



Hydrocephalus Related to CNS Malignancies in Adults

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40.1 General Presentation and Pathogenesis of Hydrocephalus

Hydrocephalus is defined as a nonphysiological accumulation of cerebrospinal fluid (CSF) in the ventricles. It is usually divided into two categories: obstructive hydrocephalus and communicative hydrocephalus. Obstructive hydrocephalus is related to a mechanical block of CSF drainage by a space-occupying lesion or congenital or acquired aqueductal stenosis. Communicative hydrocephalus is related to an increased production or decreased resorption of CSF, e.g., after

subarachnoid hemorrhage or acute or chronic meningitis [1] or after radiotherapy [2], or to a modification of CSF composition, e.g., increased protein level and presence of malignant cells, resulting in CSF malabsorption. Overall, central nervous system tumors represent the main cause of hydrocephalus [3], and approximately 5–10% of patients with glioblastoma develop hydrocephalus [4–7] as do 6–24% of patients with central nervous system metastases [8–12]. The incidence may be higher, up to 23% at presentation, in the adult population of patients with posterior fossa tumors [13].

Symptoms and signs of hydrocephalus include headache, nausea and vomiting, gait disorders, vertigo, dizziness, cognitive disorders, visual disturbances, urinary incontinence, and decreased level of consciousness. However, these symptoms and signs may be also related to expansive posterior fossa lesions [4, 8, 11, 14]. A risk of acute obstructive hydrocephalus does exist for posterior fossa lesions, eventually leading to sudden coma and death. This risk requires to manage such lesions as neurosurgical emergencies as outlined below. Conversely, symptoms and signs of hydrocephalus depend on the kinetics of its evolution, and hydrocephalus can also be largely asymptomatic when developing slowly and may be detected only by neuroimaging.

MRI with contrast enhancement is the gold standard for the diagnosis of brain tumors. In the context of hydrocephalus, it may show enlarged

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ventricles proximal to a CSF blockade in case of obstruction or throughout the ventricular system in case of communicating hydrocephalus. The Evans' index defined as the largest width between the lateral part of the frontal horns divided by the largest internal cranial diameter, measured on the same neuroimaging plane [15], has been proposed to aid in the diagnosis of normal pressure hydrocephalus, and a ventricular enlargement was defined by an index of 0.3 or more. However, significant differences can be observed depending on the level of the plane used to obtain this measure. In addition, the patient's age has to be considered—children and adolescents have narrow ventricles, and a size being enlarged in a young patient may be a normal width in the aged population. Volumetric assessment of the ventricles can also be used for the follow-up of hydrocephalus [16].

In case of newly developed or progressive clinical symptoms of raised intracranial pressure, a computed tomography (CT) scan is a widely available and quick to perform imaging modality to diagnose or rule out an acute hydrocephalus which might need immediate treatment.

40.2 Therapeutic Options

Several options are available for the management of hydrocephalus: direct surgical removal of the responsible lesion or endoscopic third ventriculostomy (ETV) for obstructive hydrocephalus, shunting either ventriculoperitoneal (VPS) or ventriculoatrial (VA) for both obstructive and communicative hydrocephalus, and external ventricular drainage as a transient emergency measure. Symptomatic pharmacological treatments such as steroids or analgesics usually have limited efficacy [14].

40.2.1 ETV

ETV is an endoscopic minimal invasive technique which involves creation of a small hole at the floor of the third ventricle to obtain a diversion of CSF into the interpeduncular cistern.

ETV can help to control intracranial pressure, avoid a procedure inserting an implant and creating a potential entry for a CSF infection, both risks associated with an EVD, and help to perform definitive surgery in better general and neurological condition [13, 17].

In a systematic literature review on 130 studies on ETV including 11,952 cases, brain tumors and cysts were the most frequent indications. The ETV failure rate was estimated at 34.7% and was higher in the first months. Complications were observed in approximately 8% and included meningitis, ventriculitis, CSF leaks, and second brain surgery [3].

Several cohorts of adult patients with posterior fossa tumors have reported success rates of an ETV between 70 and 90% [13, 18–21]. In case of persisting hydrocephalus after surgery due to a partial resection or due to failure of initial ETV mostly related to hemorrhage, a second ETV or an EVD worked [17, 22].

However, with a history of central nervous system infection, ventricular hemorrhage, high CSF protein level, or leptomeningeal metastasis, VPS or VA shunt should be used rather than an ETV [11, 23–25]. In these situations, one factor for hydrocephalus might be a block of CSF absorption on the pial surface or arachnoid granulations outside the ventricles; thus the concept of “circumventing a CSF block distal to the third ventricle” does not work [25]. Also, unfavorable anatomy for ETV (e.g., too short distance between floor of the third ventricle and the basilar tip) or any obstruction at the level of the lateral ventricles (with block of Monroe's foramen) or of the third ventricle demands a shunt procedure.

40.2.2 VPS

VPS consists in the implantation of a catheter connecting the cerebral ventricles and the peritoneal cavity. Different types of valves, either programmable or not, can be used. Improvement occurs within the first days after surgery [14]. In a cohort of 417 patients with VPS implantation for hydrocephalus, 62 fixed shunts (15%) and

355 programmable shunts (85%) were implanted. Shunt revision rates were similar between groups: 22% for programmable pressure valves and 21% for fixed pressure valves. Complications of VPS were observed in approximately 12% of the patients [26] and include infection, obstruction, bleeding, shunt malfunction, overdrainage, and formation of cystic fluid collection in the abdominal cavity sometimes referred to as abdominal “pseudocysts” [14, 26, 27]. The latter usually indicates the malposition of the distal catheter outside the peritoneal cavity and requires revision.

40.2.3 Ventriculoatrial Shunt (VAS)

VA shunt consists in the implantation of a catheter from the cerebral ventricles into the right cardiac atrium. VAS is usually considered as more challenging than VPS due to potential severe cardiopulmonary and renal complications. However, VPA represents an option for patients with contraindication to a VPS, such as multiple prior abdominal surgeries, cirrhosis with ascites, peritoneal infection, and prior severe abdominal complications of VPS. In a retrospective analysis of 496 patients presenting with idiopathic normal pressure hydrocephalus (NPH), 150 received a VAS and 346 a VPS. Post-surgery complications were observed in 36% of VAS and 42.5% of VPS. Overdrainage was the main complication observed (27.4% for VAS, 19.8% for VPS) [28]. It remains uncertain in how far such data for NPH can be extrapolated to brain tumor patients. However, in the absence of severe contraindications, currently shunting into the peritoneum (VPS) is widely preferred over VAS.

40.2.4 External Ventricular Drainage (EVD)

An EVD is a temporary measure and usually indicated as an acute emergency procedure in patients with an acutely evolving clinical deterioration due to increased intracranial pressure on

the basis of a hydrocephalus. Besides the controlled release of CSF, it allows to monitor the intracranial pressure. The main complication is infection. In a contemporary prospective cohort of 187 patients treated with an EVD and hospitalized in an intensive care unit, 31 related infections (16.6%) were observed [29]. Serum and CSF biomarkers have been shown useful to early detect infectious complications of EVD in patients with subarachnoid hemorrhage; whether this can be expanded on tumor patients is yet unclear [30].

40.2.5 Choice of Indications

The management of hydrocephalus depends on its cause and on the neurological condition. In a cohort of 243 adult patients with posterior fossa tumors, 52 patients (21.4%) had hydrocephalus at the time of admission: 39 of 52 patients had an early tumor resection, 11 of 52 patients had an ETV prior to resection, and 2 of 52 received an external ventricular drainage (EVD) initially [13]. The incidence of hydrocephalus prior to surgery was thus lower than for the pediatric population with posterior fossa tumors, where figures of 76% have been reported [31]. The risk of persistent hydrocephalus after surgery was 5.7%. Of the 191 patients without hydrocephalus prior to surgery, 4 patients (2.1%) developed post-surgery hydrocephalus. A risk factor for the need of a permanent CSF shunting procedure could not be identified [13].

In other cohorts of 36 patients treated with VPS and 16 patients treated with ETV, the efficacy was similar, 75% success rate for VPS and 69% success rate for ETV. Efficacy was higher in patients with severe symptoms. Complication rates were 19.4% for VPS and 12.6% for ETV [24]. In another report of 159 patients with hydrocephalus (123 patients treated with VPS and 36 patients treated with VTE), no revision was necessary in 69% of patients in the VPS group and 86% of patients in the ETV group. However, the complication rate was 42.7% in the VPS group versus only 9.4% in the ETV group [32]. In case of symptomatic hydrocephalus requiring CSF

diversion prior to surgery, ETV should be considered as procedure of first choice as it has the same efficacy with less morbidity and is only transient and less costly than VPS or VA shunt [21, 23, 24, 33–35]. Even more, tissue detritus and blood being spilled into the CSF during surgery of intraventricular tumors leads with a high likelihood to an obstruction of a permanent shunt system with subsequent necessity of revision—another strong argument for EVD instead of shunting in this situation [13, 23]. ETV is associated with lower rates of perioperative complications and persistent hydrocephalus after tumor resection in children; however, in adult patients, this correlation has been less well studied [17, 36].

40.3 Primary Brain Tumors

40.3.1 Glioblastoma

In a report about 841 glioblastoma patients, 64 patients (8%) underwent a VPS for symptomatic hydrocephalus [4]. Fifteen patients presented with radiographic signs of hydrocephalus at diagnosis. Symptomatic hydrocephalus was observed during the course of the disease in 49 additional patients. VPS was performed after a median of 0.4 months (range 0–25.6 months) after glioblastoma diagnosis in patients with obstructive hydrocephalus (34% of patients with symptomatic hydrocephalus) and after a median of 10.6 (0.3–461) months after glioblastoma diagnosis in patients with communicative hydrocephalus (66%). In other smaller glioblastoma cohorts, communicative hydrocephalus was observed in 5–10% during the course of disease [5–7]. Risk factors for communicative hydrocephalus include ventricular opening during surgical procedures and leptomeningeal tumor cell dissemination [6, 7]. Radiotherapy may also contribute to the development of hydrocephalus in these patients, probably by inducing fibrosis of arachnoid granulations [2].

Out of 64 patients treated by shunt, a clinical improvement was noted after CSF diversion in 61% of the patients, independent of the type of hydrocephalus: 62% of the patients with commu-

nicative hydrocephalus improved and 59% of the patients with obstructive hydrocephalus improved [4]. In another cohort of 41 patients with WHO grade III and IV glioma receiving a shunt, clinical improvement was observed in 75% [37].

In patients with glioma-associated hydrocephalus, prognostic factors for longer survival were improvement of symptoms after shunt insertion, short time between initial tumor diagnosis and shunt, and, in case of communicative hydrocephalus, later onset of symptoms during the course of the disease [4]. Complications requiring a shunt revision have been reported in 17–29% of patients [4, 37]. The administration of bevacizumab prior to the surgical procedure may be associated with a somewhat higher bleeding rate ($p = 0.026$) [37].

40.3.2 Other Primary Brain Tumors

A rate of 27–58% of hydrocephalus has been reported in adult patients with hemangioblastomas prior to surgery [38, 39], and up to 14% of patients with preoperative hydrocephalus may require a VPS for persistent hydrocephalus after surgery [38]. The rate of hydrocephalus varies from 13.7 to 32.5% in vestibular schwannomas [13, 40–43]. In a cohort of 77 patients with small-to-medium vestibular schwannomas, the rate of hydrocephalus was 11.6% [42]. In this cohort no shunt was required after surgery, whereas 16 of 49 patients (32.5%) with large vestibular schwannomas underwent VPS for persistent hydrocephalus [43]. Especially in vestibular schwannomas, an increased CSF protein level might be found which is associated with a higher risk of shunt obstruction. Thus, and since in many cases enlargement of the ventricles resumes after surgical removal of the schwannoma, upfront shunting is seldom indicated. However, in elderly and frail patients with vestibular schwannoma and concomitant hydrocephalus, it is highly recommendable to check whether the symptoms are more likely derived from the hydrocephalus. In these patients, a shunting procedure might resolve the symptoms and avoid a more risky surgical procedure since

surgical morbidity is closely linked to age in this entity [44].

In meningioma, age greater than 65 years, posterior fossa tumor location, tumor size greater than 5 cm, and Simpson resection grade II to IV were identified as risk factors of requiring a CSF diversion. In a cohort of 48 patients with meningiomas requiring a CSF shunt, the shunt failure rate was 27%, with single revision in 16.7% and multiple revisions in 10.4% [45]. Medulloblastoma and ependymoma are commonly observed in the fossa posterior, especially in the fourth ventricle, and may require postsurgical shunting due to hydrocephalus also in adult patients [13].

40.4 Brain Metastases

40.4.1 Posterior Fossa Metastasis

The incidence of brain metastases is increasing due to an improvement of therapeutic strategies which lead to improved systemic tumor control and increased overall survival in several types of common cancer. Posterior fossa metastases represent 27% of brain metastases [46]. The main tumor histology for posterior fossa metastases includes lung, breast, gastrointestinal, gynecological, and renal tumors and melanoma [11, 12]. In a cohort of 92 consecutive patients with posterior fossa metastases, 7.6% developed obstructive hydrocephalus requiring an emergency CSF shunt prior to surgical resection, and 7.1% required a CSF diversion after tumor surgery [11]. In another cohort of 50 patients, up to 24% of patients with posterior fossa metastasis presenting with symptomatic hydrocephalus required a permanent CSF drainage after resection of the metastases [12]. The risk of leptomeningeal tumor spread with potentially subsequent hydrocephalus is significantly higher with piecemeal tumor resection than with either en bloc resection or stereotactic radiosurgery [47].

In a cohort of patients presenting with hydrocephalus related to brain metastases, 16 ETV and 36 VPS were performed [24]. In this cohort no ETV was performed in patients with prior history of CNS infection or bleeding or with leptomeningeal

metastases. A comparable efficacy on symptoms was obtained after ETV (69%) and VPS (75%). While the precise prognosis of asymptomatic or symptomatic obstructive hydrocephalus is unknown [48], surgical resection or at least biopsy of identified lesions can be recommended with the aims to obtain a pathological diagnosis and to improve local control [48].

40.4.2 Leptomeningeal Metastases

Communicating hydrocephalus has been reported in 5–17% of patients with leptomeningeal metastases [9, 10, 25]. Obstructive hydrocephalus related to a block of CSF flow by metastatic nodules may also be observed. The goal of the treatment of hydrocephalus in this situation is to improve symptoms and quality of life. Adequate treatment of hydrocephalus may also help to administer other therapies which may improve the prognosis of the patients [25]. Several retrospective studies have shown 77–88% of improvement of neurological symptoms related to hydrocephalus and of the general condition after shunt placement in patients with leptomeningeal metastases [8, 33, 49]. The quality of life is usually improved [14, 24, 49]. The greatest improvements are usually seen for headache and nausea but less so for cognitive disorders, urinary incontinence, or gait disturbance [8, 24, 33, 49]. The main complications of VPS in patients with leptomeningeal metastases include infection, bleeding, obstruction or malfunction, and subdural hematoma, with an overall complication rate estimated between 9 and 15% [8]. Peritoneal dissemination of tumor cells has been reported [50–52] but seems to be rare [8, 24, 33].

Repeated CSF depletion by lumbar puncture or through a ventricular device can be an option in patients with a/pauci-symptomatic hydrocephalus treated with intra-CSF pharmacotherapy. However, intra-CSF pharmacotherapy is usually not recommended in case of symptomatic hydrocephalus which requires a VPS, especially in the absence of a valve with an on/off option. Complications of ventricular devices include obstruction, malposition, leukoencephalopathy,

and infection, although the revision rates are below 8% [53–55].

ETV represents an option for patients with obstructive hydrocephalus, e.g., secondary to brain metastases [56], but should be avoided in patients with communicative hydrocephalus as efficacy cannot be expected in these situations.

40.5 Conclusions

CSF diversion may have a role in the early diagnostic setting, sometimes as an emergency measure, or during the course of the disease in patients with primary and secondary central nervous system tumors. The method for CSF diversion should be determined according to the type of hydrocephalus (obstructive vs. communicative), the clinical presentation of the patient, and the overall medical history. CSF shunting may allow for rapid improvement of clinical symptoms and quality of life with an acceptable rate of complications and may provide the opportunity to apply further oncologic treatments. The option of CSF diversion appears to be undervalued in neuro-oncology and should be considered in patients with central nervous system tumors.

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