Profound Sensorineural Hearing Loss Following Adjuvant Steroid Delay in Pediatric Bacterial Meningitis

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Abstract: Streptococcus pneumonia is a gram positive, polysaccharide-encapsulated diplococcus associated with various pulmonary and extra-pulmonary clinical presentations including invasive diseases such as acute meningitis. It can be associated with high rates of morbidity and mortality in both the pediatric and the adult populations. The introduction of the pneumococcal conjugate vaccine which expanded to cover 13 strains allowed remarkable protection against these invasive infections. In addition, the use of adjuvant corticosteroid therapy in the last few years; in particular dexamethasone, for the management of acute bacterial meningitis reduced the incidence of severe hearing loss in both Hib and other bacterial meningitis. The IDS guidelines recommend administering the first dose of steroids just before or with the start of antibiotics due to its decreased effectiveness with the late presentations of meningitis. We present the case of a 14-year-old female adolescent refugee, with incomplete vaccination status prior to relocating to Lebanon presenting with pneumococcal meningitis. Her hospitalization was complicated by bilateral profound sensorineural hearing loss (SNHL) following a delay in steroid administration. The aim of this article is to highlight the role of vaccines in decreasing morbidity of vaccine-preventable illnesses, and the importance of early administration of steroids as adjuvant to therapy for prevention of neurologic sequeleae.

Keywords: Bacterial Meningitis, Streptococcus Pneumonia, Hearing Loss, Dexamethasone, Vaccines

1. Introduction

Vaccine Preventable Diseases and associated morbidities continue to occur in underserved communities despite availability of vaccinations. [1]

Streptococcus pneumonia – in all its serotypes - is associated with a wide array of clinical presentations, both pulmonary and extra-pulmonary. [2]

Protection against infection with Streptococcus pneumonia was made possible since 2000 by the pneumococcal conjugate vaccine which has been expanded later on to cover 13 strains and was recommended by the center of disease control (CDC) as part of childhood immunization schedule in the United States since 2010. [3, 4] However, there is a delay of almost 15 to 20 years before vaccines distributed in developed countries became available in the developing world, leaving poorer nations vulnerable to the most virulent streptococcal strains. [5]

In addition to PCV 13, Men ACWY and MenB are still not added on the official MOPH list for children older than 11 years. [6]

This gap of vaccination, added to the migration waves of undocumented refugees to Lebanon since 2011 and economic crisis in the last few years have raised concerns to the higher emergence of these infections within refugee camps thus the need to promote better prevention in poorer more vulnerable nations, in order to attain real global prevention. [7-9] Although Adjuvant dexamethasone therapy has no effect on mortality in children; this intervention significantly reduces the incidence of severe hearing loss in both Hib meningitis and non-Hib meningitis. [10]

2. Case Presentation

A previously healthy 14-year-old refugee female presented to RHUH Emergency Department complaining of a one day history of high grade fever reaching 39.5°C, and diffuse pancephalic headache of 8/10 intensity. The patient was at the 75th Percentile for weight and at the 50th percentile for height. She was unable to localize her headache and complained of inability to open her eyes due to photophobia and tiredness. Paracetamol taken every 6 hours did not alleviate her symptoms.

Her symptoms dated back to one week prior to presentation, when she noticed a decrease of her sense of smell associated with flu-like symptoms, consisting of runny nose, fatigue, and fever. The flu like symptoms resolved after 4 days but the anosmia persisted. Two days prior to presentation her headache started with increasing severity over the 24 hours before her ED presentation. In her review of systems there was no nausea or vomiting, no diarrhea, no cough or any new onset rash. Throughout this period the headache was not relieved by taking paracetamol at home which precipitated her presentation to the ED at RHUH for further evaluation.

Her past medical history was unremarkable for any motor delays, speech delays, or other neurological abnormalities.

Her family history is unremarkable. She was on no chronic home medications, and not known to have any food or drug allergies.

Upon arrival to the RHUH ED, her vital signs were as follows: heart rate 90 bpm, BP 10/60 mmHg, Respiratory Rate 23, SpO_2 98% on room air, and body temperature 39.5°C.

She complained of photophobia and persistent headache despite taking analgesics (Paracetamol) 1 hour before presetning. On her Physical exam, she was irritable but oriented to time and place and person. Fundoscopic exam in the ED was not done. Neurologic examination showed 2-mm bilaterally equal and reactive pupils to light, the cranial nerves were intact, there was no abnormal eye movements. Her motor power and spinal reflexes were within normal limits, but due to dizziness she was unable to walk for gait assessment. Neck stiffness was noted on exam as well as moderate maxillary sinus tenderness bilaterally. The rest of her examination was unremarkable.

The initial laboratory results showed significant leucocytosis with a white blood cell count of 23.7 thousand/ul and elevated neutrophils (91%) (ANC was 21567, CRP was unavailable). Rapid Antigen testing came back negative for influenza, and RSV. Covid 19 PCR testing was negative.

Brain CT without contrast was done that showed mucosal thickening of both sphenoidal sinuses with the presence of air bubbles denoting acute sinusitis. There was no mass effect detected or evidence of a bleed. Lumbar puncture was done and CSF results showed 2000 cells/μL WBCs with 85% neutrophils, and protein of 450 mg/dL. Vancomycin 20mg/kg/dose every 12 hours and ceftriaxone 100 mg/kg/day divided every 12 hours were started. Her headache and fever started to improve within 48 hours after antibiotics were started and paracetamol was given to control fever that was spacing and then subsided after 48 hours. The CSF culture grew gram positive cocci after 12 hours of incubation, and the bacteria was identified as Streptococcus pneumoniae sensitive to ceftriaxone. Her fever subsided 24 hours after the start of antibiotics.

On the fifth day of admission to the hospital, the patient noticed that she was unable to hear her parent's conversation in her room, and felt as if her ears were ringing. She was unsteady while walking. Dexamethasone was administered on the fifth day of hospitalization and continued for 10 days in addition to betahistine dihydrochloride and acetyl-leucine for the treatment of vertigo and dizziness. The dizziness improved, however the hearing loss and tinnitus persisted. Repeat CSF tap and culture on the 14th day of hospitalization was sterile. An audiogram done at discharge showed bilateral severe sensorineural hearing loss (SNHL). Based on these findings, a high dose of intra-tympanic steroids was advised by the consulted pediatric otolaryngology service, as well as an ear MRI after the course of steroids to look for the presence of ossifications as an assessment for cochlear implants. After completing her course of antibiotics and a negative CSF culture, the patient was discharged home, but her family did not follow up with ENT, or show interest to continue care at a center near their residence due to socio-economic constraints.

3. Discussion

Bacterial meningitis is caused by severe infection of the membranes (meninges) that line the brain and the spinal cord. Despite advanced antibiotic therapy and critical care it is still associated with great morbidity and mortality rates. [11] The most common causes of bacterial meningitis worldwide in the pediatric age group are Streptococcus pneumonia, Haemophilus influenza (Hi), and Neisseria meningitides. The introduction of the pneumococcal conjugate and Hi type b (Hib) vaccines has decreased remarkably the incidence of the pneumococcal and Hib diseases in the world. [12, 13]

Pneumococcal meningitis is an invasive disease with a mortality rate of 16-37% in adults and with severe neurological sequelae among those who survive (30-52%). In the literature intracranial complications rate in adults were reported to be as high as 74%. [14, 15] The prognosis in children is somewhat better with the exception of the presence of hearing damage in up to 30% of survivors. The risk of neurological sequelae is six times greater in invasive pneumococcal disease when compared to other bacterial meningitis. [14, 16] Authors reported that 20-40% of children had neurological sequelae before the introduction of PCV. [14].

The Global IB-VPD Surveillance Network coordinated by the WHO conducted surveillance data of pediatric meningitis cases from 58 countries. They found that even with the use of

the pneumococcal conjugate vaccines, the most common pathogen identified from these patients was the Pneumococcus. In addition, the majority of the children who died from bacterial meningitis had confirmed Streptococcus pneumonia infections. [12].

The Practice Guidelines for the management of bacterial meningitis recommended by the Infectious Diseases Society of America (IDSA) is to start antibiotics as early as possible. [17, 18] The maximum timeline for the start of antibiotics according to IDSA was 8 hours after considering meningitis as the possible diagnosis and according to several retrospective studies a delay after this chosen cutoff was associated with poorer outcomes. [17, 19-21].

Investigators started to introduce corticosteroids as an adjuvant treatment in acute bacterial meningitis after experimental studies in animals showed that it decreased brain edema, reduced the inflammatory reaction in the cerebrospinal fluid and contributed to an overall better outcome. Moreover, a meta-analysis conducted by Brouwer MC et al. in 2015, which included 25 studies with 4121 participants where 2511 were children, showed the importance of adjunctive corticosteroids in bacterial meningitis on both the morbidity and mortality in all ages. In children, corticosteroids decreased the rate of any hearing loss (RR 0.73, 95% CI 0.61 to 0.86) and severe hearing loss (RR 0.67, 95% CI 0.49 to 0.91), in addition to the short-term neurological damage. A reduction in the rate of any hearing loss was also noticed in adults (RR 0.74, 95% CI 0.56 to 0.98) but with non-significant effects on mortality. In children with pneumococcal meningitis studies showed that after the use of adjunctive dexamethasone, mortality has reduced from 30% to 20%. Moreover, the effects of corticosteroids on the morbidity were noticed by a reduction from 20.4% to 14.6% in hearing loss and from 11.2% to 7.35% reductions in severe hearing loss. [11].

The IDSA recommends the use of dexamethasone in pediatric patients with Haemophilus influenzae type b meningitis, in addition to its use in adults that present with pneumococcal meningitis. According to the IDS guidelines the first dose of dexamethasone must be given just before or with the start of antibiotics because a further delay beyond this cutoff would not improve outcomes. [17, 19] Studies have not shown any benefit of steroids on patients with late presentation of meningitis and its associated complications. In addition, corticosteroids should not be used in patients with septic shock where its administration may be detrimental. [22].

An evidence based summary was done in 2006 by James LR that included databases from the PubMED, the Cochrane library, and the EMBASE, where the results of this review showed the beneficial effects of adjuvant dexamethasone when given just before or with the start of antibiotics in children with meningitis due to Hib and non-Hib pathogens. In addition, the review also showed the effects of dexamethasone in the reduction of severe hearing loss that was also seen in both Hib and other bacterial meningitis [10, 23] (grade A recommendation). [24].

Concerning the type of corticosteroid in bacterial meningitis, dexamethasone was used in the majority of the studies. Dexamethasone is considered to be the corticosteroid of choice due to its longer half-life and better penetrance in the cerebrospinal fluid. [11] To our knowledge there is no clear consensus of the duration of dexamethasone to be administered; however, most studies have used a regimen ranging from 0.4mg/kg to 0.6 mg/kg administered every 6 hours and continued for four days. [10].

In the literature the concern of whether corticosteroids interfere with the eradication of meningeal pathogens by decreasing the blood-brain permeability and, therefore a reduced antibiotic concentration in the subarachnoid space, was suggested. However, two studies conducted in both children and adults showed normal levels of vancomycin in the CSF of patients treated with dexamethasone throughout the repeated lumbar punctures. [11].

A study conducted on the long-term neuropsychological outcomes in children who had pneumococcal meningitis and who were treated with dexamethasone showed a better academic performance compared to those children who were not treated with adjunctive corticosteroids. [25].

Vaccines have been introduced to prevent meningitis caused by the major bacterial pathogens; including Streptococcus pneumonia, Neisseria meningitides, and Haemophilus influenzae type b (Hib) that can result in poor outcomes. [26] The current available pneumococcal conjugate vaccines allow protection against S. pneumoniae serotypes 7, 10, and 13. [27] The global impact of this vaccine was a significant decrease in the incidence of pneumococcal meningitis. [28].

Another important bacterial pathogen causing severe meningitis is the Neisseria meningitidis. [29] This bacteria has been divided into groups based on its surface polysaccharide capsule, and from the 13 capsular groups the ones causing severe infections in humans are the A, B, C, W, X and Y. [30] For many decades polysaccharide-conjugate vaccines have been available against the serogroups A, C, W and Y and have been used as a routine vaccination program globally.

In Lebanon, Men A, C, W, Y is still not listed on the Main Pediatric Immunization Program recommended by the MOPH.

According to the Ministry of Public Health (MOPH) 2022 Meningitis quarterly surveillance report, Strep Pneumo meningitidis is the most frequent of all pathogen in Lebanon (N= 8, with 17.8% of all infections), followed by Neisseria Meningitidis (N=3, 6.7% of all infections), then Hemophilus Influenzae (N=1, 2.2% of all infections), with the majority of meningitis infections reported as neither Bacterial neither Aseptic and reported as Unspecified (N =14, 31.1%). There is no reported Men B infections in Lebanon so far.

Vaccines against Meningitis serotype B, have been developed only recently as a form of protein-based vaccine, MenB (Bexsero, GSK), and were first licensed in Europe in 2013. After Europe's licensure, more than 40 countries

worldwide have approved the MenB vaccine, however only few countries have introduced this vaccine as their national immunization program and it has not yet been implemented in the majority of the developing countries. [31, 32].

The aim of our report is to highlight two public health concerns. First, the importance of vaccination in the eradication of vaccine preventable invasive diseases in children like the streptococcus pneumonia.

Second, to underscore the importance of the use of adjunctive dexamethasone before or with the start of antibiotic therapy in children with acute bacterial meningitis to reduce the complications of meningitis in particular the hearing loss.

4. Conclusion

Pneumococcal infections are still considered a public health concern in developing countries. Vaccination remains the main preventive measure. In addition, Men A, C, W, Y should be listed on the official vaccination lists for children older than 11 year old as part of a two-dose series as recommended by the US CDC, to confer more immunity against bacterial meningitis. Once referred, a patient with suspected streptococcal meningitis dexamethasone needs to be administered with the start of antibiotics to prevent potential hearing impairment. This will reduce morbidity as well as economic and financial burden on families and the health care system.

Abbreviations

SNHL:	SensoriNeural Hearing Loss.
CDC:	Center of Disease Control.
PCV:	Pneumococcal Conjugate Vaccine
Men ACWY:	Meningococcal quadrivalente conjugate vaccine.
MenB:	Serogroup B meningococcal vaccine.
MOPH:	Ministry Of Public Health.
RHUH:	Rafic Hariri University Hospital.
ED:	Emergency Department.
ANC:	Absolute Neutrophils Count.
CRP:	C-Reactive Protein.
RSV:	Respiratory Syncytial Virus.
PCR:	Polymerase Chain Reaction.
CT:	Computed Tomography.
CSF:	Cerebral Spinal Fluid.
WBCs:	White Blood Cells.
MRI:	Magnetic Resonance Imaging.
Hi:	Haemophilus influenza.
Hib:	Haemophilus influenza type b.
IB-VPD:	global Invasive Bacterial Vaccine Preventable Diseases.
WHO:	World Health Organization.
IDSA:	Infectious Diseases Society of America.
RR:	Relative Risk.
CI:	Confidence Interval.

Declarations

Ethics Approval and Consent to Participate

Not applicable.

Availability of Data and Materials

The datasets used during this case presentation are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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