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Acquired hydrocephalus associated with superior vena cava syndrome in infants

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Abstract We report observations on children with the unusual combination of superior vena cava syndrome in infancy followed by communicating hydrocephalus. Following retrospective review of hospital discharges at a tertiary children's hospital, three children were identified in a 13-year period. Two term infants were treated with extracorporeal membrane oxygenation for pulmonary failure associated with congenital diaphragmatic hernia. These infants had septic complications of central venous lines. A post-term infant required reconstruction of the superior vena cava following cannulation for cardiac bypass surgery to repair transposition of the great vessels. Thrombosis occurred and was followed by the sequential development of superior vena cava syndrome and communicating hydrocephalus. The findings in these patients suggest that communicating hydrocephalus may be caused by superior vena cava syndrome. This is an unusual complication of therapeutic manipulation of the heart and great veins. Cerebrospinal fluid shunting may be required.

Key words Hydrocephalus · Superior vena cava syndrome · Neonates · ECMO · Catheters · Thrombosis

Introduction

Superior vena cava (SVC) syndrome in infancy is an unusual complication of the use of indwelling central lines during newborn intensive care [8, 15, 20, 22]. When the ventriculo-atrial shunt was the treatment of choice for hydrocephalus, SVC syndrome was an occasional complication [6]. Catheter-associated infection, usually due to *Staphylococcus epidermidis*, and/or thrombosis precedes the development of SVC syndrome in these patients and is presumed to be the cause of the venous obstruction [9, 27]. SVC syndrome caused in children by external compression of major veins has been attributed to lymphoproliferative disease, neoplastic processes and thoracic surgery for congenital heart disease [4, 5, 13, 18, 19].

Hydrocephalus is common in small infants and has many causes, but it is unusual in combination with SVC syndrome. Hooper [12] reported a single child in whom idiopathic extrinsic venous obstruction appeared to cause hydrocephalus. Communicating hydrocephalus presumed secondary to SVC syndrome associated with Mustard procedures for transposition of the great arteries has been reported in several small series [4, 5]. The SVC syndrome was due to obstruction of SVC blood flow at the upper end of the intra-atrial baffle and was surgically reversible. Muller et al. [16] presented an abstract documenting SVC thrombosis and hydrocephalus in three 29- to 30-week premature infants. We identified two reports of hydrocephalus associated with SVC syndrome associated with central line infection and/or thrombosis [10, 17].

Stewart et al. [24] reported four cases of communicating hydrocephalus associated with indwelling catheters but did not document the presence of SVC syndrome. Canady et al. [3] mention two patients with hydrocephalus and SVC syndrome after neonatal extracorporeal membrane oxy-

genation (ECMO). Walsh-Sukys et al. [26] identified macrocephaly and "prominent CSF spaces" in five children after ECMO. Zreik et al. [28] reported 7 cases of SVC thrombosis among 60 children undergoing ECMO, 3 of whom developed either "hydrocephalus or subdural hematoma." In this report we present three children in whom hydrocephalus appears to have been caused by thrombosis and SVC obstruction.

Case reports

The three children are being followed by the authors and their colleagues at a tertiary children's hospital. The computerized hospital patient discharge abstracts for the 13-year period 1 January 1981 to 31 December 1993 were searched using a series of strategies to identify additional patients. There were a total of 111,563 discharges, of which 2557 followed treatment for hydrocephalus and 37, treatment of SVC syndrome. No additional cases were identified.

Patient 1

This boy was born at 40 weeks of gestation with birth weight 3.4 kg and head circumference 34.3 cm. A congenital diaphragmatic hernia (CDH) was repaired on day 4 of life. He was placed on arteriovenous ECMO therapy on days 6 through 8 for progressive respiratory failure.

A Broviac catheter was inserted uneventfully in the right subclavian vein at 2 weeks of age. At 8 weeks line sepsis with *Staphylococcus epidermidis* developed, which was treated with antibiotics. At 10 weeks of age, ultrasound examination demonstrated the presence of thrombi in the aorta and associated with the catheter in the SVC. The Broviac line was removed and replaced with a left subclavian catheter that functioned without complications. The child was discharged at 5½ months of age on supplemental oxygen and steroids for chronic lung disease. He required treatment for renovascular hypertension associated with the aortic thrombus.

Serial cranial ultrasounds during the first 2 weeks of life had been normal. He had a normal cranium with a circumference of 42 cm (25th percentile) 2 weeks before discharge and cranial ultrasound examination revealed mildly enlarged ventricles and subarachnoid spaces consistent with mild atrophy. Echocardiograms 1 week and 1 day before discharge showed persistence of the SVC thrombus with extension into the right atrium.

At 6½ months of age, bilateral chest wall varicosities were noted. His head circumference had increased disproportionately to 46 cm (95th percentile). He had no other signs of increased intracranial pressure. Repeat ultrasound confirmed further enlargement of the ventricles and subarachnoid spaces. Shunt placement was planned, but his pulmonary status remained tenuous and anesthetic risks precluded elective surgery. He remained asymptomatic except for mild truncal hypotonia. His head circumference reached 50 cm ($\gg$95th percentile) by 8 months of age. A cranial CT scan revealed communicating hydrocephalus with enlarged subarachnoid spaces. At 1 year of age he was found to have bilateral 50- to 60-dB sensorineural hearing loss. His cognitive development was normal (Bayley Mental Developmental Index 104 at 32 months) with mild motor delays and a nonfocal neurologic examination. His head circumference continued to be well above the 95th percentile, reaching 59.2 cm at 40 months of age. The SVC syndrome persisted, and the remaining thrombus was found to be calcified on X-ray examination of the chest. Multiple cranial CT examinations showed stable hydrocephalus with substantial enlargement of the ventricles and subarachnoid spaces. At 66 months he was stable and attending a regular preschool.

Patient 2

This girl was born at 36 weeks of gestation with birth weight 2.8 kg and head circumference 33.6 cm. A congenital diaphragmatic hernia (CDH) was repaired at 1 week of age. She required ECMO for respiratory failure from 13 h until 12 days of age.

A Broviac catheter was placed in the left internal jugular vein at 1 month of age. Cellulitis developed and the catheter was replaced with another catheter in the same location a week later and then removed at 9 weeks of age. Cranial ultrasound examinations at 1 and 7 days of age were normal. Head circumference was 37 cm (just above 10th percentile, corrected age) at 2 months of age.

When the baby was 7 months of age her parents called attention to spongy neck masses. Clinical consultation, neck ultrasound and MRI documented the presence of multiple tortuous dilated veins in the neck and old SVC thrombosis. Cranial MRI showed enlarged subarachnoid spaces with an open aqueduct of Sylvius and no ventriculomegaly. Her head circumference was 42 cm (50th percentile) at 5 months of age and 46.6 cm (90th percentile) at 10 months of age.

By 12½ months of age, her head circumference was 49.5 cm ($\gg$95th percentile) and cranial CT demonstrated moderate enlargement of subarachnoid spaces and symmetric dilation of third and lateral cerebral ventricles. A subarachnoid-peritoneal shunt was placed at 13 months of age. Her head circumference remained above the 95th percentile, reaching 52.6 cm at 28 months. A chest X-ray at 17 months revealed paraspinal densities in the upper thorax and chest CT at 18 months showed dilated collateral vessels in the neck and upper mediastinum and enlarged azygos and hemiazygos veins. At 15 months the patient had normal scores on the Motor Assessment of Infants and the Bayley Scales of Infant Development (MDI 92, PDI 82). At 28 months a repeat CT was unchanged. At 48 months she was clinically stable, with age-appropriate developmental characteristics.

Patient 3

This girl was born at 42 weeks of gestation with birth weight 2.82 kg and head circumference 31.8 cm. She was delivered by cesarean section because of fetal distress and oligohydramnios. She underwent an arterial switch procedure at 4 days of age for transposition of the great vessels. A small tear was noted in the SVC associated with the placement of a #12 right-angle cannula for cardiac bypass. The tear was sutured, and she had an uneventful postoperative course. Between 6 and 8 days of age she developed progressive edema of the head and upper torso. Echocardiography and CT scan of the chest demonstrated thrombosis of the SVC and the innominate vein. A large thrombus was surgically removed from the SVC and innominate vein. Fogarty catheters were passed into both internal jugular veins, resulting in the removal of more thrombotic material before good venous flow was documented clinically and by Doppler examination. The SVC was enlarged with a pulmonary homograft patch. She received intensive anticoagulation therapy with heparin and warfarin. CT scan of the brain at 16 days of age demonstrated extension of the thrombus into the right transverse and sagittal sinuses. She was discharged at 25 days of age on warfarin with a normal neurologic examination.

She remained healthy at home and fed vigorously. Adequate anticoagulation was demonstrated. She gradually developed multiple dilated veins over the upper chest and neck. At 4 months of age she had relative macrocephaly (head circumference 42.5 cm, 90th percentile) with height and weight at or below the 5th percentile. The anterior fontanel was bulging and measured 6×10 cm. Cranial ultrasound and CT scan showed mild communicating hydrocephalus and mildly enlarged subarachnoid spaces without atrophy. The right transverse and sagittal sinuses were slightly ectatic.

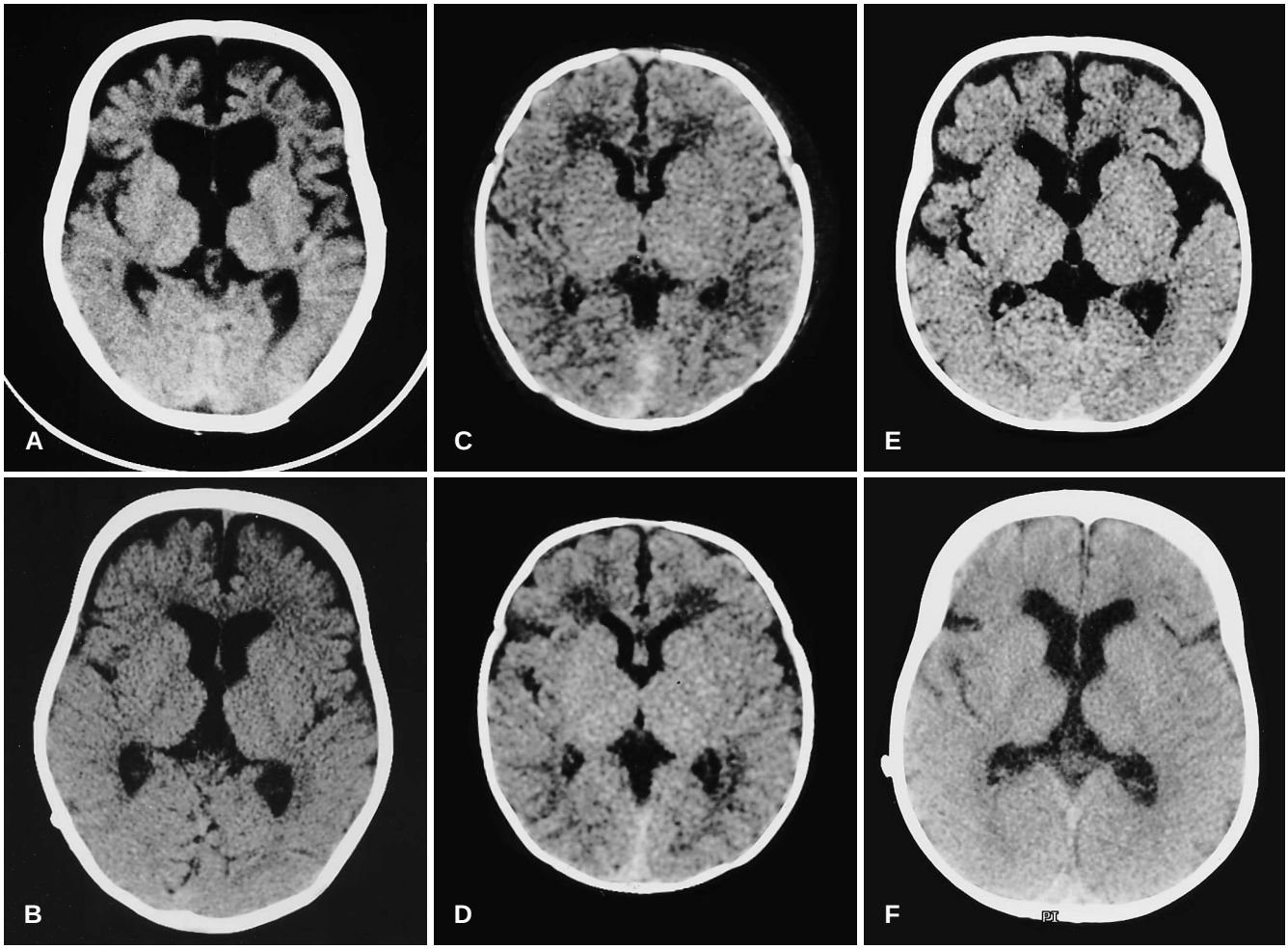

Fig. 1A–F Central nervous system CT imaging of three children with communicating hydrocephalus associated with pre-existing superior vena cava syndrome. **A** Patient 1 at 8 months of age. **B** Patient 2 at 21 months of age after placement of a subarachnoid-peritoneal shunt. Both studies reveal generalized dilatation of the ventricular system and enlarged subarachnoid spaces. **C–F** Patient 3 at 2 weeks (before onset of superior vena cava syndrome), 1 month, 4 months, and 13 months of age, respectively. The initial study is normal and there is progressive enlargement of both the ventricular system and the subarachnoid space on the two next studies, and near-complete resolution after shunting on the final study

Her head circumference at 4½ months of age was 44.0 cm (98th percentile). She obtained normal scores on the Bayley Scales of Infant Development (MDI 118, PDI 126). At 6 months, an increase in ventricular size was seen on CT, and her head circumference was just above the 98th percentile at 46 cm. She was neurologically normal and developing well. A subdural-to-peritoneal shunt was placed when the patient was 8 months of age. Her head circumference dropped back to the 98th percentile (48.25 cm at 12 months), and a CT scan at 13 months showed resolution of extra-axial fluid and marked improvement in ventricular size. At 31 months her head circumference was 51 cm (98th percentile) and repeat CT showed that both subarachnoid spaces and cerebral ventricles were normal in size.

Radiologic findings

Representative CT images are shown in Fig. 1. Note that the entire ventricular system is dilated. The enlargement of the subarachnoid spaces is at least equivalent to and sometimes greater than the lateral ventricles. There are no embryologic malformations. The degree of dilatation of the ventricles and enlargement of the subarachnoid spaces is stable and mild. One shunted patient had substantial reduction in extra-axial and ventricular fluid spaces.

Discussion and conclusions

We believe that the findings in these three children are consistent with the observations made by Haar and Miller [10] and Newman et al. [17] that SVC syndrome secondary to intravascular thrombosis may result in the development of hydrocephalus. We did not measure intracranial venous pressure, but argue that the clinical and radiologic data pre-

sented are best explained by an inadequate pressure gradient at the level of the arachnoid granulations secondary to elevated venous pressure. Bering and Salibi [2] demonstrated in experiments with dogs that complete obstruction of venous flow in the neck by acute ligation leads initially to moderate increases (200 mm of water) in both sagittal sinus venous pressure (SSVP) and cerebrospinal fluid pressure in the ventricles. Within a few days, the normal relationship of pressure in these two sites is reversed so that SSVP is higher than CSF pressure. Hydrocephalus with moderate symmetric ventricular dilatation was documented at autopsy in approximately 75% of the dogs. Rosman and Shands [21] reported similar pathologic findings in a single human example of hydrocephalus associated with SVC syndrome. Sainte-Rose et al. [23] made simultaneous measurements of intracranial pressure, SSVP and jugular venous pressure in a group of children with hydrocephalus, some of whom had venous compression at the base of the skull (e.g., achondroplasia) and some of whom had no vascular abnormalities. Intracranial pressure and SSVP were equally elevated, and jugular venous pressure was normal in both groups. Intracranial pressure but not SSVP was reduced when cerebrospinal fluid was removed from the lateral ventricles in the children with venous obstruction. Both intracranial pressure and SSVP were reduced in children without vascular abnormalities. These studies by Sante-Rose et al. support the hypothesis that increased venous pressure can lead to communicating hydrocephalus. None of the three children we report on had radiologic or clinical evidence of meningitis, hemorrhage, or any other independent disorder that could have directly disrupted the physiologic integrity of the arachnoid granulations. Neuroimaging should have detected intraventricular hemorrhage severe enough to cause hydrocephalus or obstruction of the aqueduct or the outlet foramina.

Two of our three patients underwent ECMO therapy for their neonatal pulmonary failure, and Canady et al. [3] allude to two children with hydrocephalus after ECMO therapy. Their report does not reveal whether other indwelling catheter problems were present, as in our patients. Zreik et al. [28] attributed SVC syndrome and external hydrocephalus in their patients to direct complications of ECMO. Other recent reports of outcome after ECMO therapy do not mention SVC syndrome or hydrocephalus [11, 25]. We could not confirm the high rate of transient extra-axial fluid collections (17 out of 29 infants) reported by Canady et al. [3] or the high rate of SVC reported by Zreik et al. [28] in the surviving infants who have undergone ECMO at our facility. The two infants reported here did not have extra-axial fluid collections while undergoing ECMO.

In the two of our patients who required ECMO, the developmental consequences of the stormy neonatal course have been remarkably benign and within the range reported for other children undergoing ECMO for pulmonary failure secondary to CDH [11, 25]. All three children appear to be progressing in a manner consistent with the benign neurologic course of communicating hydrocephalus caused by SVC syndrome reported by others [4, 5, 12].

Optimal long-term management remains unclear. The thrombotic area has apparently not recanalized. Despite the absence of other clinical findings, the head circumference moves further away from the 95th percentile without shunting. Placement of a subarachnoid-peritoneal shunt seems to have had little effect in patient 2, but may have been effective in patient 3. Haar and Miller [10] described short-term control of head size with a ventriculoatrial shunt in a single patient, and Newman et al. [17] described short-term success with a ventriculoperitoneal shunt.

A central venous catheter is a necessary part of the intensive care of neonates with life-threatening diseases. Thrombosis occurs with 14–21% of indwelling catheters [14, 22]. Such catheters appear to be responsible for the majority of reports of SVC syndrome in infants [9, 15, 20]. Catheter-associated infection may precede thrombosis, which it is presumed is responsible for the development of SVC obstruction. The effectiveness and safety of thrombolytic and anticoagulant therapies in this setting has not been well established [7]. Infants may require higher doses of heparin than older children or adults [1]. Anticoagulant treatment did not prevent SVC syndrome from developing in patient 3. The risk of hydrocephalus due to SVC syndrome is another cause for vigilance in the management of infants with indwelling central venous catheters or other disruptions of the integrity of the central venous intima.

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