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REVIEW PAPER

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Abdominal metastases of pediatric brain tumors via ventriculo-peritoneal shunts

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Abstract Internal drainage of cerebrospinal fluid (CSF) to the abdominal cavity via a ventriculo-peritoneal shunt (VPS) is a procedure that is commonly used for the treatment of obstructive hydrocephalus. As this condition is often caused by brain tumors blocking the natural CSF pathways, a VPS, as an artificial anastomosis, can provide the means for tumor cells to be spread with the CSF. A review of the literature reveals 35 VPS-related abdominal metastases from pediatric brain tumors; 17 in patients aged 0–9 (group A) and 18 in patients aged 10–18 years (group B); the mean age of male patients was 10.5, and that of female patients, 7 years. The male-to-female ratio was 1.9 (group A 1.1, group B 3.5), and the mean interval between shunt operation and diagnosis of metastases, 16.7 months (group A 11.6, group B 22.6 months; boys 21.6, girls 7.5 months). During the observation period, 22/30=73.3% of the patients died (group A 13/15=86.7%, group B 9/15=60%; boys 13/21=61.9%, girls 9/9=100%); their mean survival time after shunting was 18.7 months (group A 15.7, group B 23.1 months; boys 25.5, girls 9 months). The four most common sources of metastases were germinomas (9 cases=25.7%; group A none, group B 9), medulloblastomas (8 cases=22.9%, group A 7, group B 1), endodermal sinus tumors (5 cases=14.3%, group A 1, group B 4), and astrocytomas (4 cases=11.4%, group A 4, group B none). Metastases via VPS are rare, but should be considered as a possible complication and mode of systemic spread in children with primary intracranial malignancy. They have a more favorable prognosis in boys and in the second decade of life.

Key words Abdominal metastasis · Pediatric brain tumor · Hydrocephalus · Ventriculo-peritoneal shunt · Complication

Introduction

Diversion of CSF into the peritoneum for the treatment of hydrocephalus was first attempted as early as 1898 [8], but did not become established until the 1950s, following the development of modern biocompatible materials for shunt systems [31]. While ventriculo-atrial shunts prevailed through the 1960s, VPS were reinvestigated and advocated by Ames [1], resulting in their more frequent application and decreased morbidity [11, 16]. As they often occlude the CSF pathways, brain tumors are a common cause of hydrocephalus, particularly in the pediatric population, which benefits greatly from shunt insertion [27]. However, several cases have been published in which extraneural metastases of primary cerebral tumors were initiated through implanted shunt tubes. Initial reports on this manner of tumor cell spread appeared in 1954 and 1963 for ventriculo-*pleural* [40] and ventriculo-*peritoneal* [4] shunts, respectively. The present study was undertaken to review the epidemiological data on VPS-related abdominal metastases originating from brain tumors in children up to the age of 18 years.

Results

A survey of the literature published between 1960 and 1997 revealed 35 cases of VPS-related abdominal metastases originating from brain tumors in children aged 18 years or under (Tables 1, 2); 17 patients were 9 or younger (group A) while 18 children were between 10 and 18 years old (group B; Table 3); the average age of male patients was 10.5, and that of female patients, 7 years (Table 4). The most frequent histological entities were germinomas (9 cases) and endodermal sinus tumors (5), which dominated in group B and showed a marked male prevalence (8:1 and 4:1, respectively), and medulloblastomas (8) and astrocytomas (4), which were particularly common in group A (Tables 2, 3). While there was an overall male predominance, with 22 cases in boys against 12 in girls (ratio 1.9), a feature that was even more pronounced in the older age group (14 vs 4 cases, ratio 3.5), no sex prevalence could be discerned for younger patients (9 vs 8, ratio 1.1). The mean interval between shunt operation and diagnosis of metastases was 16.7 months: 11.6 in the younger, 22.6 in the older age group (Table 3); 21.6 months in boys and 7.5 in girls (Table 4). During the observation period of between 1 month and 9 years, 22 of 30 patients died (73.3%, Table 2), more of these children being in the first (13/15; 86.7%) than in the second decade of life (9/15; 60%, Table 3) and a higher percentage of the girls (9/9; 100%) than boys being affected (13/21; 61.9%, Table 4). The mean survival time of the deceased children after shunting was 18.7 months (group A 15.7, group B 23.1 months; boys 25.5, girls 9 months; Tables 2–4).

Table 1 Reported cases of peritoneal metastases of primary pediatric brain tumors via ventriculo-peritoneal shunts

Reference	Diagnosis	Sex	Age[b]	Metastasis[c]	Survival[d]
Fujimoto 1972[a]	Medulloblastoma	F	2	12	12
[17]	Medulloblastoma	F	2	1	nd
[33]	Ependymoblastoma	M	9	18	22
[35]	Endodermal sinus tumor	M	13	nd	nd
[3]	Oligodendroglioma	F	1.3	3	3
[18]	Germinoma	M	12	30	>42
[21]	Ependymoblastoma	F	1.2	5	5
[30]	Germinoma	M	11	nd	>48
[39]	Endodermal sinus tumor	M	4	9	9
	Endodermal sinus tumor	F	12	6	7
[41]	Germinoma	M	11	41	>60
	Germinoma	F	13	17	17
	Pineal tumor	M	15	60	>60
[37]	Germinoma	M	15	20	42
[15]	Germinoma	M	14	14	>54
[36]	Astrocytoma I	M	3	10	>18
[2]	Endodermal sinus tumor	M	16	4	6
[6]	Medulloblastoma	F	3	8	14
	Medulloblastoma	M	5	14	18
	Medulloblastoma	M	6	28	32
	Medulloblastoma	M	7	5	6
	Medulloblastoma	M	11	20	35
[14]	Endodermal sinus tumor	M	17	2	16
[24]	Pineoblastoma	F	12	12	nd
[20]	Astrocytoma I	M	1.6	48	60
[42]	PNET	M	1.1	16	nd
[13]	Astrocytoma	F	4	5	6
[23]	Germinoma	M	15	2	6
[29]	Germinoma	M	18	72	72
[19]	Glioblastoma	F	9	2	6
	Glioblastoma	M	13	3	7
[22]	Medulloblastoma	F	0.8	11	11
[38]	Germinoma	M	13	36	>60
[25]	Astrocytoma II	M	0.5	2	>108
[9]	Melanoma	F	16	nd	nd

[a] Cited in [22]
[b] At time of shunt operation (years)
[c] Interval between shunt operation and diagnosis of abdominal metastasis (months)
[d] Length of survival (months) after shunting (> still alive after end of observation period, *nd* no data available)

Discussion

Extraneural metastases of primary brain tumors are rare and can occur through both blood and lymphatic vessels. Spread via shunts inserted as therapeutic means to the management of tumor-related hydrocephalus and acting as artificial anastomoses between two body cavities has been limited to sporadic cases. Among patients with ventriculo-peritoneal shunts, 58 VPS-related abdominal metastases have been reported so far; on average, these patients had been 12.2 years of age at shunt insertion, reflecting the mainly pediatric types of the underlying brain tumors (unpublished data). In children aged 18 years or younger 35 such incidences have been described, amounting to 77.8% of all 45 patients whose ages could be established and confirming the more malignant and metastasis-prone character of pediatric brain tumors (unpublished data).

Medulloblastomas account for 22.9% of cases of metastases arising following tumor cell spread via VPS, although they make up only 14% of tumors in children under 20 years of age [34] and no shunt-related metastases of this entity were found in the study by Raimondi and Tomita [26]. Only germinomas account for more, namely 25.7% of cases (Table 2); this is surprising, given that these germ cell tumors only comprise 0.5% of all primary cerebral neoplasms [12] and 4.1% of all pediatric brain tumors [34]. These figures show that both medulloblastomas and germinomas are overrepresented among the sources of VPS-related abdominal metastases, which is in line with their tendency to spread via the CSF [6, 12], often causing com-

Table 2 Tumor types of 35 primary brain neoplasms causing abdominal ventriculo-peritoneal shunt metastases in children. Absolute (*n*) and relative (%) frequency, sex distribution (*M* male, *F* female), mean age at shunt operation (years), and interval in months between shunt insertion and diagnosis of peritoneal metastasis (*metastasis*) and death (*survival*); *alive* number of children still alive after observation period, *dead* number of deceased patients, *nd* no data available

Histological tumor type	*n* (%)	M/F	Age	Metastasis	Alive/dead	Survival
Germinoma	9 (25.7)	8/1	13.6	29.0	5/4	34.3
Medulloblastoma	8 (22.9)	4/4	4.6	12.4	–/7	18.3
Endodermal sinus tumor	5 (14.3)	4/1	12.4	5.3	–/4	9.5
Astrocytoma	4 (11.4)	3/1	2.3	16.3	2/2	33.0
Glioblastoma	2 (5.7)	1/1	11.0	2.5	–/2	6.5
Ependymoblastoma	2 (5.7)	1/1	5.6	11.5	–/2	13.5
Melanoma	1 (2.9)	–/1	16.0	nd	nd	nd
Pineoblastoma	1 (2.9)	–/1	12.0	12.0	nd	nd
Oligodendroglioma	1 (2.9)	–1	1.3	3.0	–1	3.0
PNET	1 (2.9)	1/–	1.1	16.0	nd	nd
Pineal tumor[a]	1 (2.9)	1/–	15.0	60.0	1/–	–
Total	35 (100)	23/12=1.9		16.7	8/22	18.7

[a] Histology not mentioned

Table 3 Clinical course and histological spectrum with regard to patient age (*metastasis* interval between shunt insertion and diagnosis of peritoneal metastasis, *alive* number of children still alive after observation period, *dead* number of deceased patients, *survival* duration of survival after shunting)

Age group	A (0–9 years)	B (10–18 years)
Number of cases	17	18
Sex distribution (M/F)	9/8 = 1.1	14/4 = 3.5
Metastasis (months)	11.6	22.6
Alive/dead	2/13	6/9
Survival (months)	15.7	23.1
Germinoma	None	9
Medulloblastoma	7	1
Endodermal sinus tumor	1	4
Astrocytoma	4	None

Table 4 Clinical course and outcome by patient's sex (*metastasis* interval between shunt insertion and diagnosis of peritoneal metastasis, *alive* number of children still alive after observation time, *dead* number of deceased patients, *survival* duration of survival after shunting)

	Male	Female
Number of cases	23	12
Age (years)	10.5	7.0
Metastasis (months)	21.6	7.5
Alive/dead	8/13	0/9
Survival (months)	25.5	9.0

pression of the cerebral aqueduct and necessitating VPS placement, with a potential risk of peritoneal metastases as a result of CSF flow into the abdomen [27]. The same applies to other maldevelopmental and/or pineal region tumors, all of which together account for 71.4% (25 of 35 cases) of metastases. Surprisingly, even histologically benign intracranial astrocytomas showed dissemination [25]. However, while germinomas and endodermal sinus tumors account almost exclusively for metastases in the second decade of life, astrocytomas and medulloblastomas are equally limited to the first decade (Table 3), corroborating the results of extensive surveys on the epidemiology of cerebral neoplasms in infancy and early childhood [7, 28].

Our review shows an incidence of abdominal metastases in male patients that is 1.9-fold that in female patients, which is higher than the general gender distribution ratio for malignant cerebral tumors (1.25, [34]). This male prevalence is even more pronounced in the group aged 10–18 years and among children with germ cell tumors. The mean age of each histological group basically follows its tumor-typical distribution (Table 2). The average interval between shunting and diagnosis of abdominal metastases is 16.7 months; in 7 patients metastases were not diagnosed until autopsy. Not surprisingly, this time span varies widely depending on the histology of the tumor; it is particularly short for glioblastoma (2.5 months) and endodermal sinus tumor (5.3 months) and markedly longer for germinoma (29 months). A virtually identical pattern is seen for survival after shunt insertion. The relatively favorable prognosis of patients with germinoma-related metastases is also indicated by the fact that they account for 5 of the 8 patients still alive within the observation period and have the longest survival time, with 34.3 months; however, three quarters of these children died of their illness.

There are marked differences in prognosis with age (Table 3) and sex (Table 4), favoring older children and boys. While among children up to 9 years of age metastases manifested themselves 11.6 months after shunting, with a postoperative survival time of 15.7 months, resulting in the demise of 13 out of 15 patients, the metastasis-free interval in the 10- to 18-year-olds was twice as long (22.6 months), with a 50% longer survival time (23.1 months) and fewer fatalities (9 out of 15). The time-lapse between shunting and diagnosis of metastases was almost 3 times as high in boys (21.6 vs 7.5 months in girls), a ratio similar to that for their respective survival times after shunt insertion (25.5 vs 9 months), while all girls (9 out of 9) but only just over half the boys (13 out of 21) died during the observation period.

As to the theoretical contraindication for precraniotomy shunt insertion – a point raised by Raimondi and Tomita [27] – our survey of 10 children who underwent both shunting and tumor removal and whose fate was known showed that 4 of the 7 patients with *pre*craniotomy VPS were still alive, while all 3 children who were shunted *after* craniotomy had died; however, owing to the limited number of cases no definite conclusion can be drawn.

The insertion of shunts is associated with a certain spectrum of well-known possible side effects, such as shunt obstruction, infection, hematomas, and overdrainage [27, 32]. Griebel and co-workers [10] found this to be the case in 57% of their 195 investigated shunt procedures. However, metastases via VPS – now the most widely used type of shunt [10, 22] and also less prone to cause complications – are very rare compared with the number of existing shunts [5] and might be avoided by the use of a filter. According to several studies, such peritoneal metastases appear to respond well to systemic chemotherapy and/or radiation [17, 18, 38]; thus, ultrasound or CT surveillance of the abdomen might be considered as part of the routine follow-up in children with VPS who are suffering from brain tumors. For most patients, however, shunts result in a highly improved quality of life and extended survival. Nonetheless, they should be considered as a possible mode of systemic spread that can therefore lead to complications in patients with primary intracranial malignancies.

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