Monozygotic Twins Discordant for External Hydrocephalus

Joseph H. Piatt, Jr.

Section of Neurosurgery, St. Christopher's Hospital for Children, and Departments of Neurological Surgery and Pediatrics, MCP Hahnemann University, Philadelphia, Pa., USA

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Abstract
External hydrocephalus (EH) is a transient, developmental condition in infancy characterized by macrocephaly and prominence of the subarachnoid spaces. The cause is unknown, but many patients have a family history consistent with autosomal dominant inheritance. This report describes a pair of monozygotic twins, only one of whom — the recipient of a twin-twin transfusion — has EH. Whatever the genotype of the twins, their discordant phenotypes suggest that the disproportionate calvarial growth that characterizes EH is set in motion — or not — during a limited, critical temporal window in fetal development.

Introduction
External hydrocephalus (EH) is a transient developmental phenomenon of infancy and early childhood characterized by macrocephaly, prominence of the subarachnoid spaces and mild ventricular enlargement. Before the era of magnetic resonance (MR) imaging and Doppler ultrasound, which allow accurate identification of extracerebral fluid collections [1, 2], EH was known by a number of misnomers, including the still popular “benign subdural effusions of infancy” [3–10]. The prominence of the subarachnoid spaces is said generally to resolve in early childhood [9, 11–13], but the temporal course of this resolution has not been documented in detail. A family history consistent with autosomal dominant transmission is commonly present [11, 14], but prominence of the subarachnoid spaces, with or without macrocephaly, has been described as symptomatic of a variety of conditions, including glutaric acidemia type I [15–22], achondroplasia [23], osteogenesis imperfecta [24, 25], Sotos syndrome [26, 27], Kniest disease [28], congenital myotonic dystrophy [29], occipital plagiocephaly [30], chronic glucocorticoid administration [31, 32] and hypomagnesemia [33].

This report describes a pair of monozygotic twins discordant for EH and takes this case as a point of departure for discussion of hypotheses about the development of prominent subarachnoid spaces and macrocephaly in infancy.
Case Report

The patient came to medical attention at 4.5 months of age because of macrocephaly.

She was one of twins, born at 34 weeks of gestation. The pregnancy had been notable for a progressive discrepancy in size between the twins, the patient being the larger one, and a presumptive diagnosis of twin-twin transfusion syndrome was made. There was oligohydramnios affecting the patient's sister. The twins were delivered by elective cesarean to prevent further growth impairment in the patient's sister. The patient's birth weight was 1,960 g (48th percentile, corrected for prematurity); her sister's birth weight was 1,600 g (13th percentile, corrected). The placenta was diamnionic and monochorionic.

The patient's neonatal course was notable only for pulmonary stenosis treated by balloon valvotomy.

Both the patient and her sister were exhibiting normal early development. At presentation, the patient's weight was 6.8 kg (95th percentile, corrected). The occipitofrontal circumference (OFC) was 42.4 cm (95th percentile, corrected). The sister's OFC was 40.0 cm (about 65th percentile, corrected). The patient's anterior fontanel was large and slack; the sister's was identical. There were no other abnormalities on general or neurological examination. The father's OFC was 58.2 cm. The mother's was 53.8 cm.

MR imaging of the head demonstrated prominence of the subarachnoid spaces and mild ventricular enlargement (fig. 1).

At follow-up at 9 months of age, the twins were developing in lockstep; both were sitting without support and pulling to stand. Both were babbling without any intelligible words. The patient's OFC was 46.7 cm (95th percentile) and her sister's was 44.7 cm (75th percentile, corrected). The patient's weight was 8.39 kg and her sister's was 6.94 kg.

Head ultrasound examination of the patient at 9 months demonstrated persisting prominence of the subarachnoid spaces in the interhemispheric fissure (fig. 2). Her sister's head ultrasound examination was normal (fig. 3).

Discussion

Because of the benignity of the natural history of EH, patients seldom require surgical intervention and do not come to autopsy. Its pathophysiology has not been studied and has not even been the subject of much conjecture. EH is commonly supposed to be the consequence of a transient disturbance of cerebrospinal fluid (CSF) circulation, perhaps on the basis of delayed maturation of the arachnoid granulations. If EH were simply a transient, congenital, communicating hydrocephalus, as this hypothesis implies, one might expect to see a more continuous spectrum of clinical conditions intermediate between EH and ordinary hydrocephalus, but in fact EH is a very distinctive entity. It is recognizable early in infancy, and it follows a stereotypical course over time. Very seldom does an infant who exhibits the typical clinical features and MR findings of EH develop overt ventriculomegaly and require a CSF shunt. An alternative hypothesis is that EH is a developmental disturbance of skull growth. It may be the result of an exaggerated responsiveness of the calvarium to the signals that link its growth to the growth of the brain during infancy. This hypothesis explains most of the clinical features of EH: brain growth and development seem to be normal in EH. There are seldom any symptoms or signs of elevated intracranial pressure (ICP) in EH despite macrocephaly. In particular, the fontanel is usually slack. The transience of the normal linkage between expansion of the cranium and its contents models the transience of the cranioencephalic disproportion of EH.
Data with which to refute one or both of these hypotheses are lacking and are not likely to be forthcoming any time soon.

Discordance between monzygotic twins for various developmental anomalies is not so uncommon, and twin-twin transfusion often plays an instrumental role in such instances [34]. A startling and well-described example is acardia. In cases of simultaneous arterial-arterial and venous-venous transfusion, the donor heart may sustain the circulation of the recipient, in which case the recipient heart ceases to develop. Placental arterial-venous anastomoses are more common, and this pattern of transfusion typically causes anemia, growth retardation and oligohydramnios in the donor. In extreme cases, the donor may perish and disappear. The recipient may experience complications of circulatory overload: plethora, cardiac failure and hydrops. In the event of the demise of the donor, the recipient may suffer a variety of ischemic complications, perhaps related to transfusion of tissue thromboplastins or to extreme hypotension in the survivor.

How then to relate the pathophysiology of twin-twin transfusion to the development of EH, a condition frequently thought to be genetically determined? Two possibilities present themselves: (1) if EH was genetically determined in the current case, then the phenotype must have been suppressed in the donor twin by intrauterine conditions; (2) if EH was not genetically determined in the current case, then the phenotype must have been promoted.

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in the recipient twin by in utero conditions. Interestingly, both of these possibilities lead to the same conclusion about the temporal period during which the phenotypic expression of EH is determined.

This family may have carried an autosomal dominant gene for EH. The father's OFC is at the very top of the normal range for adult males and suggests a family history of macrocephaly. If both twins were genetically programmed for EH, the normal development of the donor twin requires an explanation, and oligohydramnios may supply it. Oligohydramnios implies diminished urinary output, presumably due to chronic intravascular volume depletion, which may have caused diminished brain pulsatility. Diminished brain and CSF pulsatility may, in turn, have robbed the cranial vault of some of its stimulus for expansion. Snug amniotic membranes may have further restricted calvarial expansion, although there were no associated deformities suggestive of intrauterine growth restraint, such as Potter's facies or arthrogryposis [35]. That the donor twin's head growth has continued along normal curves after birth despite putative genetic programming for EH suggests a window of susceptibility during fetal development during which the craniofacial disproportion of EH must be set in motion.

Alternatively, EH may not have been genetically determined in the recipient twin, and the recipient's craniofacial disproportion may have been the result of disturbed cardiovascular physiology. The recipient presumably experienced intravascular volume expansion with elevated central venous pressures and dural venous sinus pressures. ICP may have been elevated. Furthermore, augmented cardiac filling may have increased cardiac contractility and the pulsatility of cardiac output. Thus, there may have been enhancement of ICP pulsatility as well as elevation of mean ICP, one or both of which factors may have served as a stimulus for disproportionate calvarial growth. That the recipient twin's head has continued to grow along a postnatal curve well above the 95th percentile without putative genetic programming once again suggests that the craniofacial disproportion of EH is set in motion irrevocably in response to some unknown trigger during fetal development.

Thus, although the genotype of the current case and her family is unknown, both of the possible genetic scenarios point to a limited, critical temporal window of susceptibility in fetal development during which the disproportionate calvarial growth that characterizes EH must be set in motion if it is to unfold later in infancy.

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References


