CASE REPORT

Chemotherapy-induced cerebrospinal fluid malabsorption in a shunted child: case report and review of the literature

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SUMMARY

Ventriculoperitoneal (VP) shunt insertion is one of the most common neurosurgical procedures for the treatment of chronic hydrocephalus. Although regarded as a relatively benign procedure, several complications including obstruction, infection and mechanical failure can be seen during the postoperative stage. Symptomatic sterile cerebrospinal fluid (CSF) ascites and hydrothoracies are rare complications of VP shunt surgery. The paucity of cases makes identifying the aetiological factors difficult, particularly without catheter tip migration. It is most likely that several factors interact to reduce the absorption of CSF. The authors discuss the case of a 5-year-old girl who developed CSF ascites and a pleural effusion after starting chemotherapy for a suprasellar pilocytic astrocytoma, 2 years post-VP shunt insertion, due to a secondary obstructive hydrocephalus. After the initial management of the presenting symptoms, the child's VP shunt was subsequently changed to a ventriculo-atrial shunt and the patient made an unremarkable recovery. We also review the literature pertaining to this rare complication, assessing identifiable risk factors and surgical management options.

BACKGROUND

Ventriculoperitoneal (VP) shunts remain the recommended standard of care for the management of chronic hydrocephalus. Symptomatic sterile cerebrospinal fluid (CSF) ascites and hydrothoracies are a rare complication of VP shunt surgery. To the best of our knowledge, there are only five CSF hydrothorax cases with associated ascites in the paediatric population reported in the literature. It is most likely that several factors interact to reduce the absorption of CSF. We present the first case in the literature of a chemotherapy-induced CSF malabsorption in a previously shunted child secondary to a suprasellar pilocytic astrocytoma, presenting with ascites and subsequent pleural effusion.

CASE PRESENTATION

A 5-year-old girl presented with subacute abdominal distension and dyspnoea over a 3-week period, on a background history of a suprasellar pilocytic astrocytoma and subsequent VP shunt insertion secondary to obstructive hydrocephalus, at the age of 2. Serial follow-up imaging revealed radiological progression of the tumour 6 months ago, and the patient was started on a cisplatin-based

chemotherapeutic regime. During this presentation, she was also complaining of intermittent headache associated with nausea.

INVESTIGATIONS

Abdominal examination revealed shifting dullness and a fluid thrill. There was no evidence of rebound tenderness or guarding. Liver enzyme levels and electrolytes were within normal limits. An abdominal ultrasound revealed a substantial amount of free fluid with normal liver and renal parenchyma. Albumin was not examined. The patient underwent a successful therapeutic paracentesis and externalisation of the distal VP shunt. Analysis of the CSF revealed a high protein concentration of 8508 mg/l (table 1). An attempt to convert the VP shunt to ventriculo-atrial (VA) shunt was abandoned due to inadvertent blood loss. A ventriculo-pleural shunt was placed on the right side. The patient made an unremarkable recovery and a postoperative chest x-ray (figure 1) confirmed the satisfactory position of the distal catheter.

Three weeks later, the young girl presented to the emergency department with progressive dyspnoea and shortness of breath on exertion. Clinical examination revealed a large right-sided pleural effusion which was subsequently confirmed on chest x-ray (figure 2). This was successfully drained via a thoracentesis and the distal end of the ventriculo-pleural shunt was externalised. Further analysis of the CSF revealed an elevated protein content (table 1). Three days later, a VA shunt was inserted on the left side. The patient made an excellent postoperative recovery and was discharged home. A non-contrast CT brain showed a satisfactory position of the shunt catheter.

Three days later, she represented with a 4 h history of severe headache and associated vomiting. Funduscopy did not reveal any papilloedema. Repeat CT brain revealed no change in the ventricular size (figure 3). She underwent an emergency ventriculostomy (EVD) with an opening pressure greater than 40 cm of water. 'Stiff ventricle syndrome' was diagnosed at this stage considering the high pressure with no change in the ventricular size and a technically difficult ventriculostomy due to a consolidated ventricular wall.

The VA shunt was subsequently revised to a low-pressure valve and the EVD was clamped and

To cite: O'Halloran PJ, Kaliaperumal C, Caird J. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-008255

Table 1 Fluid analysis

	Ascites	CSF	Pleural fluid
Glucose (mmol/l)	4.6	4.3	5
Protein (mg/l)	10388	3100	8508
White cell count ($\times 10^6/l$)	24	6	15
Red cell count	3	10	37
Lymphocytes (%)	100	94	97
Gram stain and culture	Negative	Negative	Negative

CSF, cerebrospinal fluid.

removed after 48 h. The young girl remained clinically well and was discharged home 1 week later.

DIFFERENTIAL DIAGNOSIS

CSF hydrothorax cases are predominantly due to migration of the distal catheter tip.¹ In cases without catheter tip migration, over 50% of patients in the paediatric population with a suprasellar glioma develop concomitant CSF ascites. Our patient did not have either an abdominal pathology or an infection and/or inflammatory source, the two most common causes of ascites with VP shunts. The patient did not have a cause for increased CSF overproduction, as evidenced by the normal appearance of the choroid plexus and the lack of enhancement (figure 3). The child did not have any history of repeated viral infections, receiving routine immunisations, and nor was there any evidence of acute shunt rejection following the initial insertion. Furthermore, no evidence of shunt degradation was seen as the shunt catheter was intact. The authors agree that although the patient was at a higher risk of developing CSF ascites due to her age, underlying pathology and elevated CSF protein concentration, we would debate the timing of her complications following the initiation of cisplatin.

Contrary to the classification of a pilocytic astrocytoma as a benign tumour, it behaves like a malignant tumour because total

Figure 2 Right-sided pleural effusion.

resection is not feasible. Cisplatin has been shown to be efficacious and well tolerated in the treatment of paediatric pilocytic astrocytomas.

It is unclear as to whether cisplatin had a direct effect on the CSF or if it expedited the malabsorptive state. Lactose intolerance, small bowel bacterial overgrowth and bile acid malabsorption frequently develop during or after chemotherapy.² Cytotoxic chemotherapy agents, such as cisplatin, have a direct effect on the gastrointestinal mucosa causing inflammation, oedema, ulceration and atrophy.^{3 4} Although our patient did not have any signs or symptoms of bowel dysfunction, it is possible that she may have had a subacute metabolic side effect accruing from the chemotherapy, hence potentiating the malabsorption of CSF. Furthermore, up to 98% of cisplatin binds to blood plasma proteins, particularly albumin. A

Figure 1 Ventriculo-pleural shunt postoperative chest x-ray. **Figure 3** CT brain pre-emergency ventriculostomy insertion.

resulting hypoalbuminaemia, although not measured in this case, reduces the colloid oncotic pressure. Consequently, the mismatch between hydrostatic pressure and oncotic pressure creates a favourable environment for the development of ascites.

We hypothesise that the cisplatin-based therapy had a major role in the development of the CSF ascites and subsequent CSF pleural effusion.

TREATMENT

Olavarria *et al* successfully demonstrated the use of a ventricular gallbladder (VG) shunt in case of postshunt ascites in three children with optic chiasmal hypothalamic astrocytomas (OCHA). The lytic action of bile and the concentrating capacity of the biliary system most likely contributed to the success of the VG shunt.⁵ The ascites and pleural effusion resolved following the insertion of a VA shunt. This procedure is well documented as the appropriate surgical management in this cohort of patients, as the main problem is peritoneal malabsorption.^{1 6 7} Other treatment options would depend on the underlying pathology, for example, in cases of CSF overproduction, choroid plexus cauterisation would be the treatment of choice.⁷

OUTCOME AND FOLLOW-UP

Following the VA shunt revision and removal of the EVD, the young girl remained clinically well and was discharged home 1 week later.

DISCUSSION

Although VP shunt insertion is regarded as a relatively benign procedure, several complications, including obstruction, infection and mechanical failure, can be seen during the postoperative stage.⁶ In addition, rare life-threatening complications such as CSF hydrothorax^{6 8–10} and ascites^{11–13} can also occur. These rare complications have been described as single entities, but few cases illustrate these complications occurring simultaneously.

CSF ascites is a result of an imbalance between CSF production and absorption. While overproduction of CSF leading to ascites can be attributed to cases such as choroid plexus papilloma and villous hypertrophy, specific to our case, CSF production is normal and is more consistent with a malabsorptive state. It is well described that children who have VP shunts placed before the age of 2 have suboptimal peritoneal absorption capacity, which may present initially as an inguinal hernia or hydrocele.^{6 14 15}

In addition, children with OCHA have elevated protein CSF content, altering the lymphatic drainage in the peritoneum reducing the absorption of CSF, a concept widely accepted in the literature.^{5 16} Gil *et al*¹² demonstrated that 57% of children with a glioma involving the optic chiasm, who required CSF diversion, developed ascites. It should be highlighted, however, that not all cases of proteinaceous CSF results in CSF ascites,^{12 13} which would imply that other causative factors are involved. Prior abdominal surgery/multiple shunt revisions,¹⁷ infection,¹⁸ immunisation,⁵ rejection,¹⁹ tumour seeding²⁰ and vascular endothelial growth factor²¹ have all been postulated as aetiological factors leading to CSF ascites. Ascites secondary to VP shunts is most commonly due to infection, whether due to the shunt source or peritonitis, and was reported in one series to have an incidence of approximately 1.3%.¹⁸ Although there is a plausible association between CSF hydrothorax and CSF

ascites in cases of unmigrated peritoneal shunts, the pathophysiology remains undefined.

Ulus *et al* illustrated that over 60% of CSF hydrothorax cases resulted from distal catheter tip migration into the thorax, which not surprisingly occurs predominately in the paediatric population. Conversely, CSF hydrothorax cases without catheter tip migration accounted for 38.9% of cases in the adult and paediatric population.¹ Furthermore, in the paediatric setting, ascites accompanied CSF hydrothorax in 58.3% of cases without catheter tip migration. A small number of CSF hydrothorax cases had neither catheter migration nor CSF ascites.

Taub and Lavyne²² classified thoracic complications of VP shunts into three types:

1. Intrathoracic trauma during placement of the shunt.
2. Migration of the peritoneal catheter into the chest—supra-diaphragmatic or transdiaphragmatic.
3. Pleural effusion accompanying CSF ascites.

The mechanism of concomitant pleural effusions occurring in the setting of pre-existing CSF ascites (without catheter tip migration) is related to the increased intra-abdominal hydrostatic pressure and cyclical negative intrathoracic pressure. CSF may pass into the thoracic cavity via congenital hiatuses such as the foramen of Bochdalek and the foramen of Morgagni. These two locations represent weak points of the diaphragm and provide potential conduits for CSF to traverse the diaphragm along the pressure gradient.^{22 23} Another possible cause is the transudative process that occurs when inflammation and/or infection exists around the catheter tip. This process takes place on the peritoneal surface of the diaphragm through the lymphatic channels. However, there is some debate as to whether the pleural fluid is transudative or not.⁷ Furthermore, the role of microcommunications in the diaphragm is discussed by Hadzikaric *et al*.⁶ The pleural membranes can offset the diminished peritoneal CSF absorption, but once a maximum threshold is reached, the pleural absorption becomes compromised by a strengthening immune response and CSF pleural effusions develop. This is a plausible explanation in the paediatric population due to the low pleural absorption rate¹ and provides a rationale as to why this complication is not commonly seen in the adult population.

We acknowledge the fact that the pleural CSF effusion may be attributed to the placement of the ventriculo-pleural shunt, a well-recognised complication of this procedure. However, we do not feel this procedure had a significant role in the development of the pleural effusion as our patient had more salient risk factors, in particular the start of a chemotherapy-based regime.

To date, there are no cases reported in the literature indicating a chemotherapy-induced CSF malabsorption.

Learning points

- Cerebrospinal fluid (CSF) hydrothorax cases are predominately due to migration of the distal catheter tip.
- Conversely, in cases without catheter tip migration, the majority of patients develop concomitant CSF ascites with a reported incidence of approximately 57%, in a paediatric population with a suprasellar glioma.

- ▶ Children with optic chiasmal hypothalamic astrocytomas have elevated protein CSF content, altering the lymphatic drainage in the peritoneum reducing the absorption of CSF, a concept widely accepted in the literature.
- ▶ Ventriculo-atrial shunt insertion is well documented as the appropriate surgical management in this cohort of patients, as the main problem is peritoneal malabsorption and may be beneficial as an initial treatment in this subpopulation.
- ▶ Although a high CSF protein concentration predisposes children to CSF ascites/hydrothorax in the presence of a suprasellar astrocytoma, the authors believe that the chemotherapy expedited CSF malabsorption in the absence of infection and abdominal pathology due to the mismatch between hydrostatic pressure and oncotic pressure, creating a favourable environment for the development of ascites.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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