Spinal cord and medullary infarction due to E. coli meningitis in neonates: experience from a Canadian tertiary hospital

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INTRODUCTION

Neonates are particularly susceptible to developing meningitis, with an incidence of culture proven meningitis estimated to be 0.3 per 1000 live births.[1] Meningitis is associated with high mortality and morbidity, and although mortality rates have declined over the last few decades, morbidity remains unchanged.[2] The most frequent source of pathogens causing meningitis is via hematogenous dissemination from primary bacteremia.[3] After group B streptococcus, *Escherichia coli* (*E. coli*) is the next most common pathogen isolated in about one-third of all early onset infections, and is the most common pathogen isolated among preterm and very low birth weight (VLBW) infants.[4–6] Clinical signs are often non-specific, ranging from lethargy to seizures.[3] Neurologic complications of neonatal bacterial meningitis include arachnoiditis, ventriculitis, vasculitis and focal infarcts but intraparenchymal abscesses and large infarcts are less common,[7] with rare reports of spinal cord infarction.[8–10] Following an index case of extensive spinal cord and caudal medullary infarction, we undertook a review of spine magnetic resonance (MR) images of all neonates with proven *E. coli* sepsis or meningitis at our institution in order to characterize the pattern of MR imaging findings, correlate these with outcomes and generate hypotheses regarding the mechanisms of spinal cord infarction.

MATERIAL & METHODS

Patient population

We performed a retrospective review of all neonates who had *E. coli* meningitis and who had undergone MR imaging of the brain and/or spine at the Hospital for Sick Children, from January 1991 to May 2021. Neonates were identified utilizing a natural language processing (NLP) based radiology text search program (Bialogics DxPro™), utilizing the terms *E.coli* sepsis and *E.coli* meningitis (figure 1). Inclusion criteria were a) proven *E.coli* sepsis and/or *E.coli* meningitis; b) onset of illness in the neonatal period (birth to 28 days of life); and c) MRI brain and spine performed within 4 weeks of illness (at minimum showing the cervical spine). Exclusion criteria were image degradation by artifacts and incomplete image acquisition. Patient demographics, clinical data at presentation, relevant laboratory results, and clinical course were collected from the hospital electronic medical records.

Image interpretation

The MR images were analyzed and co-read in consensus by 3 of the authors (A.B, H.B and S.B). The spinal cord was assessed for the presence of swelling or abnormal signal. Spinal cord and medullary infarction were diagnosed if there was a) restricted diffusion; or b) cavitation on follow up MRI. Tumefactive swelling of the caudal medulla and cervicomedullary junction was diagnosed if there was *"tumor-like"* swelling of these regions. The presence or absence of other features of CNS infection such as ventriculitis, empyema, hydrocephalus, cerebritis, perforator and cortical infarcts, and hemorrhage was also noted.. Imaging findings were correlated with autopsy results if available.

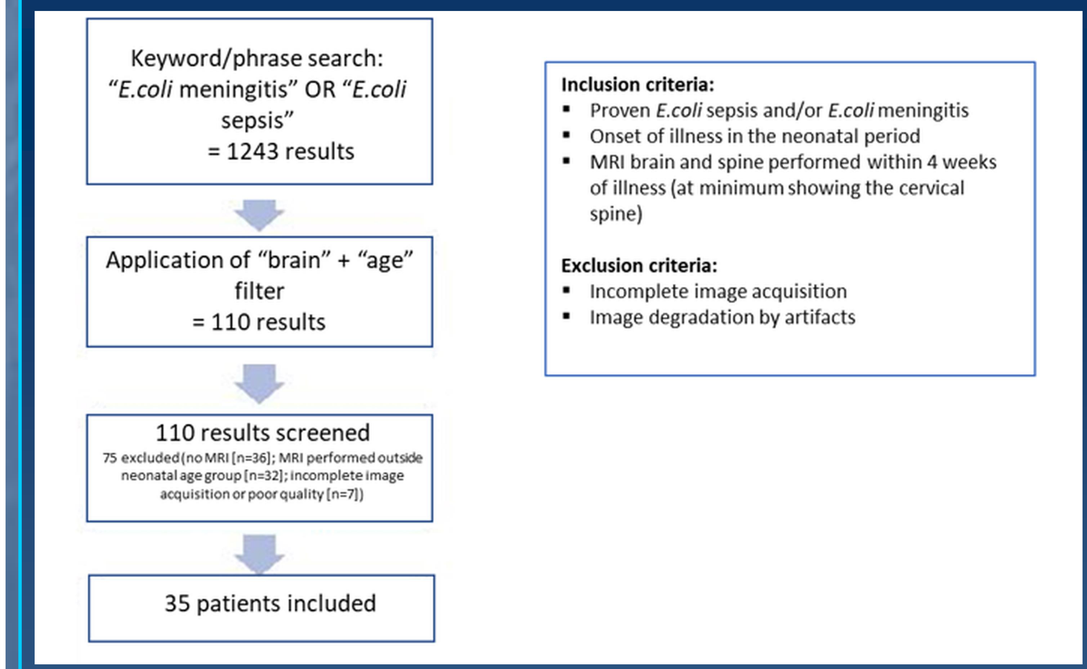

Figure 1: Identification of cases using natural language processing (NLP) based radiology text search program (Bialogics DxPro™)

RESULTS

- A total of 35 neonates met the inclusion criteria (figure 1).
- Twelve were born at full term gestational age (GA) and 23 were preterm (GA 32-37 weeks, n=9; 28-32 weeks, n=7; <28 weeks, n=7).

Group A: Neonates with spinal cord infarction

➢5/35 (14.3%)

Imaging findings:
- Holocord infarction in 3/5 (60%); cervical cord infarction in 2/5 (40%)
- Caudal medulla and CMJ involvement in 5/5 (100%)
- Tumefactive swelling and infarction in 4/5 (80%)
- Abnormal brain MRI in 5/5 (100%)

Clinical presentation and course:
- High cervical myelopathy/brainstem dysfunction in 4/5 (80%)
- Inotropic support in 5/5 (100%); unable to wean in 3/5 (60%)
- Intubation and mechanical ventilation in 5/5 (100%); unable to wean in 5/5 (100%)

Outcome:
- Death in 5/5 (100%)

Group B: Neonates without spinal cord infarction

➢30/35 (85.7%)

Clinical presentation and course:
- High cervical myelopathy/brainstem dysfunction in 0/30
- Inotropic support in 6/30 (20%); 100% weaned off
- Intubation in 22/30 (73.3%); 90.9% successfully weaned off

Outcome:
- Death in 2/30 (6.7%)

Parameter	Group A	Group B
Number	5/35 (14.3%)	30/35 (85.7%)
Ventilator	5/5 (100%)	22/30 (73.3%)
Ventilator dependent	5/5 (100%)	2/30 (6.7%)
Inotrope requirement	5/5 (100%)	6/30 (20%)
Inotrope dependent	3/5 (60%)	0/30
Death	5/5 (100%)	2/30 (6.7%)

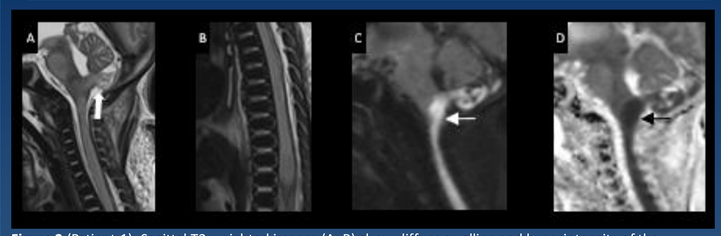

Figure 2 (Patient 1): Sagittal T2 weighted images (A, B) show diffuse swelling and hyperintensity of the medulla and spinal cord. Sagittal DWI and ADC (C, D) images show medullary and cervical spinal cord infarction. Debris extrudes into the infravermian cistern (arrowhead, A). Note tumefactive swelling of the cervicomedullary junction (arrows, C and D).

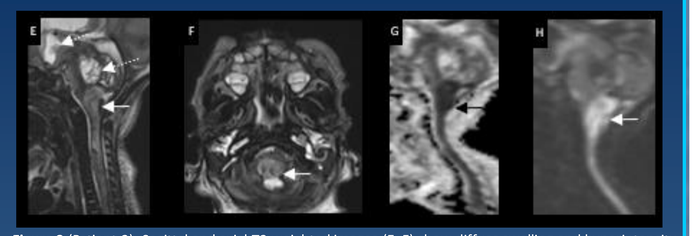

Figure 3 (Patient 2): Sagittal and axial T2 weighted images (E, F) show diffuse swelling and hyperintensity of the medulla, cervical and thoracic spinal cord; and extensive debris in the 3rd and 4th ventricles (dotted arrows in E) Sagittal DWI and ADC (G, H) images show medullary and spinal cord infarction. Note "tumefactive" swelling of the cervicomedullary junction (arrows, E-H).

DISCUSSION

Few case reports and series have described spinal cord infarction occurring in the context of E.coli meningitis.[8-10] This single institute study demonstrates imaging findings of neonates with E.coli meningitis and cord/medullary infarction, and compare outcomes between infarction and non-infarction groups.

Possible mechanisms of spinal cord infarction in our series include: a) hypoperfusion from septic shock or from involvement of brainstem regulatory centers; b) arachnoiditis with complicating vasculitis; c) vascular thrombosis as a result of disseminated intravascular coagulation (DIC); d) direct involvement of the spinal cord (bacterial myelitis); or e) a combination of these factors.

The peculiar feature seen in 4 out of 5 cases in our series was the tumefactive swelling and restricted diffusion of the caudal medulla and cervicomedullary junction (figures 1 and 2) The medulla contains a number of structures vital to the central regulation of respiration and blood pressure such as the ventral and dorsal regulatory groups (which include the pre-Bötzinger complex and the nucleus tractus solitarius), the chemosensitive center and the vasomotor center. Furthermore, an intact cervical and upper thoracic cord is needed for maintenance of normal sympathetic tone, which in turn is responsible for maintaining adequate blood pressure. In two cases, lack of spontaneous respiratory drive was possibly explained by the presence of medullary infarction. Whether upper cervical cord and lower medullary involvement in these patients also contributed to dysautonomia and resultant low blood pressure is uncertain. Nevertheless, given the severity of disease course, the need for continued inotropic support, and high mortality, a central cause for the poor cardiorespiratory drive occurring due to involvement of regulatory centers in the medulla and upper cervical spinal cord may warrant consideration.

CONCLUSION

Spinal cord and medullary infarction are a lethal complication of E.coli meningitis. Diffusion weighted imaging is invaluable in making the diagnosis. Possible mechanisms for infarction include hypoperfusion due to shock, with medullary infarction resulting in poor respiratory drive and vasomotor tone also potentially contributing to the pathogenesis and overall mortality in these cases. The presence of high cervical myelopathy and/or brainstem dysfunction, inotropic and ventilator dependence may predict the presence of infarction, and MR imaging of the spine is advisable in these patients.

LIMITATIONS OF THE STUDY

Retrospective study- therefore dedicated imaging of the whole spine was not available in all cases. Smaller cord infarcts, especially in the thoracic and lumbar levels may have been missed. Diffusion imaging parameters were not standardized, especially as images were acquired over a 30-year period utilizing various MRI scanners with differing capabilities.

DISCLOSURES: None

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