mainly to improvements in neonatal intensive care and the increased survival of the premature infant in whom the lesion occurs almost exclusively. This paper will review PVH/IVH and then discuss the problem of posthemorrhagic ventricular dilation, a common sequel of PVH/IVH.

Incidence of PVH/IVH

The use of routine CT scans within the first week of life has shown a 45% incidence of PVH/IVH in infants whose birth weight is less than 1500 g (Ahmann et al, 1980; Papile et al, 1978). More recent studies with real-time ultrasound scans of the head have demonstrated a similar incidence (Holt and Allan, 1981; Levene et al, 1981).

Neuropathology

PVH/IVH in the premature infant originates in the abundant fragile capillaries of the subependymal germinal matrix located at the head of the caudate nucleus and foramen of Monro. The hemorrhage may remain confined to the subependymal region or it may spread throughout the ventricular system and extraventricular subarachnoid space. A major sequel of PVH/IVH is obliterative arachnoiditis which may develop over a period of days to weeks, principally in the posterior fossa, and which in turn may impair cerebrospinal fluid (CSF) reabsorption and lead to ventricular dilation (Larroche, 1972). Extensive IVH may extend into periventricular parenchymal tissue resulting in a porencephalic cystic lesion (Pasternak et al, 1980).

Pathogenesis

There is a strong relationship between PVH/IVH and insults related to both prematurity and hypoxia. Pathological studies of the vascular formation in the premature brain indicate a disproportionate arterial supply to the deep regions of the cerebrum (including the germinal matrix). Consequently an increase in total cerebral blood flow will cause excessive perfusion of, and probable rupture of the capillaries of the germinal matrix. Ineffective cerebrovascular autoregulation may also cause excessive blood flow to the germinal matrix, (Lou et al, 1979). This is thought to be a result of immaturity and/or prior hypoxic-ischemic insult. Therefore, wide fluctuations in systemic blood pressure (a common occurrence in the premature newborn) may cause changes in the cerebral circulation in a "pressure-passive" fashion. Experimental and human studies suggest a relationship between increases in systemic blood pressure and the occurrence of PVH/IVH (Goddard et al, 1980; Reynolds et al, 1979; Fujimura et al, 1979; Milligan, 1980). A relationship has also been demonstrated between PVH/IVH and both increased carbon dioxide tension in cord blood at birth (Kenny et al, 1978) and pneumothorax (Hill et al, 1982; Lipscomb et al, 1981).

Asphyxia, which often accompanies premature delivery, may play a role in the pathogenesis of PVH/IVH through: (1) impairment of cerebrovascular autoregulation, (2) an increase of cerebral perfusion (an immediate response to

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asphyxia), (3) increased cerebral venous pressure (secondary to transient myocardial ischemia and heart failure), and (4) hypoxic-ischemic injury to the endothelium of the capillaries of the germinal matrix, predisposing them to rupture.

Clinical Features

Recent studies with CT and ultrasound scanning of the head have demonstrated that PVH/IVH need not, as hitherto considered, occur in association with disastrous clinical deterioration, but may be clinically "silent". In a recent prospective study a lesion was predicted from clinical findings in only 50% of the cases (Lazzara et al, 1980).

Diagnosis

The diagnostic approach to PVH/IVH has been altered recently by the increasing availability of CT and ultrasonography. In the modern Neonatal Intensive Care Unit, it appears reasonable to perform routinely within the first week of life, portable real-time ultrasound scans in infants with birth weight less than 1500 g. In addition, such scans should be performed in infants above this birth weight in whom the diagnosis of PVH/IVH is suspected on clinical grounds. However, the optimal timing of such scans has not been determined.

In the newborn, real-time ultrasound scanning is the most suitable technique for diagnosis of PVH/IVH and for assessment of ventricular size (Bejar et al, 1980; Allan et al, 1980; Pape et al, 1979). A major advantage of this technique over CT scanning is that it may be performed at the bedside with little or no disturbance to the infant, obviating transport of a sick infant to the CT scanner. A second advantage is that ionizing radiation is not involved and thus, the procedure may be used serially to enable accurate timing of PVH/IVH and assessment of changes in ventricular size.

Prognosis

The short-term outcome is related in large part to the severity of hemorrhage and may be considered in terms of death or rapidly progressive hydrocephalus. With respect to long-term outcome, the following mechanisms of brain injury may play an important role: perinatal hypoxic-ischemic insult; impairment of cerebral perfusion at the time of hemorrhage as a result of increased intracranial pressure (ICP) and/or systemic hypotension; injury to periventricular white matter; destruction of germinal matrix; and posthemorrhagic hydrocephalus.

POSTHEMORRHAGIC VENTRICULAR DILATION

Following IVH, ventricular dilation may occur as a result of an obliterative arachnoiditis affecting principally the posterior fossa (Larroche, 1972) or, less commonly, because of obstruction within the ventricular system by clot or other debris. Although with moderate to severe lesions, increase in ventricular size may occur at the time of IVH, it usually does not become progressive until one to three weeks later (Korobkin, 1975; Volpe et al, 1977). Of particular importance is the observation that the classical clinical signs of hydrocephalus (ie. inappropriate increase of head circumference, suture diastasis and bulging of anterior fontanelle) often do not occur for days to weeks following the onset of ventricular dilation (documented by CT or ultrasound scan) (Volpe, 1981; Hill and Volpe, 1981b). The absence of classical signs of hydrocephalus and sustained increase in ICP in this context most probably is a consequence of increased compliance of periventricular tissue (as a result of its immature state of development and/or prior hypoxic-ischemic or compressive injury). The presence of a large subarachnoid space over the cerebral convexities in the premature infant may also contribute to this phenomenon (Pape and Wigglesworth, 1979).

Following PVH/IVH a state of ventricular dilation with normal ICP is common (Hill and Volpe, 1981b). This apparent paradox may be explained by an accumulation of CSF (secondary to impairment of reabsorption) which causes ventricular dilation rather than sustained increase in ICP. This is presumably due to the high compliance of periventricular tissue. Thus, it is simpler for the excessive accumulation of CSF to compress periventricular tissue than to expand cranial volume. This state of ventriculomegaly with normal ICP is somewhat analogous to normal-pressure hydrocephalus in adult patients (Hakim et al, 1976; Geschwind, 1968). The continued accumulation of CSF within the ventricular system may thus be accommodated by progressive increase in ventricular size (at normal ICP) until the limits of periventricular compliance are exceeded at which time continued accumulation of CSF may occur only in association with an increase in cranial volume. It is at this time the classical signs of hydrocephalus appear.

Recent studies have demonstrated that the ventricular dilation which follows IVH need not necessarily be progressive (Hill and Volpe, 1981b). Of the 20 premature infants with posthemorrhagic ventricular dilation who were followed with serial measurement of ICP and ventricular size, ICP was normal initially (Fig. 1). Subsequently, in 9 of these 20 infants there was spontaneous arrest with or without resolution of ventricular dilation within 31 days of onset. In the remaining 11 cases there was progressive in-

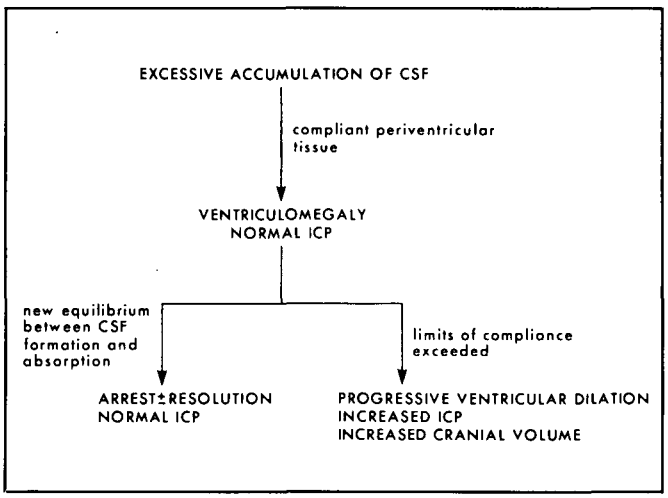

Figure 1 — Evolution of ventricular dilation following intraventricular hemorrhage in 20 infants. Initially all had ventriculomegaly and normal ICP. Subsequently, in 9, there was spontaneous arrest, and in 11, there was progressive hydrocephalus.

crease in ventricular size, initially at normal ICP but subsequently with elevation of ICP (ie. progressive hydrocephalus). The spontaneous arrest of ventricular dilation presumably is a result of resolution of the arachnoiditis (which is responsible for impaired reabsorption of CSF) and return to equilibrium between the formation versus reabsorption of CSF (prior to exceeding the limits of periventricular compliance). The above data demonstrate the occurrence of spontaneous arrest with or without resolution of ventricular dilation following IVH in approximately 50% of cases. Similarly, Ahmann et al, (1981) observed some degree of hydrocephalus in 51% of 106 survivors of IVH and subsequent spontaneous arrest or regression of ventricular dilation in one half of these.

Progressive hydrocephalus with increased ICP may be detrimental, but it is not known if ventriculomegaly with normal ICP is harmful; experimental animal and human data suggest that it may be. Ventricular dilation may cause periventricular edema and astrocytosis (Weller and Schulman, 1972; Rubin et al, 1976) and there may be alterations in the protein and lipid content of periventricular tissue (Fishman and Greer, 1963). Futhermore, diminution of cerebral blood flow in patients with normal-pressure hydrocephalus is suggested by experimental studies (Wozniak et al, 1975) and human studies in both adults (Matthew, 1975) and children (Hill and Volpe, 1982). These observations raise the possibility that ventriculomegaly, albeit with normal ICP, may be harmful.

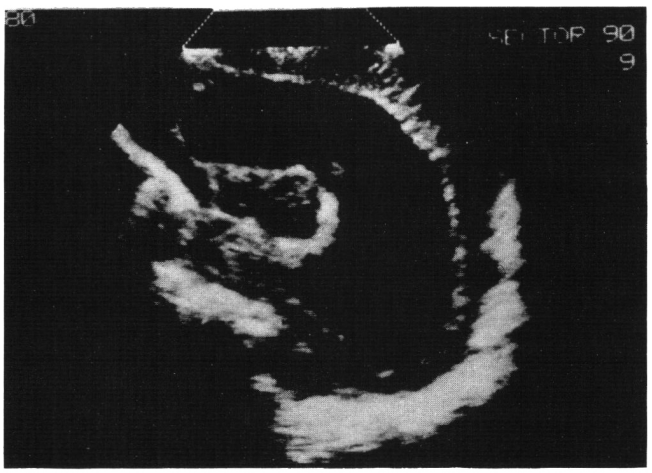

Figure 2 — Real-time ultrasound scan of head: sagittal view. Note markedly enlarged lateral ventricle.

Table 1: Management of Ventricular Dilation Following IVH

1. Observation - serial assessment of ventricular size
2. Drugs to decrease CSF production
   - carbonic anhydrase inhibitors (acetazolamide, furosemide)
   - osmotic agents (glycerol)
3. Serial lumbar punctures
4. Ventriculostomy
5. Ventriculoperitoneal shunt

Management of Posthemorrhagic Ventricular Dilation

Following the diagnosis of PVH/IVH, serial measurement of ventricular size (preferably with real-time ultrasound) (Fig. 2) and if possible, ICP (with a non-invasive method) are indicated at approximately one-week intervals. Such surveillance is of value because of the unreliability of clinical observation alone to detect the occurrence of significant ventricular dilation prior to the occurrence of clinical signs of hydrocephalus (Volpe, 1981; Hill and Volpe, 1981b).

At present there is no entirely satisfactory method for the management of posthemorrhagic ventricular dilation in the premature infant. The methods for treatment of posthemorrhagic ventricular dilation are listed in Table 1. A decision regarding the timing and method of treatment is made difficult by the occurrence of spontaneous arrest in approximately 50% of cases (Hill and Volpe, 1981b).

When rapid ventricular dilation with intracranial hypertension develops, ventricular drainage is indicated. External ventriculostomy has been used in infants who, because of their small size or severe illness, are considered unsuitable candidates for the more definitive therapy of ventriculoperitoneal shunting. In our own experience, removal of the ventriculostomy after approximately seven days is necessary because of the increased risk of infection beyond this period. In the study of Harbaugh et al, (1981), drainage was continued for up to 41 days (mean 21 days) without complication by use of a subcutaneously tunneled catheter. Following removal of the ventriculostomy, ventricular size may remain stable for a period of days following which there is usually recurrent ventricular enlargement and increase in ICP requiring further ventricular drainage preferably by ventriculoperitoneal shunt. However, in the small premature infant, the latter procedure is associated with a high incidence of shunt blockage, infection or skin breakdown.

In cases with slowly progressive ventricular dilation with normal ICP, surveillance of ventricular size and measurement of ICP with a non-invasive technique (Hill and Volpe, 1981a) may be all that is needed. Several non-surgical modes of therapy have been evaluated recently. These include drugs to decrease CSF production and serial lumbar punctures (for more detailed review see Volpe, 1981 and Tarby and Volpe, 1982). These methods of treatment may serve as temporizing measures to prevent excessive accumulation of CSF (and subsequent ventricular enlargement) until such time that equilibrium of CSF production versus absorption is re-established.

Drugs which have been used to decrease production of CSF are listed in Table 1. The rationale for the use of carbonic anhydrase inhibitors is derived from experimental animal studies (McCarthy and Reed, 1974): inhibition of carbonic anhydrase by acetazolamide causes a decrease in CSF formation of 50% but the effect is often transient. Experimental studies demonstrate value in the combined use of acetazolamide and furosemide (McCarthy and Reed, 1974): the use of high doses of acetazolamide (100 mg/kg/day) and furosemide (1 mg/kg/day) appeared to cause arrest of ventricular dilation in three of six cases (Bergman et al, 1978). However, because carbonic anhydrase occurs in myelin and may thus be important during myelination, high doses of acetazolamide must be used with caution. In a further study, 55 infants with progressive hydrocephalus of varied etiology were treated with acetazolamide (up to

100/mg/day) and furosemide (1 mg/kg/day) for up to six months (Shinnar et al, 1982). Only 25 of the 55 required shunting. Complications of therapy included acidosis, dehydration, diarrhea, appetite suppression and, rarely, hypocalcemia.

The rationale for the use of osmotic agents also derives from animal experiments which demonstrate an inverse relationship between serum osmolarity and CSF production Hochwald et al, 1976a; Hochwald et al, 1976b). Preliminary studies with glycerol suggest that it may be of value in selected cases (Taylor et al, 1981). Our practise has been to begin with a dose of 1 g/kg by mouth every six hours and to increase the dose over one week to 2 g/kg/dose. Serum osmolarity, electrolytes, blood urea nitrogen and glucose are monitored. In cases where there is arrest of ventricular dilation, the drug has been continued for up to six months (Tarby and Volpe, 1982).

The use of serial lumbar punctures to prevent excessive accumulation of CSF, has been reported by several groups (Mantovani et al, 1980; Ahmann et al, 1980; Chaplin et al, 1980; Papile et al, 1980). Recent studies suggest a potential value for this mode of therapy in selected cases (Hill et al, 1981). The removal of relatively large quantities of CSF (ie. 15 to 20 ml) was necessary to effect significant decrease in ventricular size (determined by ultrasound scanning before and after each lumbar puncture). Clearly, communication between ventricles and lumbar subarachnoid space is essential for this method of treatment to be effective. In cases where ventricular size can be decreased by removal of such relatively large volumes of CSF, progressive ventricular dilation may be prevented or delayed until there is spontaneous arrest or until ventriculoperitoneal shunting is feasible in those cases in whom spontaneous arrest does not occur.

It must be stressed that when the above methods of treatment are begun at a stage when ventricular enlargement is slowly progressive and ICP is normal, results are difficult to evaluate because of the known occurrence of spontaneous arrest in 50% of such cases (Hill and Volpe, 1981b; Ahmann et al, 1981). Alternatively, if such treatment is begun only after there is rapid increase in both ventricular size and ICP, it is unlikely to be of permanent value.

In summary, a reasonable approach to the management of ventricular dilation following IVH in the premature infant is as follows (see also Fig. 3). In infants with slowly progressive ventricular dilation and normal ICP, observation with serial ultrasound scans, (preferably with simultaneous measurement of ICP), the use of drugs to decrease CSF production or the use of serial lumbar punctures may be considered. On the other hand, if there is rapid progression of ventricular dilation with elevated ICP, ventricular drainage is indicated.

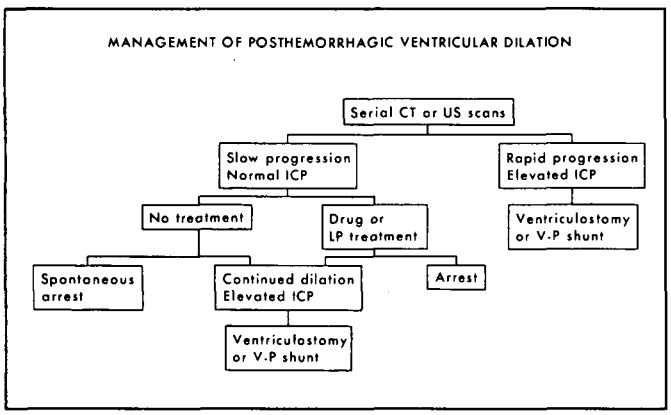

Figure 3 — Approach to management of posthemorrhagic ventricular dilation.

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