

Case Report

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Recurrent Meningitis Secondary to Cervical Neuroenteric Fistula in an Infant with Klippel Feil Syndrome and Esofage Duplication: A Unique Case Report



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Abstract

We present a patient with recurrent bacterial meningitis due to different gram-negative bacilli as result of a neuroenteric fistula, oesophageal duplication and Klippel-Feil syndrome.

Keywords: Recurrent meningitis; *Clostridium hathewayi*; Neuroenteric fistula; Oesophageal duplication; Klippel-Feil syndrome

Introduction

Recurrent bacterial meningitis (RBM) in children is an uncommon potentially life-threatening infection that is associated with high rates of morbidity and mortality. The clinical presentation in children is frequently nonspecific, thus diagnosis often gets delayed or missed. RBM is usually associated with a predisposing factor such as congenital defects due to cerebrospinal fluid (CSF) leak or spinal defects, and occasionally secondary to immunodeficiencies, including antibody, complement deficiency or hyposplenism, so the major task, is to identify underlying causes of RBM [1]. The differential diagnoses procedure is based on the age of the patient, the type of cultured microorganism and the associated structural problems. The most common bacterial pathogen causing RBM is *Streptococcus pneumoniae* (50%), followed by *Neisseria meningitidis* (25%), *Hemophilus influenzae* (6.9%), *Escherichia coli* (4.2%), *Proteus* spp. (0.9%) the presence of gram-negative bacilli (GNB), should prompt the search for a neuroenteric defect [1,2].

Case Presentation

A 2 month and 15 days old girl was admitted to the Paediatric Intensive Care Unit (PICU) with fever, lethargy, and poor feeding. She was born after an uncomplicated pregnancy and spontaneous vaginal delivery at 38+5 weeks with normal birth weight. Vaccination completed for her age including one dose of pneumococcal vaccine. She previously had been discharged from another hospital on day 21, after a 2-week hospitalization to treat a *Proteus mirabilis* neonatal meningitis, where she received ampicillin and cefotaxime, with complete recovery. On initial assessment, the following features were identified: reduced level of consciousness (response only to painful stimulus); afebrile, normotense, tachycardia (heart rate 190bpm); prolonged capillary refill time (>5seconds peripherally); cold peripheries; tachypnoea (respiratory rate 60) and the arterial oxygen saturation was 96% with room air. The patient looked ill, irritable and had a full anterior fontanelle. The rest of the examination was

unremarkable. After fluid resuscitation and a septic workup, the initial empiric therapy included vancomycin and meropenem after a dose of dexamethasone, because of concern for possible sepsis and meningitis. The hemogram and the C-reactive protein (CRP) were normal and Procalcitonin (ProCT) was 6.71ng/ml (normal values < 0, 5ng/ml). CSF was turbid and showed 740WBC/mm³ with 70% neutrophils, 30% monocytes. CSF protein was 156mg/dl, glucose 35mg/dl (simultaneous blood glucose 80mg/dl) and gram stain did not reveal any findings. Blood culture was sterile.

Culture of her CSF grew *Escherichia coli* susceptible to cefotaxime and amoxicillin-clavulanic acid. After this result became available, vancomycin was suspended. A brain MRI (T1 flair signal) was performed and revealed several areas of leptomeningeal highlight probably attributable to meningitis. It was also performed a barium enema that was normal and a radionuclide cisternogram was negative for CSF leak or sinus tracts via nasopharynx and auditory canals. The results of tests for HIV infection and immunodeficiency workup were negative.



Figure 1: Klippel-Feil anomaly.

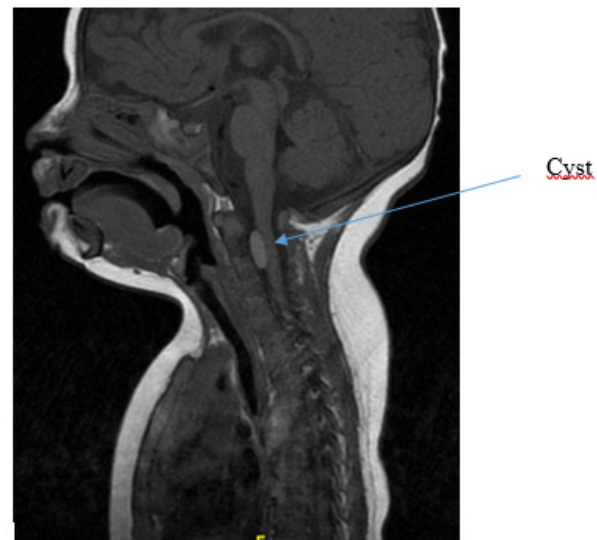


Figure 2: Brain and spinal cord MRI with contrast.

The patient was discharged after a complete treatment of 21 days of meropenem and two control CSF sterile with complete recovery. At 4 months of age, one week after discharge, she was readmitted to the PICU with fever, tachycardia, tachypnoea, lethargic, hypotonic and poor feeding. Laboratory studies showed a normal total white blood cell count with mild predominance of

neutrophils without any immature forms. She had anaemia with 8,3g/dL, haematocrit 25.9%, mean corpuscular volume (MCV) 78.2fL; platelets were 206.000 and CRP was 14.2mg/dl. Blood, CSF, urine and stool samples were collected for bacterial and virological study. CSF was turbid and revealed a leukocyte count of 1.440 WBC/mm³ with 70% neutrophils, glucose level of 8mg/

dl (the serum glucose level was 90mg/dl). Gram's staining of a sample of her CSF showed several gram-negative, rod-shaped bacteria. Empirical antimicrobial therapy was started again with meropenem. The microbiology laboratory informed 24 hours later about the growth in CSF of gram-positive cocci in clusters, and vancomycin was added. *Clostridium hathewayi* susceptible to meropenem, clindamycin, amoxicillin-clavulanic acid and metronidazole grew in blood culture. In addition, in her CSF grew a *Staphylococcus epidermidis*. Brain and spinal cord MRI evidenced a cervical hemivertebrae fusion from C2 to C5 in the context of a Klippel-Feil anomaly (Figure 1); the presence of a

1.4cm cystic intradural and extramedullary mass and a fistulous lesion with a 2.5cm craniocaudal diameter, communicating the C3-vertebral body with the left retropharyngeal space (Figure 2 & 3). The esophagogram confirmed the presence of a tubular mass connecting the retropharyngeal space with the oesophagus (Figure 4). With the diagnosis of neuroenteric cyst, esophagus duplication and Klippel-Feil syndrome, the patient was dismissed with prophylactic treatment with cefibuten until the surgery was scheduled. However, she was re-hospitalized at 7 months of age, with a history of irritability and poor feeding during 5 days, without fever or other symptoms.

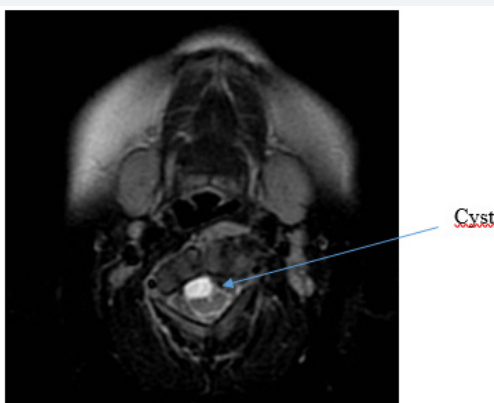


Figure 3: Brain and spinal cord MRI with contrast.

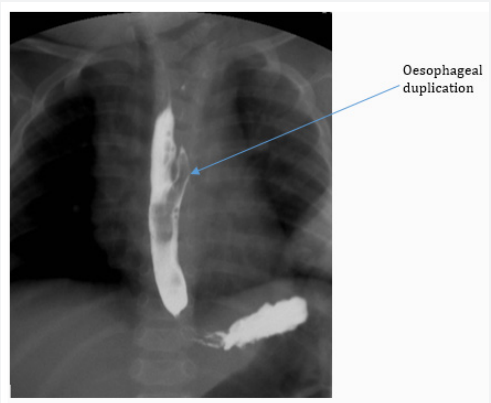


Figure 4: Esophagogastroduodenal study. Oesophageal duplication.

Physical examination revealed an irritable but alert infant with a normal anterior fontanel, hypotonic and somnolent; she was febrile with an axillary temperature of 38.6°C, poorly perfused, respiratory rate of 45 breaths per minute and tachycardia (192bpm), and with normal oxygen saturation. Laboratory testing performed at admission revealed a peripheral WBC count of 14.90cells/mL, with 67.2% segmented neutrophils, 25.2% lymphocytes and 4% monocytes. Measurement of hemoglobin and platelet count, serum electrolytes, creatinine, creatine phosphokinase, and transaminase values were within normal. CRP 1.53mg/dl and Procalcitonin 6.71ng/ml. Lumbar puncture

revealed a turbid CSF with leukocyte count of 8000 WBC/mm³ with absolute neutrophils (98%), no detectable glucose and a protein level of 448mg/dl. Gram's staining of a sample of her CSF showed several gram-negative bacilli and empiric treatment with meropenem was started. In blood and cerebrospinal fluid grew an *Acinetobacter genospecies* susceptible to tigecyclin, imipenem, piperacillin-tazobactam, gentamycin, and amoxicillin-clavulanic acid. Two weeks later, the child underwent a surgical procedure in collaboration by neuro and paediatric surgery teams. The oesophageal duplication was removed through a thoracic approach. The retropharyngeal lesion through a right cervicectomy although

the intradural cystic mass was resected through a laminectomy of the C3 vertebral body. The bone defect was repaired with protesic material to avoid leakage of CSF. Histological examination of the excised tissue showed a cyst covered by ciliated cuboidal cells, similar to respiratory tissue, confirming the diagnosis of Neuroenteric cyst. However, a non-symptomatic CSF collection developed ventrally to the C3-vertebral body. Conservative treatment failed and the collection was finally removed, and CSF leakage closed. Six years after surgery the patient is doing well, asymptomatic without any neurological sequelae and no other episodes of meningitis.

Discussion

RBM is uncommon in children. It has been estimated that 1.3% of all of bacterial meningitis develop recurrences [3]. A recurrence is defined as a new episode occurring at least 3 weeks after CSF sterilization. It may be due to the same or a different microorganism. The type of bacteria isolated can lead to suspicion of the predisposing condition or the possible underlying deficiency. Tebruegge et al. [2] described that 59% of RBM were related to anatomical problems, 36% to immunodeficiencies, and 5% to chronic Para meningeal infections. The 48% of the anatomical problems were cases of traumatic head injury with secondary CSF fistula, followed by inner ear abnormalities (26%) and Neuroenteric cyst (9%). Neuroenteric cyst (NE) is a rare congenital abnormality that develops during the third week of embryonic life, is a foregut duplication cyst that results from failure of separation of ectoderm from the endoderm. It has a variety of clinical presentations depending on size and location [4,5]. There are two major histologic patterns suggesting respiratory or gastrointestinal tract origins. The histology in our patient suggested a respiratory tract origin of the cyst. These cysts generally occur in the spine, like our patient and rarely occur intracranially [6]. Although NE cysts are benign lesions, the natural history of untreated intraspinal NE cysts is unfavorable. The proper treatment of NE cysts is complete surgical removal [7]. Congenital vertebral anomalies are frequently seen in patients with NE, suggesting a common error in embryological development. Klippel-Feil syndrome is a congenital spinal malformation characterized by the failure in segmentation of two or more vertebrae, primarily affecting the cervical spine, accompanied by a spectrum of neurologic anomalies [8]. Vertebral body anomalies, as seen in Klippel-Feil syndrome can be found anywhere from the cervical to the sacral region, indicating a connection between the neural canal and the gastrointestinal system [9]. This congenital anomaly likely results when the embryonic connection between notochord and endoderm fails to reabsorb. Gray et al. [10] describe an association of NE, fistulae and gastrointestinal duplications in 5% of the Klippel-Feil patients.

Our patient had four episodes of bacterial meningitis with different microorganism. This case is unique because of

the anatomical defect and also because of the etiology due to *Clostridium hathewayi*, in our best knowledge this is the first report of disease caused by this microorganism in children. *C. hathewayi* was first reported in 2001 by Steer et al. [11] is an anaerobic, endospore-forming, gram-negative stain rod-shaped bacteria with subterminal, oval-to-round endospores. Its growth in blood cultures has been reported in a few cases in the literature. Elsayed et al. In 2004 described a 27-year-old man with acute cholecystitis, hepatic abscess, and bacteremia [12]; Woo et al. in 2004 causing bacteremia in a 39 old patient with acute appendicitis [13]; Linscott et al. in 2005 reported a septicemia due to *Clostridium hathewayi* and *Campylobacter hominis* [14]. Dababneh et al. in 2014 bacteraemia and surgical site infection after uterine myomectomy in a 42-year-old woman [15], Tena et al. in 2014 a Fournier's gangrene in 73-year-old man [16] and Randazzo in 2015 an acute appendicitis in 60-year-old man [17]. It is possible that *Clostridium hathewayi* only grew in blood culture and not in CSF because of the special needs for its grow and the isolation of *S. epidermidis* as well. We think that *C. hathewayi* was a time pathogen and *S. epidermidis* would be likely contaminated due to the high cell counts in CSF. In summary, the development of RBM due to a variety of microorganism should prompt the investigation of an anatomical defect, particularly a neuroenteric fistula when GNB are involved.

Conflicts of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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Celia Gil L. MD PhD and Belén Joyanes A. MD PhD from department of Pediatric and Arribi A, MD department of Microbiology of Clínico San Carlos Hospital. Madrid. Spain.

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