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Case Report

Continuous intraventricular vancomycin for treatment of ventriculitis using IRRAflow®: A case report

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ABSTRACT

Background: Ventriculitis usually occurs as the result of infection and results in the inflammation of the ependymal lining of the ventricular system. Mortality rates remain high despite treatment.

Case Description: We present the case of a 66-year-old man who presented with altered mental status and progressively became comatose. He was found to have fulminant ventriculitis due to a ruptured intracranial abscess. He was treated with bilateral IRRAflow® catheter (IRRAS, Stockholm, Sweden) placement through which continuous irrigation with vancomycin was initiated.

Conclusion: This treatment was safe and led to improvement in the patient's neurologic examination, imaging findings, and cerebrospinal fluid profiles.

Keywords: IRRAflow® system, Technology, Ventriculitis

BACKGROUND

Ventriculitis is defined as inflammation of the ependymal lining of the ventricular system and usually occurs as the result of infection. Ways in which infection can seed the ependymal system include meningitis, rupture of intracranial abscesses, trauma, and catheter-associated spread.[12,13] The mortality associated with ventriculitis caused by intraventricular rupture of an intracranial abscess tends to be high, with rates from 26% to 72.7% reported in various case series depending on the route of infection and the organism responsible.[10,14] Intraventricular antibiotic administration has been posed as a potential treatment of these aggressive infections with some positive results.[5]

The advent of self-irrigating catheter systems, such as the IRRAflow® (IRRAS, Stockholm, Sweden), has expanded interest in applications for this technology with early reports of use in the treatment of chronic subdural hematomas and intraventricular hemorrhage.[2,7] In addition to the standard "drain-only" option available on a typical ventricular drain, the IRRAflow® can be set to irrigate small volumes at a fixed rate through its dual lumen catheter. Typically, normal saline is used as the irrigation solution, although in theory this technology could be used as a

drug delivery system. We present a case report of a patient treated with continuous intraventricular vancomycin for ventriculitis using the IRRAflow® system for this purpose.

CASE DESCRIPTION

The patient was a 66-year-old man with a medical history of hepatitis C and benign prostatic hypertrophy who presented originally to our institution with altered mental status following 1 week of headaches. He attended a religious event and after arriving home was found in front of his computer, attempting to use it even though it was turned off. His examination on arrival was remarkable for disorientation, a right homonymous hemianopia, and nonsensical speech. Computed tomography (CT) of the head demonstrated a left occipital lesion concerning for intracranial abscess with intraventricular extension [Figure 1]. This was confirmed on contrast-enhanced magnetic resonance imaging (MRI) that also demonstrated diffuse enhancement of the lateral and third ventricles [Figure 2a and b].

Figure 1: Computed tomography of the head demonstrating a mixed density left occipital lesion with the presence of hypodense material extending into the lateral ventricle.

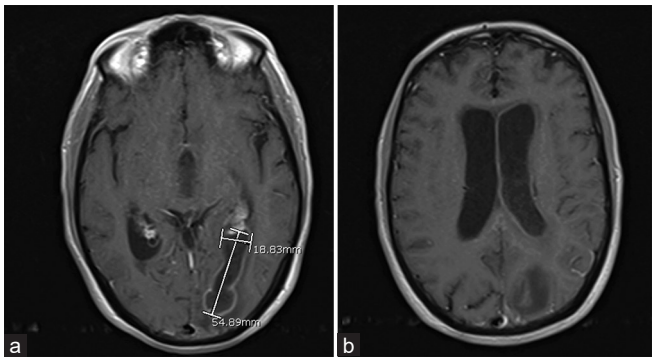

Figure 2: Magnetic resonance images (a and b) of the brain showing a ring-enhancing left occipital lesion with intraventricular enhancement consistent with intraventricular rupture of an intracranial abscess.

Soon the patient began to have a seizure, becoming unresponsive with right gaze deviation and hypertonicity in his extremities. Despite treatment with several milligrams of intravenous (IV) lorazepam and 1000 mg of fosphenytoin, he continued to seize requiring intubation and heavy sedation with a continuous infusion of propofol. To treat the hydrocephalus associated with his ventriculitis, a left-sided Kocher's point IRRAflow® catheter system was placed and set to drain-only mode [Figure 3]. Blood and cerebrospinal fluid (CSF) cultures were submitted for pathologic analysis, and the patient was admitted to the intensive care unit. IV antibiotic therapy was initiated consisting of vancomycin (1250 mg every 12 h), ceftriaxone (2 g every 12 h), and metronidazole (500 mg every 8 h). Continuous electroencephalography (EEG) was used to target a pattern of burst suppression. Overnight, the IRRAflow® catheter became clogged with thick pus, and a second right-sided IRRAflow® catheter was placed [Figure 4]. Gradually, his sedation was weaned off. Despite discontinuation of the sedation, his neurologic examination findings were extremely poor. His pupils were reactive, but he had weak corneal reflexes and minimal motor response to noxious stimuli. EEG was continued to monitor for any seizure activity, although none was captured.

On hospital day 2, irrigation with normal saline was started through the IRRAflow® system bilaterally at a rate of 40 mL/h. A single dose of intraventricular vancomycin (10 mg) was given through the system on hospital day 3, and irrigation was resumed following a 1-h clamp of the system to allow distribution of the antibiotic therapy. On hospital day 4, the normal saline irrigation solution was replaced with 50 mg of vancomycin diluted in 1 L of normal saline. This solution was continuously irrigated through the system at 60 ml/h bilaterally. In addition, 4 mg of IV dexamethasone was administered every 6 h.

Over the subsequent days, the patient's neurologic condition began to improve. By hospital day 6, he was extubated. He

Figure 3: Computed tomography of the head used to confirm placement of the IRRAflow® catheter within the left lateral ventricle.

Figure 4: Computed tomography of the head demonstrating placement of the second IRRAflow® catheter within the right lateral ventricle.

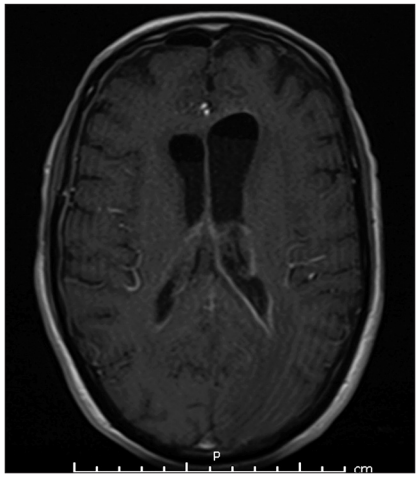

Figure 5: Magnetic resonance imaging of the brain following IRRAflow® treatment showing decreased ventricular abscess burden.

was conversant and following commands. In the interim, blood and CSF cultures were positive for *Streptococcus intermedius*. The IV ceftriaxone and metronidazole, as well as the intraventricular vancomycin were continued at the previous doses. An extensive workup was conducted to explore the source of the infection, including CT of the abdomen, pelvis, face, and sinuses. These were all negative. A human immunodeficiency virus test was negative. No source was able to be identified.

During the patient's hospital course, CSF profiles obtained on a daily basis showed continued improvement [Table 1]. Inflammatory marker tests were also regularly obtained, and the values down trended. Even the drainage from the IRRAflow® system began to clear, going from thick, and proteinaceous pus to a thin straw-like fluid. Repeat MRI completed approximately 1 week after the patient's presentation demonstrated decrease in the abscess burden and ventricular enhancement [Figure 5].

Despite improvement in the patient's clinical status following treatment, he was significantly debilitated. Discussions were had with the patient's family who emphasized that the patient's previous state of function was excellent, and he would not want aggressive measures if his function would not return exactly to its previous state. As such, the patient's family proceed with comfort care measures, and the patient subsequently died several weeks later.

DISCUSSION

Spontaneous intraventricular rupture of an intracranial abscess is a devastating complication with a mortality rate approaching 80% in one series.[16] The high rate of mortality is due to acute hydrocephalus and rapid dissemination of infectious materials throughout the CSF space leading to fulminant meningoencephalitis.[16] In those who are fortunate enough to survive the acute phase, the ongoing inflammatory process leads to scarring of the ependymal surface ultimately leading to septations and loculated hydrocephalus.[9] Treatment of septations, once they have already formed, can be accomplished through a neuroendoscopic procedure in which the septations are broken up and the inflammatory debris drained.[6]

One factor that influences the treatment of ventriculitis is the ability to achieve adequate penetration of antimicrobial agents into the brain due to significant purulence.[4] To combat this, intrathecal antibiotics have been proposed.[8] In their case series, Isono *et al*. report that early ventricular drainage, along with intraventricular antibiotics, dramatically improved outcomes in patients with intraventricular rupture of an intracranial abscess.[3] In addition, they found that early, aggressive ventricular irrigation can prevent formation of septations and improve prognosis. Similarly, Remeš *et al*. demonstrated the rapid sterilization of CSF following intrathecal antibiotics administered to 34 post-neurosurgical patients with meningitis or ventriculitis, with nearly 50% of patients demonstrating sterilization within 24 h.[8] Only 3 of the 34 patients demonstrated adverse drug reactions, which supports the safety of this intervention.

Despite the positive outcomes reported by Isono *et al*. and Remeš *et al*.,[3,8] large case series and randomized controlled trials are lacking. In addition, there is no clear consensus on the use of intrathecal antibiotics for ventriculitis within the neurosurgical community.[15] von Spreckelsen *et al*. queried 121 neurosurgical programs across Germany regarding their treatment of ventriculitis.[15] Of the 33 respondents, 30% of programs did not utilize intrathecal antibiotics, 36% considered intrathecal antibiotics on a case-by-case basis,

Table 1: Cerebrospinal fluid profiles.

	Hospital Day 0	Hospital Day 3	Hospital Day 4	Hospital Day 5	Hospital Day 7	Hospital Day 8
Appearance	Turbid	Turbid	Cloudy	Turbid	Turbid	Cloudy
Color	Tan	Yellow	White	White	White	White
Erythrocytes (cells/mm^3)	Unable to count due to clumping of cells	Unable to count to due to degenerative cells	Unable to count to due to degenerative cells	350	30	60
Nucleated cells (cells/mm^3)	Unable to count due to clumping of cells	Unable to count to due to degenerative cells	Unable to count to due to degenerative cells	12350	1950	1270
Neutrophil segmented (cells/mm^3)	91	Unable to count to due to degenerative cells	Unable to count to due to degenerative cells	97		97
Glucose (mg/dL)	1	4	1	2	1	5
Lactate (mmol/L)	18.4	16.4	2.2	1.6	0.6	1.3
Protein (mg/dL)	1126	494	39	30	<7	21
Microogranisms	Present	Present	None seen	None seen	None seen	None seen
Culture	*Streptococcus intermedius*	*Streptococcus intermedius*	*Streptococcus intermedius*	No growth	No growth	No growth

and 21% utilized intraventricular antibiotics routinely. Introducing antibiotics directly into the intraventricular space is thought to improve the bioavailability of antibiotics in the central nervous system (CNS). The utilization of irrigation may decrease the risk of seizures or aseptic meningitis associated with intraventricular antibiotic administration.[11]

Given the high mortality of intraventricular rupture of an intracranial abscess and the lack of evidence-based treatment protocols, we elected to mimic the promising protocol reported by Isono *et al*.[3] The use of the IRRAflow® system allowed us to expand on this by providing continuous irrigation of the ventricular system and constant cycling of antibiotics directly into the CNS. Our hope was that aggressive irrigation would help to clear the inflammatory byproducts of the abscess, thus preventing the scarring of the ependymal surface that can occur.[9] We also felt continuous antibiotic irrigation was needed to promote penetration of the drug through the proteinaceous material within the ventricle. We used dexamethasone in the patient described in this case because steroid use may be beneficial in controlling vasogenic edema in patients with intracranial abscesses.[1] We also felt that there may be some benefit in preventing inflammatory scarring of the ependyma but that has not been proven.

Following the implementation of our therapy, the patient had dramatic improvement in his neurologic status within 3 days. He began to follow commands and was able to have a conversation. Repeat MRI demonstrated a notable improvement in the size of the patient's abscess and intraventricular pus burden. Finally, the CSF profiles also showed remarkable improvement. Given his family's wishes to pursue palliative options, it is difficult to say whether this novel treatment would have benefited the patient in the long term or prevented the need for shunting. In retrospect, aggressive irrigation with the IRRAflow® system on initial placement may have prevented the need for a second device. We were hesitant to begin irrigation until the patient's intracranial pressure (ICP) stabilized because he did not have a neurologic examination to follow due to requiring heavy sedation. Despite our initial concerns, ICPs began to normalize after irrigation was started. This is an important learning point for future use of this device as only a single IRRAflow® is likely needed as long as it remains patent. Based on our experience, we advocate for aggressive irrigation to promote drainage of viscous materials, such as pus or clotted blood, to reduce ICP.

At present, several ventricular catheters are available, such as the Codman and Integra systems. To the best of our knowledge, the IRRAflow® system is the only self-irrigating ventricular catheter system on the market. Comparison of the IRRAflow® with other available devices is somewhat limited because of this, although we noted some advantages and disadvantages during this case. Continuous infusion is not possible with conventional external ventricular drainage systems; therefore, a benefit of the IRRAflow® system was that medications could be administered into the ventricular system without halting drainage. Clamping of the system to allow for proper distribution of intraventricular medications, such as vancomycin or tissue plasminogen activator, can be associated with elevations in ICPs. Although manual irrigation through the Codman and Integra systems can be performed, a clear advantage of the IRRAflow® is that this process is automatic, occurring on a minute-by-minute basis.

It is unclear whether this confers a benefit in the treatment of the underlying disease process; however, it certainly simplifies patient care.

Disadvantages of the IRRAflow® system are mainly centered on the lack of familiarity with the system. As noted in the case discussion, the IRRAflow® was used without irrigation when it was initially placed because of concern for elevation of the patient's ICPs, whereas the standard Codman system available at our institution would typically have been manually irrigated to promote drainage of the intraventricular pus. As our experience with the device has increased, we have become more comfortable initiating aggressive drainage early on. Similarly, the initial rate of irrigation was based on our comfort level and not an evidence-based protocol. Given that the IRRAflow® is a new device, these protocols will need to be developed as neurosurgeons familiarize themselves with the device. Finally, determining the reliability of ICP measurements using waveforms from a pressure transducer is not currently available with the IRRAflow® system. At our institution, a transducer is typically attached to the buretrol, which is leveled at the tragus. Waveforms from the transducer are referenced when we examine ICP to ensure the recordings are accurate. Lack of a waveform was one of the factors contributing to our hesitancy to initiate irrigation earlier. We did attach a transducer directly to the IRRAflow® catheter outflow port later in the patient's clinical course to obtain pressure waveforms. Although the expected three-peak waveform was present, the transducer needed to manually be leveled each time the pressures were checked.

The limitations of the research presented here include its retrospective nature and inclusion of a single patient. Larger retrospective and prospective studies examining a wide variety of neurosurgical pathologies are needed to determine the benefit of the IRRAflow® system and create evidence-based treatment protocols.

CONCLUSION

The use of an IRRAflow® catheter for continuous delivery of intraventricular irrigation with vancomycin is a technically feasible and safe treatment for ventriculitis. In our case, it led to marked improvement in neurologic status, imaging findings, and CSF profiles.

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Declaration of patient consent

The authors certify that they have obtained the appropriate patient consent.

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Conflicts of interest

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