

Abdominal Neuroblastoma and Early Onset Acinetobacter Septicemia in a Newborn

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ABSTRACT

Background: Neonatal sepsis is a leading cause of mortality and morbidity in the first month of life. The underlying risk factors for early-onset infection (in the first 3 days of life) are prematurity, low birth weight, maternal history of infection, difficult delivery, male gender, twin pregnancy, and congenital malformations. Acinetobacter is a nosocomial infection and rarely caused the early-onset-sepsis and meningitis. The most common neonatal tumor is neuroblastoma; however, it is not defined as a risk factor for early-onset sepsis.

Case report: A 13-day-old newborn female was referred to our hospital due to ventriculitis, persistent meningitis, and an abdominal mass. She was a term neonate delivered by cesarean section from a mother with a nearly normal pregnancy with no complications, such as chorioamnionitis, prolonged rupture of membrane, urinary tract infection, preeclampsia, and diabetes.

A fetal abdominal mass was detected on the left kidney in prenatal sonography. The patient was admitted to the Neonatal Intensive Care Unit in the first minutes of life because of respiratory distress and cyanosis. Subsequently, mechanical ventilation, endotracheal surfactant instillation, and antibiotic therapy were prescribed.

Due to the deterioration of the general condition, fever, seizure, and hematuria on the third day, sepsis workup and changing the antibiotics were performed. Blood culture and cerebrospinal fluid (CSF) were positive for Acinetobacter baumannii. Persistent positive CSF culture led to the diagnosis of ventriculitis which was confirmed by brain computed tomography scan (CTS) and ventricular tap. The condition of the patient got better after intraventricular amikacin injection in addition to intravenous colistin and piperacillin.

Postnatal sonography and CTS confirmed the abdominal neuroblastoma. Chemotherapy was initiated after the complete treatment of sepsis, meningitis, and ventriculitis. This case report presents a term and female neonate with early-onset neonatal sepsis and meningitis, caused by an unusual microorganism, and a prenatal history of abdominal neuroblastoma.

Conclusion: By this case report, the clinicians are suggested to consider the Acinetobacter baumannii as the cause of fulminant sepsis and meningitis in a term neonate with no underlying risk factors for infection.

Keywords: Meningitis, Neonatal Sepsis, Neuroblastoma, Ventriculitis

Introduction

Neonatal sepsis is a leading cause of mortality and morbidity in the first month of life (1). One of the most common indications of admission in neonatal wards and Neonatal Intensive Care Units (NICUs) is early-onset (on the first 3 days of life) or late-onset sepsis (>72 hours) (2). Early-

onset sepsis (EOS) is reported in 1.9-5.1% of the term and 5-21% of the preterm infants (3).

However, prematurity and low birth weights are the most important risk factors for neonatal sepsis and meningitis, even term neonates are vulnerable to microbial invasion and its

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complications (4). Other maternal and neonatal predisposing factors for early-onset infections are maternal infections during pregnancy, such as urinary tract infection, chorioamnionitis, prolonged (>24hour) rupture of membranes (PROM) (5), as well as intrapartum unwanted events, including difficult and prolonged delivery, intrapartum usage of forceps or vacuum, neonatal asphyxia, male gender, twin pregnancy, and congenital malformations (6). The most common responsible microbial pattern for EOS is streptococci group B (GBS), *Escherichia coli* (7), and *Listeria monocytogenes*; however, the less common pathogens include Coagulase-negative staphylococci, *Klebsiella*, *Pseudomonas aeruginosa*, *Haemophilus influenzae*, and *Acinetobacter* (8). Regarding the changing of microbial patterns in neonatal nursery and NICUs in recent years, less frequent bacterial pathogens in the past are more common recently.

Acinetobacter is an aerobic Gram-negative bacillus, which commonly isolated from the hospital environment and is a kind of nosocomial infection. This microbe has more than 50 species, and *baumannii* is the most common subtype species with a tendency to live in a watery environment (9). Some recently published articles reported a higher incidence of early-onset *Acinetobacter* infection more than the late-onset ones (10).

Considering that the *Acinetobacter* infection is nosocomial, the underlying risk factor for this infection, such as carbapenem and ampicillin use, central venous catheter usage, and total parenteral nutrition are introduced by some studies (11). *Acinetobacter* meningitis may occur following a traumatic head injury, metastatic infection during bacteremia of the patients, and neurosurgery (12).

In some studies, the probability of early-onset neonatal sepsis with this pathogen is reported as high as 32% (10) and in some published studies, the incidence of *Acinetobacter* EOS and meningitis is estimated at 13% (13).

Brain hypoperfusion, transient hypoxia, or metabolic acidosis concurrent with neonatal infections, are the predisposing factors for neurologic complications, such as seizure, ventriculitis, arachnoiditis, hydrocephalus, and subdural empyema (14). Meningitis with septicemia increases the probability of these neurologic complications.

Ventriculitis refers to the inflammation of the lining of the ventricles and ventricular fluid which may be associated with obstruction to cerebrospinal fluid flow and hydrocephaly.

Ventriculitis is a common complication of neonatal meningitis occurring in up to 20% of the cases (15). The diagnosis of ventriculitis was considered in persistence meningitis despite the appropriate antibiotic regimen and confirmed with neuroimaging and/or ventricular tap.

The most common tumor in neonatal period is neuroblastoma with an incidence of 0.61 per 100,000 live births, and almost 28-39% of all malignancy in the first month of life is related to this malignancy (16). The most common site of presentation in neonatal neuroblastoma is an adrenal gland (90%) (17). The prenatal detection of neuroblastoma is reported as high as 80-85% (18). In post-natal periods, neonatal neuroblastoma can be completely asymptomatic and the diagnosis of neonatal and infantile neuroblastoma may be incidental in the evaluations of some other problems in the patient (19). Regarding that neonatal sepsis has some mentioned underlying risk factors, such as prematurity and low birth weight, maternal chorioamnionitis, and PROM, birth asphyxia (4) neuroblastoma is not defined as a risk factor for neonatal sepsis. Although sepsis is considered a consequence of the admission of neonates with neuroblastoma in the NICU, it can be detected as a nosocomial infection followed by neonatal manipulations, such as surgery, catheterizations, blood sampling, and other procedures. However, there are some case reports in congenital neuroblastoma mimicking early-onset neonatal sepsis (20).

In this presentation, we report a term female neonate with a prenatal diagnosis of abdominal mass and fulminant bacteremia and meningitis with *Acinetobacter* and ventriculitis as a complication of this infection.

Case report

A 13-day-old female newborn was referred to Mofid Children's Hospital, Tehran, Iran, due to surgical interventions for ventriculitis, persistent meningitis, and an abdominal mass. She was born in the 38 weeks (+5day) of gestation with a birth weight of 3000 g from a 30-year-old, gravid 2, live 2, and abort 0 mother and a 37-year-old father which suffering from congenital spherocytosis. The parents did not have consanguinity. The first sibling is a 4-year-old healthy male.

The mother had a nearly normal pregnancy with no complications, such as chorioamnionitis, PROM, urinary tract infection, preeclampsia, and diabetes although a prenatal history of polyhydramnios with no needs for any special medication or intervention was reported. The

delivery mode was a cesarean section at Imam Hussein Hospital affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran. In prenatal ultrasonography, an abdominal mass was detected on the left kidney.

The newborn was admitted to the NICU of his maternity hospital during the first minutes of life due to respiratory distress and cyanosis. The first laboratory tests consisted of White blood cell (WBC):8000 per microliter, Polymorph nuclear (PMN):32.5%, Lymphocyte (LYM):58%, Hemoglobin 16.1g/dl and Hematocrit:48.5%, Platelet: 252000 per microliter, C reactive protein (CRP):1mg/dl, Blood culture: negative.

Due to severe respiratory distress and respiratory failure in the patient, mechanical ventilation, endotracheal surfactant instillation, and antibiotic therapy (ampicillin and amikacin) were prescribed for the treatment of congenital pneumonia, primary pulmonary hypertension, and neonatal sepsis. Given that, hyaline membrane disease was the other differential diagnosis of respiratory failure of the patient at the first h of life, the prescription of endotracheal surfactant seemed logical.

Unfortunately, due to the deterioration of the general condition, fever, seizure, and hematuria on the third day of admission, sepsis workup consisted of taking blood culture and lumbar puncture (LP) and urine culture was re-ordered, and the antibiotic regimen was changed empirically to meropenem and vancomycin. Laboratory finding in this time was WBC: 3700 per microliter, PMN:59.5%, LYM:36.8%, Hemoglobin:10.8 g/dl and Hematocrit:30%, Platelet: 125000 per microliter, CRP: 43mg/dl, and positive blood culture for *Acinetobacter*.

In the LP, the results were WBC: 4800 per microliter, PMN:30%, LYM: 70%, Red blood cell: 1600 per mm³, Protein: 277mg/dl, Sugar:5 mg/dl, Cerebrospinalfluid culture (CSF): *Acinetobacter Baumannii*, similar to blood culture.

Seizures were controlled by phenobarbital injection. Regarding that the first blood culture was sterile and after 2 days of hospital stay, the next one was positive, the nosocomial infection was considered for the diagnosis of the patient. Moreover, because of the persistent fever in the neonate and the result of the antibiogram, the antibiotic regimen was changed again to ampiculbactam and colistin. Unfortunately, with the persistent positive CSF culture despite appropriate antibiotic regimen with an impression of ventriculitis, the patient was referred to our hospital for surgical interventions.



Figure 1. Bilateral Ventriculomegaly

Figures 1-3 illustrate the brain CTS and magnetic resonance image results of the patient.

In our hospital, the extra ventricular device shunt was inserted by a pediatric neurosurgeon for eradicating the intraventricular infection and intraventricular amikacin injection for 4 weeks. In addition to the systemic intravenous antibiotic injection with colistin, meropenem and ampiculbactam were continued for 5 weeks.

Fortunately, the normal CSF analysis, negative blood, and CSF cultures in concurrence with the improvement of the neonatal condition confirmed the good response of the patient to medical and surgical modalities. Regarding lack of prenatal and intrapartum risk factors for early-onset neonatal sepsis in a term female neonate, such as PROM,



Figure 2. White Arrow: Ventricular dilation with debris in the dependent part of the lateral ventricle.
Orange Arrow: Diffuse Hypodensity in the periventricular area and white matter

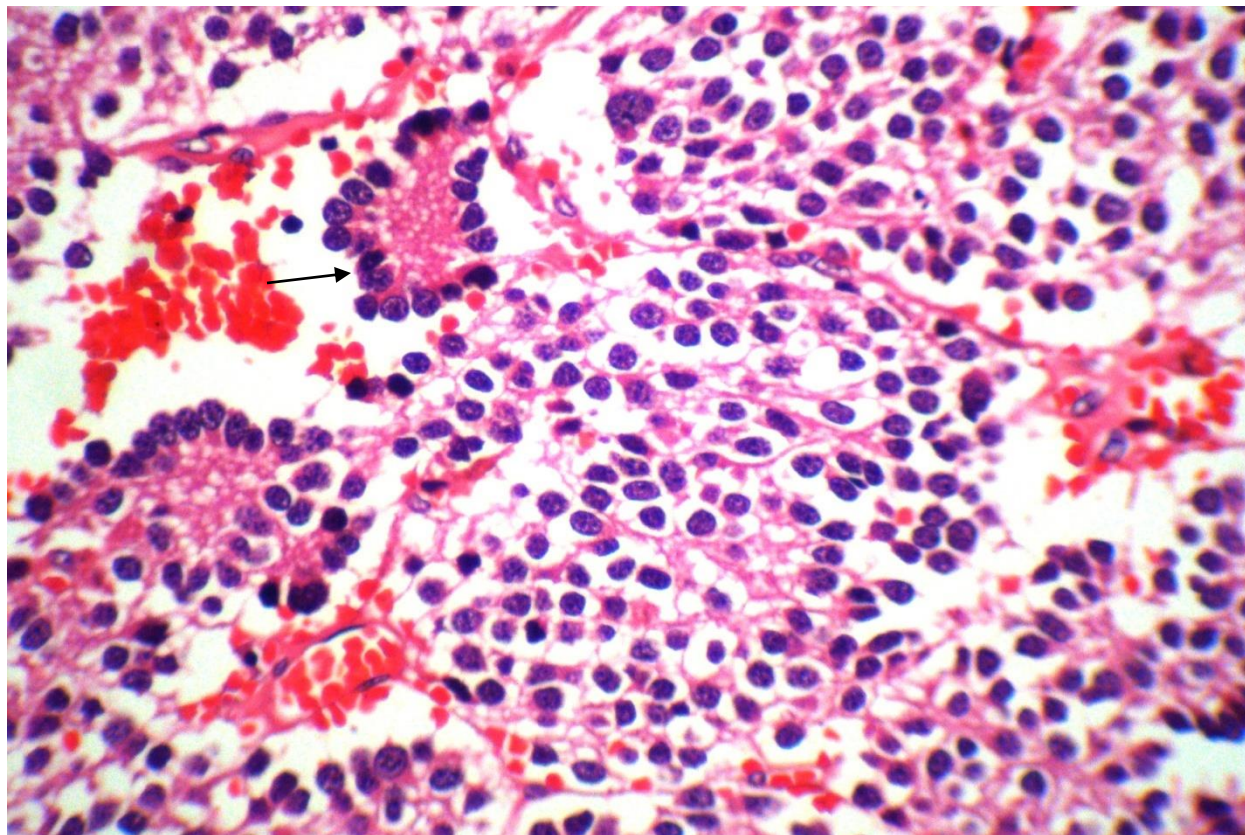


Figure 3. A poorly differentiated neuroblastoma with rosettes, less than 5% ganglion cell differentiation, and low mitotic karyorrhectic index (Hematoxylin and Eosin×200).

maternal chorioamnionitis, and other infections, concurrence with early-onset isolation of an unusual microorganism in the blood and CSF of the patient, assessment of underlying congenital immunodeficiency disorders was performed. However, no specific immunodeficiency syndromes were detected. As mentioned before, in prenatal ultrasonography of the mother, an abdominal mass was detected. In postnatal ultrasonography, a round echogenic mass with a size of 30×33 mm in the left upper pole of the left kidney or left adrenal gland with a suggestion of neuroblastoma was detected. In abdominal CTS, the diagnosis of neuroblastoma was confirmed. Figure 2 illustrates the abdominal CTS of the patients.

Urine vanilylmandelic acid and hemophilic acid were in the normal range. Bone marrow aspiration was reported normal and negative for N-MYC amplification.

After the end of antibiotic treatment courses, surgery for left side adrenalectomy was performed by a pediatric surgeon at the age of 40-day-old. Pathologic evaluation of the excised abdominal mass revealed a partly encapsulated, brown, and ovoid solid mass with homogenous

brown cut surfaces and a dimension of 3×3×2 cm. Microscopic examination showed a poorly differentiated neuroblastoma attached to the adrenal gland with a moderate amount of neuropil, several rosettes, less than 5% ganglion cell differentiation, low mitotic karyorrhectic index (<100 per 5000 cells;< 2%), as well as foci of calcification, and extensive hemorrhage with hemosiderin deposition (Figure 3).

Eventually, the infant was transferred to the hematology and oncology sections of the hospital for chemotherapy under the supervision of a qualified pediatric oncologist.

Discussion

In this case report, we presented a term female neonate with abdominal neuroblastoma and early onset fulminant septicemia, congenital pneumonia, meningitis, and ventriculitis with *Acinetobacter baumannii*. The patient was admitted to the NICU at the first minutes of life because of respiratory distress and cyanosis.

Regarding the well-known correlation between early-onset neonatal infections with underlying maternal or neonatal risk factors, we found no

obvious predisposing risk factors for this fulminant EOS and meningitis with an unusual microbe.

Moreover, concerning a high association of late-onset sepsis with meningitis in neonatal periods, the concurrence of meningitis with EOS is an uncommon event (21). Given that the most common microbial etiology of EOS and meningitis are Gram-positive bacteria (22), some recently published articles indicated the changes in the microbial pattern of neonatal infections. In a study conducted by Utpala Devi on bacterial etiologies of neonatal meningitis, Gram-negative bacteria were the predominant cause of this infection in 48% of the patients, compared to Gram-positive ones that were detected in 39% of the cases.

The most frequent Gram-negative bacteria detected in the aforementioned study were *Acinetobacter baumannii* (18%), *Klebsiella* (12%), and *Pseudomonas* (9%) (23). *Neisseria meningitidis* and *E. coli*, *Serratia*, *Cronobacter sakazakii*, and *Roseomonas* were detected with lower incidence (25). In another study performed by Boscabadi, the incidence of *Acinetobacter* infection was estimated at 17% (24).

In a 10-year retrospective review by Melese Abate Reta on neonatal bacterial meningitis, the prevalence of *Acinetobacter* meningitis was reported 13%, and all cases in this study had early-onset initiation and low birth weight < 2500 g (14).

Considering that *Acinetobacter* is a naturally nosocomial infection, on the other hand, the low incidence of early-onset neonatal meningitis with *Acinetobacter*, it seems that the presence of additive predisposing factors besides the common factors is necessary. In a case report by Adil Fouad et al, the two patients with ruptured meningomyelocele were introduced with *Acinetobacter* meningitis. Both cases had imipenem resistance *Acinetobacter*, and colistin was prescribed for treatment after the surgery of their lumbosacral lesion (25). Our patient had no detectable risk factor for this devastating infection.

Ventriculitis is a less common consequence of meningitis; however, the incidence of this complication is more in neonatal periods, compared to older ages. In this case report, no response to broad-spectrum antibiotic therapy led to consider this diagnosis. The definitive diagnosis of ventriculitis was obtained by the presence of WBC and bacteria in the sample of the intraventricular tap. In a study carried out by Shih-Ming Chu on neurologic complications of

neonatal infections, in 1037 bacteremia episodes, 36 (3.5%) patients had the involvement of neurologic systems. The most common microorganisms were GBS and *E. coli* in 41.7% and 16.7% of the patients, respectively. The rate of meningitis and ventriculitis in patients with neurologic dysfunctions was estimated at 66.7%. Moreover, the incidence of neurologic complications in late preterm (gestational age 33-36 weeks) and term infants with early-onset initiation of the disease was more than the others. Ventriculitis was reported in 22.8% of the patients (14).

The presence of neuroblastoma as an underlying risk factor for EOS, meningitis, and ventriculitis is not specified. In a literature review for the accompaniment of these two disorders in neonatal periods, there was no correlation or association between them. This concurrency may be an incidental finding; however, a kind of impairment in the immune system due to congenital and prenatal neuroblastoma can be suggested for the susceptibility to this grave neonatal infection. Probably, the common environmental or genetic risk factors will be known for these two disorders in the future.

Conclusion

By this case report, the clinicians are suggested to consider the *Acinetobacter baumannii* as the cause of fulminant sepsis and meningitis in a term neonate with no underlying risk factors for infection.

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Conflicts of interest

The authors have no conflicts of interest regarding the publication of the study.

Author contribution

Dr. Nouripour and Dr. Fallahi determined the conception or design of the case report. Dr. Kazemian and Dr. Alizadeh performed the acquisition, or interpretation of the data. Dr. Fallahi, Dr. Taslimi, and Dr. Radfar drafted and revised the study critically for important intellectual content. Dr. Fallahi approved the final version of the study to be published.

Dr. Nouripour and Dr. Fallahi investigated and resolved the agreement to be accountable for all aspects of the study in ensuring that questions

related to the accuracy or integrity of any part of the work are appropriate.

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Ethical Consideration

This case report includes no personal information that could lead to the identification of the patient.

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