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Case Report

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CNS Complication of Group A *Streptococcal* Meningitis in Children: a Comprehensive Case-Based Literature Review

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ABSTRACT

Group A *Streptococcus pyogenes* meningitis rarely results in central nervous system complication. Chronic hydrocephalus is a well-known complication of bacterial meningitis. To date, no reports have focused on acute central nervous system complications and neurological outcome of Group A *Streptococcus pyogenes* meningitis. An unusual association of acute hydrocephalus requiring emergent neurosurgical intervention in a 6-year-old girl with Group A *Streptococcus meningitis* is presented. Based on reported cases since 1966, authors present the results of a comprehensive acute neurological complication and outcome. Our report highlights a need for vigilance and timely needed emergent surgical intervention in minimizing acute hydrocephalus in children with Group A *Streptococcus* meningitis.

KEYWORDS: *Streptococcus pyogenes* meningitis; Central Nervous System complication; Acute hydrocephalus; Surgical intervention; Children.

ABBREVIATIONS: CNS: Central Nervous System; CSF: Cerebrospinal fluid; CT: Computerized Tomography.

INTRODUCTION

Streptococcal infections are common in children. Unlike Group B *Streptococci septicemia*,[1] Group A *Streptococcus* (*S. pyogenes*) typically affects children beyond the neonatal period. Occasionally, this causes acute meningitis, glomerulonephritis, or rheumatic heart disease.[2] Group A Streptococcus infection is a rare cause of bacterial meningitis. Hydrocephalus is a relatively rare complication of acute bacterial meningitis in children. Nonetheless, it has been reported in 20% of infants and children. Acute Central Nervous System (CNS) complications including hydrocephalus are not unique to *Stretococcus pyogenes* causing meningitis. They have been reported in children with viral and other bacterial meningitis.[3]

We report an unusual association of acute hydrocephalus in a 6-year-old girl with Group A *Streptococcal* meningitis and provide the results of a comprehensive literature review on acute CNS complications and neurological outcome in children 17years and under.

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CASE REPORT

A 6-year-old girl presented to the Emergency Department with vomiting and neck pain for 24 hours. She had headache for five days and intermittent fever and sore throat for the past two weeks. She had no seizures and had received no antibiotics. A non-contrast Computerized Tomography (CT) scan of the brain prior to the lumbar puncture was normal. Treatment with intravenous vancomycin and ceftriaxone was initiated.

On admission to the Pediatric Intensive Care Unit, her vital signs were stable and temperature was 37.6 degree C. Her throat was red and congested but the tympanic membranes were normal. Her skin had no lesions. She had decreased alertness and her neck was hyper-extended in a fixed position. Pupils were 4 mm and reactive to light. Fundoscopic examination revealed no papilledema. Deep tendon reflexes were hyperreflexic and on plantar stimulation, her toes were up going.

The Cerebrospinal fluid (CSF) studies revealed an elevated intracranial pressure, a white blood cell count of 7644 mm^3, red blood cells 10,000 mm^3, protein 440 mg/dl and glucose 20 mg/dl. Serum glucose was 102 mg/dl. CSF smears revealed Gram-positive cocci in pairs and chains. The blood and CSF culture yielded *S. pyogenes*. Genotyping for the streptococcal isolates was not obtained. The CSF polymerase chain reaction for herpes simplex virus type 1 and 2 DNA for both, was negative.

Hospital Course

Ten hours after admission, she had an acute increase in heart rate from 80 to 133 beats per minute and blood pressure from 124/69 to 156/47 mm Hg. Her pupils became asymmetric and reacted sluggishly to light. Her Glasgow Coma Scale score declined from 13 to 9. Following endotracheal intubation, mechanical ventilation, and administration of 1 gram/kilogram of mannitol, a contrast-enhanced brain CT scan was performed which revealed communicating hydrocephalus with no herniation or abscess (Figure 1A). An urgent frontal external ventricular drain was placed. A follow up brain CT scan revealed relief of the hydrocephalus (Figure 1B).

The ventriculostomy tube was clamped on day 12 and was removed on day 15. Intravenous ceftriaxone was continued for 21 days. She received physical, occupational, and speech therapies throughout the hospitalization. She was discharged on the 23rd day of admission with no focal motor, cerebellar, or sensory deficits.

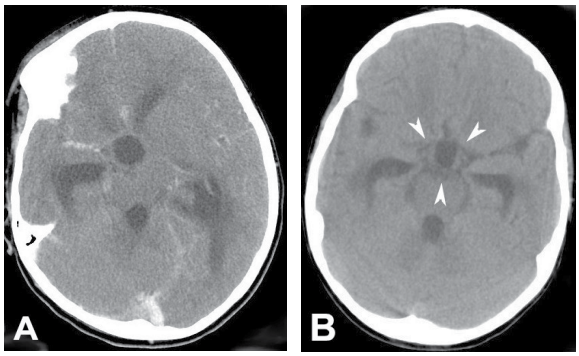

Figure 1: An axial Computerized Tomography (CT) of the brain at the fourth ventricle level shows communicating hydrocephalus, figure A was obtained before and figure B was after surgical placement of a ventricular drain which is not seen at this level.
A. Contrasted CT scan of the brain 10 hours after initiating parenteral antibiotics shows a global enlargement of the ventricular system. Note the complete effacement of the basal cisterns.
B. A follow up non-contrasted CT scan of the brain 8 hours after surgical placement of a ventricular drain shows a decrease in ventricular size, reappearance of basal cisterns (arrows heads), and also the disappearance of the left parietal hypodensity suggesting no parietal infarction.

DISCUSSION

Increased intracranial pressure caused by communicating hydrocephalus may be the result of long standing hydrocephalus, increased CSF production, decreased CSF absorption, or tonsillar herniation. Streptococcal infection produces many virulence factors and toxins.[4]

A clinical and epidemiologic study for the last 45 years reported the incidence of GAS meningitis in pediatric population 0.06 cases per 100,000 children per year. The case fatality rate was 43%. Neonatal age and the presence of an associated toxic shock syndrome were identified as risk factors for death. A distant focus of infection was present 36% in the Brazilian case series which were more than half of the patients in the literature. No single virulence determinant could be associated with death.[5]

Literature Search and the Results

We performed PubMed online search for English literature for *Streptococcal pyogenes* meningitis in children 0-17 years and under. We used terms "Group A *Streptococcal* meningitis", "*Streptococcal pyogenes* meningitis", "with and without" and "CNS complications" and "acute and chronic hydrocephalus" with a variable combination. Bibliography of the reports was searched for additional information.

The results of our literature search with CNS complications are shown in Table 1.

Clinical Demography

With the exception of 7 neonates, the mean age for children with CNS complications was 6.1 years. Of 44 children, 30 (68%) children had a known focus of infection. In fourteen (32%) children the focus of infection was unknown

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Case #	Age/ Sex	Infection Focus	Central Nervous System Complication		Year [Reference]
			Acute	Chronic or Outcome	
1	6 d/M	Erysipelas	Seizures	No sequellae	1966[6]
2	8 d/M	Unknown	Seizures	Death	1967[7]
3	13 d/F	Cellulitis of both feet	Focal Seizures	Death	1984[8]
4	14 d/F	Cystic gingival lesion	Seizures,	No sequellae	1983[9]
5	24 d/F	Unknown	Seizures, Brain Abscesses	Death	2000[10]
6	26 d/M	Paronychia	Seizures, Communicating Hydrocephalus	No sequellae	1984[8]
7	28 d/M	Unknown	Seizures and Brain Abscess	No sequellae	2008[11]
8	1 m/F	Unknown	Seizures	Death	1967[7]
9	1 m/F	Unknown	Meningitis and Multiple Brain Abscess	NA[a]	1988[12]
10	1.5 m/M	Otitis Media	Seizures	Severe Motor Deficits	1979[13]
11	NA/NA	Unknown	NA	Hydrocephalus, Porencephalic cyst	1986[14]
12	2 m/M	Tonsillitis	Seizures and Subdural effusions	Moderate Motor Deficit, Cystic Hygroma	1998[15]
13	2 m/NA	Ulcerated and Infected hemangioma	Infantile spasm and Seizures	Encephalomalacia, Infantile spasms,Profound Developmental Delay	2004[16]
14	2.5 m/M	None	Seizures and SIADH	Seizure Disorder, Optic atrophy, Microcephaly, Psychomotor Retardation	1983[9]
15	2.5 m/F	Infected hemangioma	Seizures	Psychomotor Retardation	1987[17]
16	2.5 m/M	Pharyngitis	Focal Seizures	Hearing loss	1988[18]
17	3 m/M	Infected BCG [c]scar	Generalized Seizures	No sequelae	2000[19]
18	3 m/F	Chicken pox	Hydrocephalus	No sequelae	2003[20]
19	7 m/F	None	Seizures	Death	1992[21]
20	11 m/NA	Unknown	NA	Bilateral Subdural Hygroma	1976[22]
21	17 m/M	Otitis media	Generalized Seizure, Brain Abscess	No sequelae	2006[23]
22	18 m/M	Dermal sinus of nose and Otitis Media	Recurrent Meningitis	No sequelae	1976[24]

23	2.5 yr/M	None	Seizures and Increased intracranial pressure	Death	2001[25]
24	3 yr/M	Otitis media	Seizures	Partial blindness, Deafness, Mental Retardation	1984[26]
25	3.5 yr/M	Pharyngitis and Mastoiditis	Cerebral Abscess	Left sensorineural hearing Loss	2012[27]
26	4 yr/M	Otitis media	SIADH	No sequelae	1983[9]
27	4.5 yr/NA	Cochlear implantation	Hearing Loss	Language Delay	2005[28]
28	5 yr/NA	Right Mastoiditis	Right Facial Nerve Palsy	No sequelae	2007[29]
29	6 yr/NA	Unknown	NA	Cranial Nerve IV Palsy	1976[22]
30	6 yr/F	Pharyngitis	Communicating hydrocephalus	No sequelae	Present
31	8 yr/M	Otitis media, Pneumonia	Seizures	Neuropsychological deficit	1981[30]
32	8 yr/M	Sore throat	Seizures	No sequelae	1983[9]
33	8 yr/F	Unknown	Coma	No sequelae	1983[9]
34	8 yr/F	Unknown	(Toxic Shock-Like Syndrome)	Death	1994[31]
35	8 yr/M	Otitis Media, Pharyngitis	Subdural effusion, Hemiparesis, and Seizures	Headaches and Attention Deficit Disorder	2010[32]
36	10 yr/M	Unspecified illness	Brain Abscess	No sequelae (abscess required surgical drainage)	2001[33]
37	11 yr/NA	Multiple Otitis media	Cranial Nerve III Palsy	Cranial Nerve III Palsy, Subdural Hygroma	2001[34]
38	12 yr/F	Pharyngitis, Otitis media	Coma and Hemianopia	Persistent Hemianopia	1983[9]
39	12 yr/F	None	Brain Abscess	No sequelae	1988[35]
40	13 yr/F	Sinusitis	Seizures	Moderate Motor Deficit	1992[36]
41	14 yr/NA	Posttraumatic meningitis	Cerebrospinal fluid leak	Severe Psychomotor Retardation	1990[37]
42	15 yr/M	Occipital Fracture	Cerebrospinal fluid leak	No sequelae	1999[38]
43	15 yr/F	Tonsillitis	Seizures and Cerebral abscess	No sequelae	2010[32]
44	17 yr/M	Pharyngitis, sinusitis	Cavernous Sinus Thrombosis	No sequelae	1999[38]

Table 1: Lists increasing age-based case Reports of central nervous system (CNS) complicationsin children with Group A *Streptococcal* meningitis since 1966 [6-38].

d: days; M: male; F: female; m: month; yr: year ;
aNA, data not available; bSIADH, Syndrome of Inappropriate Anti-Diuretic Hormone;
cBCG, Bacillus Calmette–Guérin

The table is based on the results of our search on PubMed for English literature for children age 17years and under with central nervous system complications caused by *Streptococcal A meningitis*. Our search identified 40 studies with 43 children, excluding the current report (Case # 30). Twenty seven (68%) studies were isolated case reports. Six reports reference number 7, 9, 22, 32, 38 and 8, had 2 cases each. The study number 8 included 6 cases. The children who presented with menigeal manifestations of headache, photophobia, and neck stiffness, but no CNS complications were excluded from this report.

or was not described. Amongst children with known focus, 13 (43%) had otitis media and/or pharyngitis. Tonsillitis, infected hemangioma, cellulitis, or erysipelas, and 1 patient had sore throat. Other minor but significant foci of infection included skull fracture, infected dermal sinus, and mastoiditis.

Central nervous system complication

The most common acute CNS complication secondary to *Streptococcal* meningitis was seizure 24/44 (55%) followed by brain abscess 8/44 (18%). Other acute complications included hydrocephalus, CSF leak, meningitis, cranial nerve palsy and subdural effusion, except one case, the complication was unknown.

Neurological Outcome

Regarding outcome, 18/44 (41%) patients including ours had no sequelae. 10/44 (23%) cases developed a slowing of speech or physical movement with or without a decreased cognitive ability, 3/44 (7%) cases with hearing loss, 2/44 (4.5%) cases with cranial nerve palsy, 2/44 (4.5%) cases developed partial or complete blindness, only 1/44 (2.3%) developed chronic hydrocephalus. In one case the outcome was unknown (See Bar Graph).

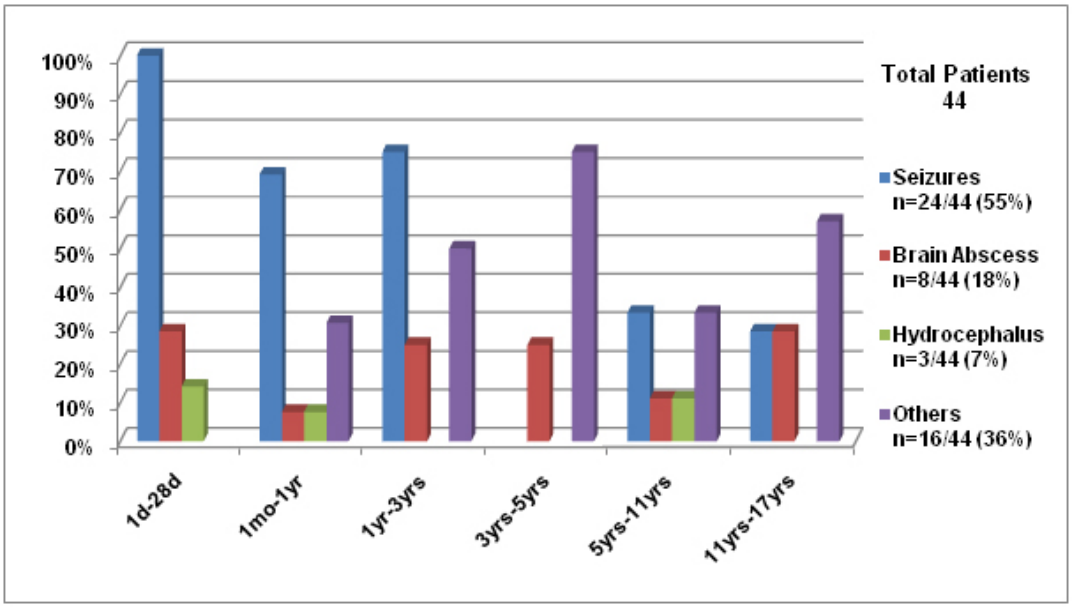
In addition, 7/44 (16%) children died from complications of Group A Streptococcus meningitis, secondary to cardio respiratory insufficiency, Waterhouse Friderichsen syndrome, and Toxic shock-like syndrome. It is unclear why previously healthy children with Group A streptococcus meningitis developed significant CNS complications?

In contrast to our case, two previous cases of acute hydrocephalus were reported during early infancy. Acute onset hydrocephalus in our case was likely due to the combined effect of untreated prolonged pharyngitis, and initial delay in diagnosis and treatment. We suggest that a high CSF protein together with pleocytosis impeded absorption of CSF by arachnoid villi at the superior sagittal sinus. Such functional blockage causing chronic hydrocephalus has been reported in the presence of proteinaceous and cellular debris in CSF[39] and also after intracranial hemorrhage.[40]

Alternatively, the term "communicating hydrocephalus" which could be acute or chronic is defined to mean that the CSF within the ventricles communicating with subarachnoid space CSF. But the CT scan panel A shows CSF within the ventricles and an obliterated subarachnoid space. Arguably, there is no evidence that the ventricles and subarachnoid space are in communication with each other (a broader definition of obstructive hydrocephalus), and therefore, this is not "communicating hydrocephalus". Additionally, hydrocephalus is not caused by increased CSF production or by tonsillar herniation. Instead, in our case, the non-communicating hydrocephalus is caused by ventriculitis resulting in obstruction to the outflow of CSF through the fourth ventricle.

CONCLUSION

Our case illustrates that Group A Streptococcal meningitis induced acute hydrocephalus is rare. A timely instituted surgical intervention may prevent other CNS complication. The review of published cases reveals that central nervous system complications including hydrocephalus are



Bar Graph: The bar graph shows age-based CNS complications of Group A *Streptococcal meningitis* in children age 0-17 years.

Others complications reported were meningitis, subdural effusions, infantile spasms, Syndrome of Inappropriate Antidiuretic Hormone secretion (SIADH), increased intracranial pressure, hearing loss, third and forth cranial nerve palsies, coma, and cavernous sinus thrombosis.
Seizure, the most common CNS complication, occurred between births to 12 months. Hydrocephalus and cerebral abscess occurred between births to 10 years. Cerebrospinal fluid leak exclusively occurred between 10 to17 years of age. There were no reports of intracranial hemorrhage secondary to Group A *w*.

rare. Since prompt antibiotic therapy can minimize risk for acute CNS complications, prompt identification and emergent medical and neurosurgical interventions should be undertaken for an optimum outcome in children with Group A *Streptococcal* meningitis.

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CONFLICTS OF INTEREST

The authors have no financial considerations to disclose or competing interests in relation to this article.

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