

Candida parapsilosis Shunt Infection: A case report

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ABSTRACT

Shunt infections are common complications of ventriculoperitoneal shunt (VPS) placement; its incidence varies from 0.3% to 40%. Bacterial infections are still the most common etiology of shunt infections, while fungal cases remain to be rare causes. Because of the latter, fungi are usually not considered in the initial diagnosis of shunt infections. Moreover, shunt infections have non-specific manifestations and have insidious nature, which make diagnosis difficult to render. Physicians who are not experienced in the management of fungal infections may lack the proper knowledge in handling shunt infection cases, which in turn leads to a delay in the administration of appropriate treatment and increase in patient morbidity. We report a case of fungal shunt infection caused by *Candida parapsilosis*.

INTRODUCTION

Infection is a major cause of morbidity in children with cerebrospinal fluidshunting procedures. About 99% of these infections are secondary to a bacterial etiology. Fungal infections account for about one percent of cases, most of which are due to *Candida albicans* and *C. tropicalis*. We report a case of fungal shunt infection caused by *C. parapsilosis* together with the different diagnostic tests and the antifungal therapy needed for children with shunt infection.

CASE REPORT

The patient is a four-month old male with a chief complaint of head enlargement. He was born preterm at eight months age of gestation to a 20-year old G1P0 mother via caesarean section at the Aquinas Hospital in Legazpi,

Keywords: Shunt infection, *Candida*, *Candida parapsilosis*

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Albay. Maternal history was unremarkable, except, for a fetal ultrasound done at eight months age of gestation, which showed

congenital hydrocephalus. At birth, the patient had good cry and activity but with poor suck. He was diagnosed with neonatal sepsis and was admitted at the Neonatal Intensive Care Unit for 12 days and treated with unrecalled IV antibiotics; he was discharged improved. At that time patient had a normal head circumference but according to the cranial ultrasound, he had congenital hydrocephalus. Patient was advised to consult with a pediatric neurologist.

At the age of one month, the patient was noted to have gradual head enlargement with no other accompanying signs or symptoms. The patient's parents consulted with a private physician who ordered for a computed tomography scan to be done; it showed hydrocephalus. The patient then underwent ventriculoperitoneal shunting. Four days after the procedure, he developed fever and was treated for one week with parenteral oxacillin and acetazolamide 250 mg/tablet given ¼ tablet, once a day. The patient was discharged improved.

At three months and two weeks old, three weeks PTA, the patient developed undocumented fever accompanied by loose, watery stool and poor suck. He was admitted at a local hospital and started on ceftazidime and vancomycin which were eventually shifted to cefepime twice a day and completed for 2 weeks. Because of noted increase of the head circumference, lumbar tap was done with alleged normal results. Patient was then diagnosed to have a shunt malfunction. They were advised that removal and reinsertion of the VPS should be done. Due to financial constraints, they sought consult at PGH and patient was subsequently admitted.

Pertinent physical examination on admission revealed the patient to be afebrile and with stable vital signs. He had an enlarged head of 47 cm; anterior fontanel was full but not bulging. There was no rebound upon pressure on the VPS. The rest of the physical examination was

unremarkable. Patient received one dose each of BCG, Hepatitis B, DPT and OPV. He was breastfed up to two months old then shifted to mixed feeding with infant formula. Patient has social smile but was unable to lift his head.

Because the patient did not have any other signs and symptoms of infection such as fever, the primary consideration on admission was shunt malfunction, probably, secondary to mechanical failure. However, because he presented with fever, diarrhea and poor suck during the course of his illness, shunt infection was also investigated. The patient's CBC showed leukocytosis of $35 \times 10^3/\mu\text{L}$, he was then started on Oxacillin (200mg/kg/day) and Gentamicin (5 mg/kg/day). He underwent ventriculoperitoneal shunt removal and right frontal ommaya reservoir insertion. Intra-operative CSF specimen showed 27 WBC with lymphocytic predominance of 83%. Culture of CSF and ventriculoperitoneal shunt tip grew *Candida specie*. Repeat CBC showed a decrease in the WBC from $35 \times 10^3/\mu\text{L}$ to $25 \times 10^3/\mu\text{L}$.

After ten days of antibiotics, repeat CSF studies showed further increase in the WBC and protein levels. Culture again grew *Candida specie*. Parenteral Fluconazole (6mg/kg/day) was started. Oxacillin and gentamicin were completed for two weeks. Despite nine days of fluconazole, CSF studies showed persistently elevated WBC count and further increase in the protein levels. CSF culture grew *Candida specie*, not albicans. A repeat CT scan showed significant accumulation of subdural fluid with a decrease in the degree of ventricular dilatation. Fluconazole was shifted to Amphotericin B. Patient's ommaya reservoir tip was removed and was sent for culture, which grew 10,000 CFU *Candida parapsilosis* (MAKI Method) sensitive to amphotericin B. This was continued for 22 days. (Plan of 28 days was interrupted because of difficulty in IV access). Repeat CT scan showed decrease in the subdural fluid in the right hemisphere and neither ependymal nor subdural enhancement. Subsequent CSF determinations showed a decreased WBC count ($12 \times 10^3/\mu$) cultures. Patient was discharged improved.

DISCUSSION

Most pediatric patients with hydrocephalus are treated with ventriculoperitoneal shunt placement. CSF shunts have a ten-year failure rate of more than 50%. The most common complication is mechanical, followed by shunt-related infection. Infection is a major cause of morbidity in children with CSF shunting procedures. Its incidence varies from 0.3% to 40%. Almost two thirds of shunt-related infections occur within one month after placement of the shunt; 90 % of infections manifest within six months. The incidence of shunt-related infections is significantly higher in infants in the first six months of life than in older children³. Bacterial infection is still the most common cause, while fungal cases are considered rare causes of shunt infections; hence, they are not usually considered in the initial diagnosis. Furthermore, there is a lack of established guidelines in the proper management of these cases. Physicians who are not experienced in the management of fungal infections may lack the proper knowledge in handling shunt infection cases, which in turn leads to a delay in rendering appropriate treatment and an increase in patient morbidity.

Etiologies of ventriculoperitoneal shunt (VPS) infections vary depending on the country and institution. In the United States, coagulase negative staphylococcus is the most common offending agent in patients with shunt infection, followed by *Staphylococcus aureus*, while fungal infections account for only <1% of the cases³. In a study done at the Philippine General Hospital, the pathogens isolated among pediatric patients with VPS infection were *Staphylococcus aureus*, *Klebsiella sp.* and *Acinetobacter*⁴. *Candida* infection was rare with only one documented in 130 infections (3.7%). In a review on the impact of *Candida* infections on medical devices, the overall rate of VPS infection is between 6% to 15%². The proportion of infection due to *Candida* is 1% and mortality due to *Candida* infection ranges from 9% to 30%. The most common *Candida* species in this review were *C. albicans* and *C. tropicalis*. A recent literature review on *Candida* Infection of Cerebrospinal Fluid Shunt Devices included 38 cases from 1958 to 1996. *C. albicans* was the most frequently isolated

species found in 78.9% of cases followed by *C. tropicalis*; *C. parapsilosis* was found in 5.2% of cases. The reported mortality due to the *Candida* infection was 5.8%. Risk factors identified were bacterial meningitis preceding the *Candida* episode (36.8%), the use of broad spectrum antibiotics (57.8%), and the use of steroids (18.4%)¹.

Candida are commensal organisms; and the interruption of normal host defense is necessary for its pathogenicity. Risk factors for *Candida* infections include immunocompromised states, diabetes mellitus, antibiotic use, indwelling devices, intravenous drug use, and hyperalimentation fluids. *Candida parapsilosis* has increasingly been reported to cause significant infections in the pediatric age group. In neonates, increasing number of blood stream infections has been documented⁸. In a UK national surveillance study, *Candida parapsilosis* comprised 25% of all cases of invasive fungal infection in very low birthweight infants¹⁰. *Candida parapsilosis* was reported to cause 5.2% to 17% of *Candida* shunt infections^{1,9}. Specific risk factors for *C. parapsilosis* are foreign-body insertion, neonates, and hyperalimentation. It is frequently recovered from skin samples and occurs more frequently in patients with venous catheters; hence, a cutaneous origin is postulated for this infection².

The initial signs and symptoms of most patients with shunt-related infections are non-specific. Therefore, it is prudent to keep in mind that only a minority of patients will have the classic signs and symptoms of CNS inflammation. In a study by Montero et al, the classical manifestations of meningoenzephalitis were found in only 10.5%. The most frequent presenting symptoms and signs were fever 28.3% and hydrocephalus 28.3%¹. In a local study by Aragon et al, seizure, irritability and nuchal rigidity were seen in only about 10% of the patients⁴. In some instances, complications of shunt obstruction may constitute as the only presenting symptom⁵. The non-specific manifestations and the insidious onset in many of the cases make diagnosis difficult. The only definitive diagnostic test is direct observation and culture of the CSF. Test for CSF glucose

concentration, differential cell count, gram stain and culture should be requested. Protein concentration is of limited help in the evaluation of shunt infections because high protein levels are found in many patients with shunt malfunction but with no infection. A low glucose level suggests an infection, but it may also be normal. Pleocytosis is indicative of a shunt-related infection³. Physicians dealing with shunt infections should consider a fungal etiology in the differential diagnosis of patients, when they have risk factors for acquisition of this infection and are not responsive to antibiotic treatment. Appropriate fungal studies should be requested so that proper management may be given.

There are four classes of drugs for the treatment of invasive fungal infections (IFIs): the polyenes, triazoles, echinocandins, and nucleoside analogues. Most isolates of *Candida parapsilosis* are sensitive to the newer triazoles, flucytosine and amphotericin B⁷, although, fluconazole-resistant isolates have been reported. Currently, there is no published RCT on the use of these different antifungal agents for the treatment of *Candida* shunt infection in children. Blyth, et al, did a systematic review that included trials among children with IFIs. No adequately-powered, comparative trials in pediatric candidemia or invasive candidiasis have been performed⁶.

The expert panel of the Infectious Diseases Society of America recommended lipid formulation of amphotericin B (3-5 mg/kg/day) for the initial treatment of CNS *Candida* infections in adults because of a lower risk of nephrotoxicity compared to the conventional Amphotericin B. This may be given in combination with or without Flucytosine. Fluconazole, on the other hand, is recommended only as a step-down therapy and an alternative for patients amphotericin B is contraindicated. For the duration of treatment, the panel recommended that therapy should continue for several weeks until all signs and symptoms, CSF abnormalities and radiologic abnormalities have been resolved⁷.

In pediatric patients, the preferred agents are still conventional amphotericin B (1 mg/kg/day) or the lipid preparation given parenterally. If

ventricular fluid remains positive after five to seven days therapy with amphotericin, addition of flucytosine (150mg/kg/day divided every 6 hours) is recommended³. Intraventricular administration is reserved for patients with persistently poor response. There is no established recommendation for the duration of treatment of fungal shunt infection in children. However, the recommended duration of therapy for candidal meningitis is at least four weeks after the resolution of signs and symptoms⁶. The role of other newer antifungal drugs has not yet been fully ascertained.

In summary, we presented a case of fungal shunt infection in a four-month old male, who presented with head enlargement, but with no other manifestations of infection to the central nervous system such as fever, nuchal rigidity or seizure. Fungal studies grew *C. parapsilosis*. Eradication of the infection in this case consisted of the administration of amphotericin B for a total duration of 22 days and removal of the infected shunt.

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