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CLINICAL ARTICLE

Antibiotic impregnated external ventricular drainage and third ventriculostomy in the management of hydrocephalus associated with posterior cranial fossa tumours

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Abstract
Background The effectiveness of antibiotic pre-treated ventricular catheters in reducing the risk of CSF infections (determined on CSF cultures) resulting from the use of per-operative external ventricular drainages (EVD) and the success rate of post-operative endoscopic third ventriculostomy (ETV) in the management of persistent hydrocephalus after posterior cranial fossa tumour removal are assessed.
Method Forty-seven children (group I) were prospectively managed by means of per-operative antibiotic impregnated EVD, post-operative ICP monitoring, and ETV. The results of this group were compared with those of a control group composed by 44 children treated with the same protocol as above except for the use of not-impregnated catheters (group II).
Findings The rate of positive CSF cultures due to EVD resulted significantly lower in group I (2.1% vs 31.8%); there was no clinical evidence of CSF infections. The success rate of ETV was the same in both groups (75%). Failures of ETV occurred in the patients with subarachnoid tumour seeding and/or tumour extension to the basal cisterns. All the children of group II with failed ETV also showed a bacterial growth in the CSF.
Conclusions Antibiotic pre-treated catheters in our experience considerably limited EVD-related bacterial growth in the CSF. Preoperative hydrocephalus resolved in 60% of the cases after tumour removal, thus confirming recent data from the literature against the routine use of preoperative ETV. In our experience postoperative ETV had a high success rate; poor results were obtained in children with tumour seeding and/or the evidence of positive CSF cultures.

Keywords Antibiotic impregnated ventricular catheters · Endoscopic third ventriculostomy · Hydrocephalus · Posterior cranial fossa tumours

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Introduction

The management of hydrocephalus in children with posterior fossa tumours (PFT) has always raised a great deal of discussion. The debate has had a further peak since the extension of the use of endoscopic third ventriculostomy (ETV) as an alternative to internal shunts also in this subset of patients. The proposal to perform ETV in all patients with preoperative hydrocephalus, prior to tumour resection [27], has been questioned by many authors in recent years [11, 22]. The criticism is justified by the high rate of unnecessary procedures related to this protocol and the not negligible risk of complications of ETV procedures (5–20%), including procedure related deaths [5–8, 12, 20, 22]. Moreover, it has been well established that both ETV is not always effective in treating preoperative hydrocephalus and then that it does not prevent persistent hydrocephalus in all cases [22, 26]. On the other hand, more than twenty years of clinical studies have demonstrated that there is no

clear advantage of pre-craniotomy extracranial CSF shunts in this kind of patients, so as the risks of acute (trans-tentorial herniation) and long-term complications (shunt dependency, shunt malfunction/infection, trans-shunt metastases) are too high to justify the routine use of this kind of procedures [4, 9, 15, 18, 19, 21, 28, 31].

Actually, most authors have come back to consider early tumour removal as first option in the management of hydrocephalus in PCF tumour patients, eventually preceded by corticosteroids therapy and associated with per-operative external ventricular drainage (EVD) [13, 17, 22, 28]. The incidence of persistent postoperative hydrocephalus in contemporary series has been reported to range between 10 and 40% [11, 22, 30]; internal shunting and ETV have been both alternatively considered for the surgical treatment of persistent post-operative hydrocephalus [11, 22, 26, 28]. When per-operative EVD is utilized the main disadvantage is the risk of CSF infection, which has been reported with occurrence rates as high as 40% [25, 30, 31].

In the present paper we evaluated if per-operatively placed antibiotic impregnated ventricular catheters can modify the risk of EVD related positive CSF cultures if compared with non pre-treated catheters in a study aimed at assessing the success rate of post-operative endoscopic third ventriculostomy in children with persistent hydrocephalus after PCF tumour removal.

Methods and materials

Two groups of patients were considered for the present study (Table 1). Group 1 was represented by all patients with posterior fossa tumours and pre-operative hydrocephalus treated at the Paediatric Neurosurgical Unit of the Catholic University of Rome, between May 2003 and March 2006; all these patients were managed prospectively with the following protocol: a) an antibiotic impregnated ventricular catheter (Bactiseal ®) was per-operatively positioned in the right occipital horn; b) After tumour removal the ventricular catheter was left in place for at most seven post-operative days and was used for intracranial pressure (ICP) monitoring and CSF subtraction (ICP values>15 mmHg.); c) Patients with persistent hydrocephalus underwent endoscopic third ventriculostomy (ETV) within the first post-operative week; d) Patients unresponsive to third ventriculostomy underwent VP shunt implantation. *Group 2* (Table 1) was a retrospectively reviewed group represented by a comparable cohort of patients with posterior fossa tumours managed at our Institution between November 2000 and May 2003; the protocol followed in these patients was the same as above, with the exception of the use of non antibiotics pre-treated external ventricular drainages.

In all cases the severity of pre-operative hydrocephalus was calculated based on the Evans Index (EI) defined as the ratio between the maximum width of the frontal horns of the lateral ventricles and the maximum bi-parietal diameter (<0.3=normal) on admission MR study. Hydrocephalus was defined as moderate if the EI was between 0.3 and 0.4 and was defined as severe if the EI was >0.4. Extension of tumour removal was verified with a contrast enhanced CT scan in the first postoperative 24 hours. Intravenous antibiotic prophylaxis (Cefazolin 30 mg/Kg) was administered per-operatively and until the removal of the external ventricular catheter in both groups. CSF samples were obtained every 2 days during the EVD period. We considered as positive CSF culture the first detection of a bacterial growth in one of the CSF cultures in the absence of clinical signs, while CSF infection was defined by occurrence of clinical and/or radiological signs suggestive of leptomeningitis or ventriculitis. In all patients with one positive CSF culture the ventricular catheter was immediately substituted and a 10-day cycle of tested antibiotic therapy was administered intraventricularly. Patients with persistent hydrocephalus underwent ETV employing a rigid 30° scope (Storz®-Decq endoscope).

Results were statistically analyzed (chi-squared test, Fisher exact test).

Table 1 Comparison between persistence of post-operative hydrocephalus and age, tumour location and severity of pre-operative ventricular dilatation

Antibiotic impregnated EVD (Group 1)			Non pre-treated EVD (Group 2)	
	No. of cases	Persistent Hy	No. of cases	Persistent Hy
Age <3 yrs	13	6 (46.1%)	17	13 (65%)
Age >3 yrs	34	10 (29.4%)	27	7 (25.9%)
Tumour inside the IV ventricle	27	16 (59.3%)	35	19 (54.5%)
Tumour outside the IV ventricle	20	0/20	9	1/9 (11.1%)
Moderate pre-operative hydrocephalus	17	0/17	9	0/9
Severe pre-operative hydrocephalus	30	16 (53.3%)	35	20 (57.1%)

Results

Group 1: Antibiotic impregnated EVD group

Clinical features

Between May 2003 and March 2006, 47 patients (M/F: 29/18, mean age: 6.5 yrs) were treated at the Paediatric Neurosurgical Unit of the Catholic University of Rome for a posterior fossa tumour with associated hydrocephalus. At admission hydrocephalus was severe in 30 cases (30/47=63.8%) and moderate in the remaining 17 patients (17/47=36.2%). Neuroradiological investigations documented an extension of the tumour inside the IV ventricle in 27 children (27/47=57.4%). Tumour removal was complete in 33 patients (70.2%), subtotal in 9 (19.1%) and partial in 5 cases (10.6%) (Table 2). Histological diagnosis documented a medulloblastoma in 21 patients (44.6%), a pilocytic astrocytoma in 15 patients (31.9%), ependymoma in 7 cases (14.9%), gangliogliomain 2 patients and a teratoid-rabdoid tumour and choroids plexus papilloma in one case each (Table 3). Sixteen of these 47 patients showed the persistence of the hydrocephalus in the postoperative period and underwent ETV. Only two variables resulted statistically related with the persistence of post-operative hydrocephalus: 1) The extension of the tumour inside the IV ventricle (p=0.001); 2) The severity of pre-operative hydrocephalus (p=0.003). These two variables were strictly dependent, seen that 23 of the 30 patients with preoperative severe hydrocephalus (23/30=77%) had the tumour located inside the IV ventricle.

Complications related to the protocol and ETV success rate

No case of pseudomeningocele or CSF leak from the surgical wounds was recorded. Complications related to the protocol were represented by one positive CSF culture (*Staphylococcus epidermidis*), occurred during the post-operative EVD time (1/47 patients: 2.1%), without clinical signs of CSF infection; this patient was treated with ventricular catheter substitution and a 10 days cycle of intraventricular antibiotic therapy (vancomycin: 10 mg/day), which allowed the resolution of the CSF bacterial growth. The success rate of ETV was 75% (12/16 patients). Two of the four patients who needed secondary VP shunt implantation had a metastatic involvement of the subarachnoid spaces documented at the pre-operative MRI (histological diagnosis: medulloblastoma in both cases); the remaining two children in which ETV failed had an extension of the tumour to the cerebellopontine angle (histological diagnosis: ependymoma in one case and cerebellar peduncle pilocytic astrocytoma in the second case), possibly impairing CSF circulation beside the stoma. No operative mortality, neither complications related to the ETV procedure were recorded.

Table 2 Comparison between extension of tumour removal and persistent post-operative hydrocephalus

Antibiotic impregnated EVD (Group 1)			Non pre-treated EVD (Group 2)	
Extension of tumour removal	No. of cases	Persistent Hy	No. of cases	Persistent Hy
Total	33	9 (27.3%)	24	9 (37.5%)
Subtotal	9	5 (55.5%)	10	5 (50%)
Partial	5	2 (40%)	9	6 (66.7%)

Group 2: Non pre-treated EVD group

Clinical features

This retrospectively reviewed group was composed by 44 children (M/F: 22/22, mean age: 6.2 yrs), affected by a posterior fossa tumour, with associated hydrocephalus, treated at the Paediatric Neurosurgical Unit of the Catholic University of Rome between November 2000 and May 2003. At admission hydrocephalus was severe in 35 cases (35/44=79.5%) and moderate in the remaining nine patients (9/44=20.5%). Neuroradiological investigations documented an extension of the tumour inside the IV ventricle in 35 children (35/44=79.5%). Tumour removal was complete in 24 patients (54.5%), subtotal in 10 (22.7%) and partial in nine cases (20.4%) (Table 2). Histological diagnosis documented a medulloblastoma in 15 cases (34.1%), a pylocytic astrocytoma in 20 cases (45.4%), an ependymoma in 5 cases (11.3%) and a fibrillary astrocytoma, ganglioglioma, choroid plexus papilloma and teratoid-rabdoid tumour in one case each (Table 3). Twenty children of this group (20/44 cases=45.4%) showed the persistence of an active ventricular dilation in the post-operative period, which was managed through ETV (Table 3).

Complications related to the protocol and ETV success rate

No case of pseudomeningocele or CSF leak from the surgical wounds was recorded. In this subset of patients we observed a higher rate of post-operatively detected positive CSF cultures (14/44 cases: 31.8%) all documented during the EVD period. CSF microbiological examination documented the presence of a *Staphylococcus epidermidis* in 9/14 (64.3%) patients; a *Staphylococcus hominis* in 2/14 cases (14.3%) and a *Staphylococcus aureus*, *Serratia marcescens* and *Pseudomonas aeruginosa* in one case each. No patients showed clinical signs of meningitis. At the first positive CSF culture all patients were treated with immediate substitution of the external ventricular catheter and 10 days of intrathecal antibiotic therapy based on tested antibiotic sensitivity, without clinical consequences.

Table 3 Comparison between tumour histology and persistent post-operative hydrocephalus

Antibiotic impregnated EVD (Group 1)			Non pre-treated EVD (Group 2)		
Histology	No. of cases	Persistent Hy	Histology	No. of cases	Persistent Hy
Medulloblastoma	21	7 (33.3%)	Medulloblastoma	15	6 (40%)
Pilocytic astrocytoma	15	4 (26.6%)	Pilocytic astrocytoma	20	9 (45%)
Ependymoma	7	5 (71.4%)	Ependymoma	5	3 (60%)
Ganglioglioma	2	0	Ganglioglioma	1	0
Choroid plexus papilloma	1	0	Choroid plexus papilloma	1	1 (100%)
Teratoid-Rhabdoid tumour	1	0	Teratoid-Rhabdoid tumour	1	1 (100%)
			Fibrillary astrocytoma	1	0

Complications directly related to the ETV procedure were represented by one case of transient hyperthermia (1/20: 5%) which had its onset few hours after ETV and spontaneously resolved after eight weeks. No mortality was recorded.

The overall ETV success rate was 75% (15/20 cases). All the five patients in which ETV failed had subarachnoid tumour seeding at the preoperative MR examinations and had the detection of a positive CSF sample (*S. epidermidis* in two cases, *S. hominis*, *S. aureus* and *S. marcescens* in each of the remaining three cases) in the EVD post-operative monitoring time.

Discussion

The management of hydrocephalus associated with posterior fossa tumours is an old and unresolved subject. In the paper of Shijman et al. [28], the personal rules followed by five experienced neurosurgeons in this context were compared. The only two agreement points in the panel perspective were: 1) no indication for pre or intra-operative CSF diversion in the absence of hydrocephalus and 2) Emergency tumour removal in patients who have no hydrocephalus but are in a bad clinical status. Per-operative EVD in case of compensated hydrocephalus was the treatment modality preferred by three of the five panel members the remaining two preferring EVD made 48 hours before surgery, and surgery without any previous procedure for hydrocephalus, respectively. A general agreement was given on not recommending pre-operative placement of a permanent shunt confirming previous literature data on this subject [1, 11, 22, 24–26, 30, 31]. Our policy is to place an external occipital ventricular drainage just after the sub-occipital craniotomy and before the opening of the dura. The ventricular catheter is left in place for the first days after tumour excision in order to monitor the intracranial pressure and transiently draw the CSF in case of elevated ICP values (ICP>15 mmHg). ETV is performed in patients with persistent abnormal ICP recordings. The advantages of a per-operatively positioned external ventricular drainage have been pointed out by many authors: intra-operatively a reduction of the posterior fossa pressure can be obtained in most of the cases allowing an easier tumour removal. Post-operatively, intracranial pressure monitoring represents an early warning system for immediate post-operative complications (i.e. tumour bed swelling or haemorrhage), leading to the possibility of early intervention; when needed, it also provides the possibility for the egress of haemorrhagic and protein laden CSF, a factor which may lessen the incidence of permanent shunt dependency. The main disadvantage is the risk of CSF infection. Most series report CSF infection rates of 6–15% [25, 31], with non pre-treated external ventricular catheters. The overall incidence of clinical CSF infection in our series was nil, while positive cultures accounted for 18.6%; however, as we removed the contaminated catheter immediately after the first positive CSF culture, we can not evaluate how many early positive cultures would have led to a clinically manifest CSF infection when untreated. Actually, none of our patients progressed to a clinical condition of infection following the catheter removal and re-implant of a new catheter for the intra-thecal antibiotic administration. Such a data makes our series not exactly comparable with the literature where only symptomatic infection rates—that is clinical signs/symptoms other than CSF alterations—are usually reported [25, 31], and even infection-related deaths have been observed [25]. Actually, in the group of children with non pre-treated EVD, the rate of CSF positive cultures was higher than the infection rate commonly reported in the literature (14/44 cases: 31.8%). Microbiological examinations documented a staphylococcal contamination of the CSF in 12/14 of the children in this group (85.7%). Since May 2003 an antibiotic pre-treated ventricular catheter (Bactiseal ®) has been prospectively introduced in place of the non pre-treated one. Rifampicin and Clindamicin impregnated shunts (Bactiseal ®) have been reported to significantly reduce the internal shunts infection rate [2, 29]; their action is directed against Gram positive bacteria, especially staphylococci (including *Staphylococcus aureus*), which represent the leading cause of external and internal CSF shunts infections [3, 14, 23, 29], a finding which is confirmed in our series. In vivo studies have documented

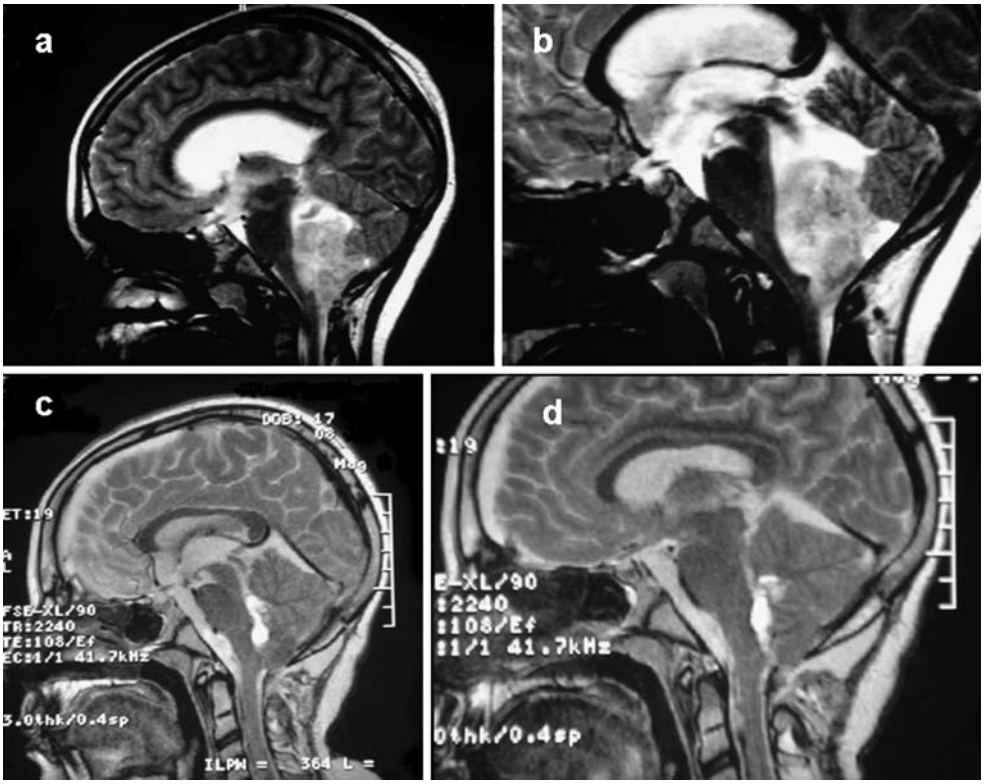

Fig. 1 Pre-operative T2-weighted sagittal MR views of a 12-yr old child with a posterior fossa ependymoma and hydrocephalus (**a, b**). The brainstem is anteriorly displaced with an almost complete obliteration of the pre-pontine arachnoid cistern. T2-weighted sagittal MR views of the same patient after tumour removal and ETV (**c, d**), documenting the reopening of the pre-pontine arachnoid cistern and the resolution of the hydrocephalus

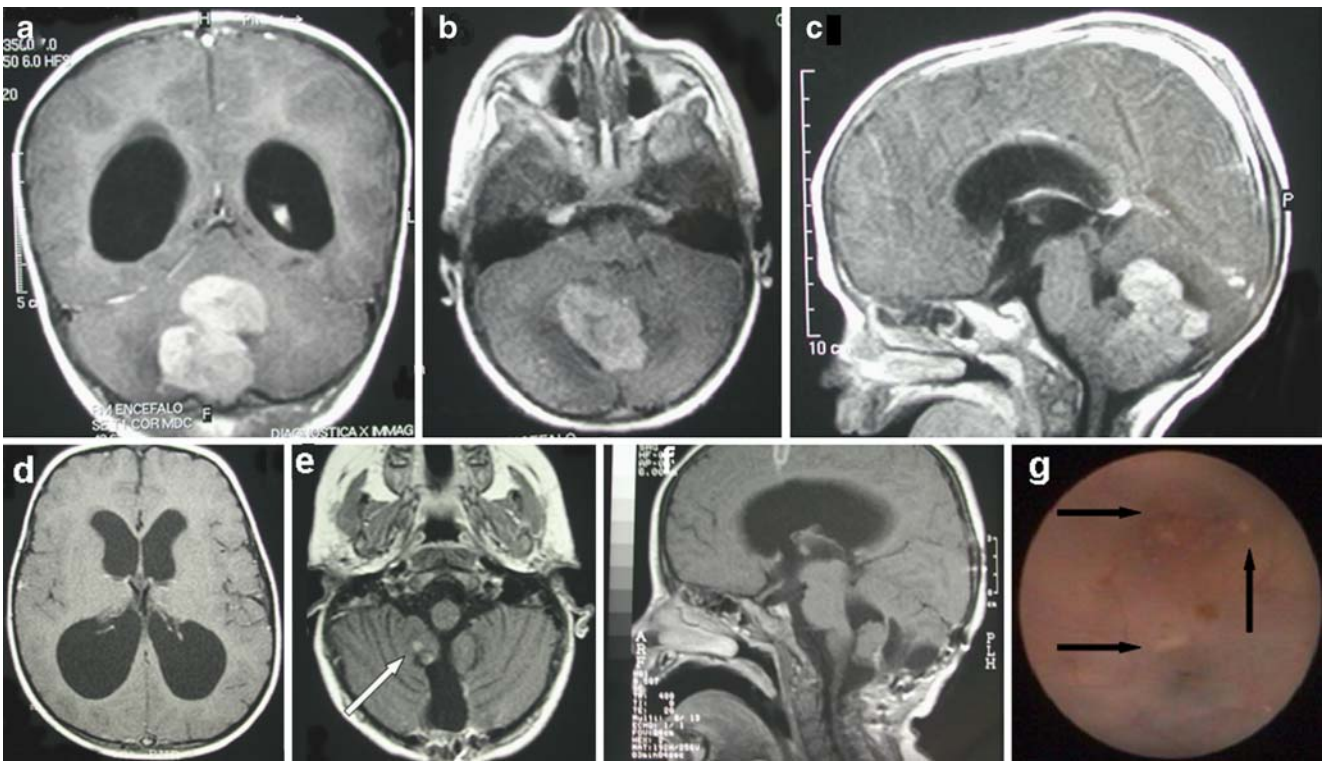

Fig. 2 T1-wighted preoperative coronal (**a**), axial (**b**) and sagittal (**c**) views of a 3-yr old child with a posterior fossa medulloblastoma and hydrocephalus. T1-weighted axial (**d, e**) and sagittal (**f**) views of the same patient after tumour removal and ETV, demonstrating the persistence of the hydrocephalus and possible secondary localizations along the surgical pathway (*white arrow*). Endoscopic intra-operative view (**g**) showing multiple secondary localizations of the primary tumour on the floor of the third ventricle (*black arrows*)

that antimicrobial activity of Bactiseal® shunts lasts against all strains up to 50 days after their implantation [23]. One of the aims of the present study was to assess whether these antibiotic impregnated catheters could actually reduce the rate of CSF positive culture. The use of this system as external ventricular drainage in our experience has proved to decrease the risk of bacterial growth in the CSF during the post-operative EVD time. Drug elution from the antibiotic impregnated catheters could have been responsible for such a phenomenon. Only 1/47 children (2.1%) presented positive CSF cultures in this group with a statistically significant reduction of the incidence of CSF contaminations if compared with children who underwent the implant of non pre-treated external ventricular drainages ($p=0.003$). Since in the control group the absence of progression of CSF positive cultures into CSF infections was obtained by the early substitution of the EVD and by an adjunctive antibiotic therapy, the main advantage of Bactiseal in the case group was to avoid a further surgical procedure and a prolonged antibiotic administration with subsequent reduction of the duration of the hospital stay. More clinical trials are needed to verify the effectiveness of this system when clinically evident CSF infections are concerned.

An alternative management strategy for children with hydrocephalus associated with posterior fossa tumours is to perform an endoscopic third ventriculostomy (ETV). Routine performance of ETV before tumour removal, once proposed to control hydrocephalus related admission symptoms of increased intracranial pressure [27], has actually been almost abandoned, hydrocephalus resolving in 60 to 90% of these children after tumour removal, with a consequent too high rate of unnecessary endoscopic procedures related to this protocol and the overall increased surgical risks [5–8, 10–12, 20, 22] (Fig. 1a,b). Moreover, the role of pre-operative ETV in reducing the rate of post-operative hydrocephalus has not been confirmed in more recent series [26]. Actually, ETV is proposed in many papers as an alternative to extra-thecal shunting in children with persistent hydrocephalus after tumour removal [11, 16, 22, 30]; however, due to its relatively recent employment in this context there is a noticeable lack of information about the results of post-operative ETV. Jones et al. [16] reported post-operative ETV to be successful in one of two patients, the second procedure being technically impossible to perform due to haemorrhage. Sainte-Rose et al. [27] performed ETV in 8 patients after posterior fossa surgery and in further three previously shunted children as secondary procedure, with an overall success rate of 100%. A lower success rate was recently reported by Ruggiero et al. [26], ETV failing in 2 out of four post-operatively treated children. The overall success rate of post-operative ETV in our series was 75% (27/36 patients), which is in the range of what has been previously reported for other obstructive hydrocephalus aetiologies. No difference in the results was observed comparing the two groups analyzed. Factors negatively influencing the success of the procedure in our series were: a metastatic involvement of the sub-arachnoid spaces (7/9 cases: 77.7%), post-operative CSF positive bacterial cultures (5/9 patients: 55.5%, all occurred in the group of children with non pre-treated external ventricular drainages) and extension of the tumour to the cerebello-pontine angle (2/9 patients: 22.2%). Subsequently, we speculate that these phenomena could prevent the CSF circulation beside the stoma (Fig. 2) or reduce its re-absorption.

In conclusion our results support the hypothesis that a staged and selective management of the hydrocephalus in children with posterior cranial fossa tumours should be considered as an appropriate alternative for these patients. The per-operative use of antibiotic pre-treated EVD could help in the post-operative EVD period lowering the possibilities of contamination of the CSF which usually precede a clinically manifest CSF infection. Post-operatively it allows a proper screening of the children who may require a permanent shunting procedure. Concerning post-operative ETV, our series is the larger to our knowledge, reported in the literature. The rationale of performing an ETV post-operatively in this subset of patients is that blood products and scarring are common and physiological occurrences at the level of the fourth ventricle and its outlet foramina after posterior fossa tumours removal and might create the conditions for a persistent obstructive ventricular dilatation.

The high success rate in our series seems to confirm this hypothesis and suggest that this procedure should be considered, not only for benign histological diagnoses, but also in children in whom a short survival is expected. Indeed extra-cranial shunts complications (shunt infection, mechanical shunt block, shunt metastases) might be particularly difficult to be accepted in patients with posterior fossa tumours, who often already have a critical early and late clinical course.

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Comment

This MS compares two groups of children with tumours. In both groups the patients received post - craniotomy EVD for pressure monitoring and CSF sampling. In Group 1, all received an antimicrobial EVD while the historical control Group 2 received a plain catheter. In terms of infective complications, study outcomes were infection rate, the need for EVD revision and hospital stay related to infection management. The policy for both groups included CSF sampling every 2 days, and immediate catheter replacement when a positive culture was reported. Probably because of this, no cases of clinical CSF space infection were seen in either group. However, the "infection" rates in Groups 1 and 2 were 2.1% and 31.8% respectively. Sampling of CSF during EVD without clinical indication (eg fever) is held to be a risk for infection. However, the findings here raise questions about this, and suggest that, if done with proper precaution, it might be clinically advantageous. The authors have reported a sequential study with historical controls, yet the results in terms of infection prevention are interesting. Prospective randomised controlled trials, with sufficient patients, are needed, as the authors say.

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This group have provided further information to a growing body of knowledge with respect to the use of antimicrobial impregnated catheters in reducing, and virtually eliminating infective complications. An interesting, unexplained observation is that in patients in which this particular technology has been used, there

appears to be a general reduction of infective complications, including organisms not known to be particularly susceptible to the specific antimicrobial agents employed in this group of catheters. This may be an interesting area of future study. A further area of interest is the use of silver impregnation technology which extends the range of organism susceptibility.

Reduction of infections in children who have a documented higher infection risk in foreign material use is a high priority. Collecting information of sufficient statistical power a further challenge.

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