

Candida albicans ventriculoperitoneal shunt infections: Immunocompetent preterm pediatric case series and an extensive review of literature

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Abstract

Cerebrospinal fluid shunt devices are increasingly being used for decompression, and despite excellent results, obstruction and infection are concerning complications, with underlying fungal etiology a rare consideration. In this study, we focus on pediatric shunt infections caused by *Candida albicans* in an extensive literature review and by reporting two additional cases. Very limited information regarding diagnosis and treatment of the Candidal shunt infections is available. Prematurity and use of broad spectrum antibiotics have been postulated as risk factors, and a CSF analysis prior to surgical placement of the shunt should be implemented as standard practice. Based on our cases, we suggest establishing the diagnosis based on a single positive fungal culture, and to initiate with intravenous and intraventricular antifungal therapy for two weeks, switching to oral antifungal medication for a total of 43 days in an outpatient setup without immediate ventriculoperitoneal shunt removal.

Abbreviations: CSF: Cerebrospinal Fluid, EVD: External Ventricular Drain, ICP: Intracerebral Pressure, LP: Lumbar Puncture, MRI: Magnetic Resonance Imaging, VP: Ventriculo-Peritoneal

Introduction

Cerebrospinal fluid shunt devices are commonly indicated for the treatment of hydrocephalus in infants, and have served to improve survival and reduce mortality. However, ventriculoperitoneal shunt infection is a serious complication, commonly with an underlying bacterial etiology [1,2]. Candidal infections remain a rare complication of neurosurgery [3], but are associated with a significant mortality, morbidity, and cost. The emerging importance of *Candida* as a nosocomial pathogen prompted us to undertake a review of published literature over the last sixty years, revealing a total of 23 cases of *Candida albicans* shunt infections in children under the age of two [4-13]. We report an additional two cases of *Candida albicans* ventriculoperitoneal shunt infection in immunocompetent preterm infants, and discuss the unique features and treatment of our cases in light of those reported previously.

Cases

Case 1

A four-month old female infant presented to the Emergency with complaints of fever, cough, squint and increasing head circumference one month after the insertion of a ventriculoperitoneal shunt. Her past medical history was significant for preterm delivery and neonatal sepsis with no seizures. At the age of three months, an MRI was performed for increasing head circumference and vomiting, establishing a diagnosis of non-communicating hydrocephalus, for which a ventriculoperitoneal shunt was placed. This procedure was

performed elsewhere, and a CSF analysis was not performed prior to surgery. On presentation at our hospital a month later, her initial CSF analysis showed occasional leukocytes, a protein concentration of 290 mg/dl, a glucose concentration of 22 mg/dl, and yielded *C. albicans* sensitive to amphotericin-B, Fluconazole and Voriconazole. The culture was positive only this once after which serial CSF examinations revealed sterility with persistence of high protein and low glucose levels. Treatment with antibiotics, intrathecal amphotericin-B and Fluconazole was promptly started, and her shunt was removed 2 weeks after initial presentation. Intermittent serial fontanelle taps were performed alongside, in progressively increasing intervals, to address high pressure-related symptoms. After 43 days of antifungal therapy, she recovered completely without necessitating reinsertion of a shunt device, and has had no signs of elevated intracerebral pressure to date.

Case 2

Around the same time, a five-month old male infant presented to our clinic with inflammation and purulent discharge along the tract of a previously inserted ventriculoperitoneal shunt. Past medical history was significant for preterm delivery and neonatal sepsis. He had been subsequently diagnosed with hydrocephalus for which a ventriculoperitoneal shunt was placed at his local hospital without

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Key words: *candida albicans*, ventriculoperitoneal shunt, infection

Received: January 14, 2017; **Accepted:** February 07, 2017; **Published:** February 10, 2017

prior CSF analysis. Since his presentation at our clinic appeared predominantly bacterial, the VP shunt was immediately removed and multiple antibiotics were started. However, *C. albicans* was isolated from the first culture of CSF, with a leukocyte count of 200/cm³, a protein concentration of 356.5 mg/dl, and a glucose concentration of 18 mg/dl. Intrathecal amphotericin-B was administered for 43 days along with Vancomycin, and the ventriculoperitoneal shunt was eventually re-inserted due to persistently elevated intracerebral pressure (Table 1).

Discussion

A thorough review of published English literature over the last sixty years from 1956 to 2014 revealed a total of 53 cases of Candidal ventriculoperitoneal shunt infections, suggesting that *Candida albicans* remains a rare causative organism complicating neurosurgical shunt procedures [3]. Of the 39 cases described, 23 were children under the age of two years [4-13]. Females accounted for 68.8% (11/16), 13 were preterm infants, and a history of prior use of antibiotics was seen in six of nineteen reported cases. The most common presenting complaints were fever (8 of 20 infants), vomiting (6 of 20 infants), and hydrocephalus (4 in 20 infants). Outcomes were not reported for three of the 23 children; the rest were treated successfully. Therapy included shunt removal and administration of systemic antifungals for most of the patients. Amphotericin-B was the most commonly prescribed antifungal (75%), with five patients receiving it via both the intravenous and intraventricular route. Baradkar [4] treated his four cases of *C. albicans* shunt infection with systemic amphotericin without clarifying if the shunt was removed. Other drugs that were used successfully were Fluconazole [7], Flucytosine [12], gentian violet [5] and Caspofungin [10] (Table 2).

Although *Candida* constitutes the normal flora of the genitourinary tract and skin [14], certain predisposing factors have been implicated in its pathological acquisition. These include indwelling catheters, steroids, immunosuppression, malignancy, cerebrospinal fluid leakage and bowel perforation or abdominal surgery [1,3,4,11,14-16]. Prematurity and the use of prior antibiotics have also been identified as risk factors, and are congruent with our observations.

Our first case presented with fever and hydrocephalus while the other had a predominantly bacterial presentation, with mucopurulent discharge along the tract of the ventriculoperitoneal shunt. CSF was promptly sent for cytology and culture, and antibiotics were started. In both cases, only the first CSF culture was positive for *Candida albicans* with increased protein and decreased glucose levels; serial CSF examinations revealed sterility. Initial literature review revealed insufficient data, in terms of well-defined guidelines and lack of a

proper criterion, to diagnose a case of Candidal shunt infection, and its optimal treatment. We suggest that a high index of suspicion should be maintained, that diagnosis should be made on a single positive culture, and treatment should be promptly initiated if the patient is symptomatic with an indwelling device and deranged CSF parameters. This is comparable to recommendations made by Geer *et al.* [17].

Generally, treatment includes shunt removal, administration of antifungal therapy and placement of a new shunt [2,6,16]. However, our cases were managed differently. Case 1 was started on intraventricular and intrathecal amphotericin-B with the shunt in situ initially for two weeks. Instead, serial fontanelle taps for raised intracerebral pressure (ICP) were performed, with intervals lengthening over time, i.e. on days 3, 7, and 18. Eventually, all high pressure signs settled and the infant had a shunt-less outcome. The CSF became sterile within the first week but medical therapy was continued for a total of 43 days, due to persistence of low CSF glucose and high protein levels. Based on this observation, we propose that the indication for shunt reinsertion should not be solely based on CSF protein levels, but should also assess and incorporate the patient’s clinical response. Serial anterior fontanelle taps proved to be a cost-effective intervention in our limited resources setting; also preventing serious complications such as external ventricular drain (EVD) related overdrainage, and reinfection. A fontanelle tap works by improving CSF flow dynamics by exerting an intermittent flow challenge and thus, may result in an ideal shunt-less resolution of hydrocephalus, as in our case.

On the other hand, the seemingly bacterial presentation of Case 2 necessitated immediate shunt removal and administration of antibiotics, including intrathecal Vancomycin, Amikacin and systemic antibiotics. A positive Candidal culture of the cerebrospinal fluid was unexpected, for which we recommended administration of amphotericin and Fluconazole. After several negative bacterial culture reports, ventriculoperitoneal shunt revision was performed to treat persistent hydrocephalus, with outpatient serial fontanelle taps to address raised ICP signs. The persisting high protein levels despite negative cultures were thought to be a reaction to the intrathecal antibiotics. Fever and lethargy were dealt successfully with Fluconazole administered for 43 days. Our study shows that shunts exposed to fungal infections behave similarly to patients with *Mycobacterium tuberculosis* infection, where the shunts are left in situ during treatment. Based on this, we suggest that shunt removal is not mandatory in fungal infections, as opposed to some studies [6,15,18] that state otherwise, and that these infections can be treated in an outpatient setup. Although administration of intrathecal antifungals is deemed controversial [17], the two new cases reported in our study have had rapid and absolute recovery with it.

Table 1. Summary of clinical characteristics of our 2 cases of Candidal VP shunt infection.

	Case 1	Case 2
Age	5 months	4 months
Gender	Female	Male
Preterm	Yes	Yes
Sepsis	Yes	Yes
History of broad spectrum antibiotics use	Yes	Yes
Hydrocephalus	Yes	Yes
VP shunt placement	Yes	Yes
CSF analysis prior placement	Not done	Not done
Presenting complaints	Fever, hydrocephalus, low birth weight	Colonization and infective tract of VP shunt
CSF culture	<i>C. albicans</i> (only 1st culture)	<i>C. albicans</i> (only 1 st culture)
Immediate shunt removal	No	Yes
Treatment	Antifungal therapy	Antibiotics followed by antifungal
Shunt Replacement	No	Yes

Table 2. All cases of *Candida albicans* shunt infection reported to date in children ≤ 2 years

Pt. No.	Reference	Age/ Sex	Underlying condition	Clinical presentation	Prior bacterial infection	CSF culture	Rx	Outcome
1	[9]	Child	Shunt revision	NR	NR	<i>C. albicans</i>	NR	NR
2	[5]	2mo/F	Lumbosacral meningocele	Hydrocephalus	+	<i>C. albicans</i>	Ventricular aspiration + shunt removal	Cured
3	[5]	2/F	Communicating hydrocephalus	Meningoencephalitis	+	<i>C. albicans</i>	Gentian violet + shunt removal	Cured
4	[12]	2mo/M	IVH	Hydrocephalus	NR	<i>C. albicans</i>	5FC + ivt antibiotic + shunt removal	Cured
5	[8]	NR	Perforated bowel wall	NR	NR	<i>C. albicans</i>	NR	NR
6	[8]	NR	Spontaneous shunt infection	NR	NR	<i>C. albicans</i>	NR	NR
7	[15]	47d/F	Prematurity, aqueductal stenosis	Hydrocephalus	+	<i>C. albicans</i>	amB iv + shunt removal	Cured
8	[15]	19 mo/F	IVH	Meningoencephalitis	+	<i>C. albicans</i>	amB iv + shunt removal	Cured
9	[15]	3mon/F	Congenital hydrocephalus	Hydrocephalus	+	<i>C. albicans</i>	amB iv + amB ivt + shunt removal	Cured
10	[15]	1mo/F	Meningomyelocele	Hydrocephalus	+	<i>C. albicans</i>	amB iv + amB ivt + shunt removal	Cured
11	[7]	2mo/F	IVH	Fever, shunt malfunction	-	<i>C. albicans</i>	Fluconazole iv + shunt removal	Cured
12	[6]	6mo/F	Prematurity, hydrocephalus	Poor activity level	-	<i>C. albicans</i>	amB iv + shunt removal	Cured
13	[6]	5mo/M	Prematurity, hydrocephalus	Poor activity level	-	<i>C. albicans</i>	amB iv + ivt + shunt removal	Cured
14	[6]	6mo/M	Prematurity, hydrocephalus	Shunt malfunction	-	<i>C. albicans</i>	amB iv + shunt removal	Cured
15	[6]	3mo/M	Prematurity, hydrocephalus	Fever, shunt malfunction	-	<i>C. albicans</i>	amB iv + shunt removal	Cured
16	[6]	8mo/M	Prematurity, hydrocephalus	Fever, shunt malfunction	-	<i>C. albicans</i>	amB iv + shunt removal	Cured
17	[11]	7mo/F	IVH	Abdominal symptoms	-	<i>C. albicans</i>	amB iv + amB ivt + shunt removal	Cured
18	[11]	2/F	Choroid plexus papilloma	Abdominal symptoms	-	<i>C. albicans</i>	amB iv + amB ivt + shunt removal	Cured
19	[4]	NR	Prematurity, hydrocephalus	Fever, vomiting	-	<i>C. albicans</i>	AmB iv	Cured
20	[4]	NR	Prematurity, hydrocephalus	Fever, vomiting	-	<i>C. albicans</i>	AmB iv	Cured
21	[4]	NR	Prematurity, hydrocephalus	Fever, vomiting	-	<i>C. albicans</i>	AmB iv	Cured
22	[4]	NR	Prematurity, hydrocephalus	Fever, vomiting	-	<i>C. albicans</i>	AmB iv	Cured
23	[10]	8mo/M	Prematurity, IVH grade III	Hydrocephalus	-	<i>C. albicans</i>	removal of Omay reservoir + caspofungin	Cured

Conclusions

In conclusion, the authors recommend maintaining a high index of suspicion, and establishing a diagnosis of *Candida albicans* ventriculoperitoneal shunt infection in the presence of one positive CSF culture in a symptomatic patient with an indwelling device, without discounting it as a contaminant. Treatment with systemic and intrathecal amphotericin-B or Fluconazole should be promptly started and can be switched to oral Fluconazole therapy for a total of 43 days. Follow-up CSF cytology and cultures should be performed, but elevated protein levels in the absence of other findings should not be solely used as an indicator of infection resolution and shunt function.

Further research is required in the form of a three-arm randomized or pragmatic clinical trial comparing the different decompression options – EVD, fontanelle taps, and serial lumbar punctures - in patients requiring temporary CSF drainage. External ventricular drainage makes inpatient care necessary and carries a high chance of overdrainage and nosocomial infections as compared to serial fontanelle taps. Ommaya reservoir is an alternative option that can be utilized for drainage of CSF as well as administration of intrathecal antibiotics. Nonetheless, fontanelle tap is emerging to be a good initial choice for neurosurgeons in a limited-resource setting as it requires a single tap to relieve the pressure, is more economical and manageable, can be carried out in an outpatient setup, provides a source for CSF challenge and has a lower risk of complications.

Acknowledgements

The authors would like to extend their gratitude and appreciation to Dr Fatima Mir, Assistant Professor of Pediatric Infectious Diseases, for her valuable input.

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