OMCR

Oxford Medical Case Reports, 2021;1,4–7

doi: 10.1093/omcr/omaa120
Case Report

CASE REPORT

Seizure activity and anion gap metabolic acidosis secondary to adverse effect of nalidixic acid—a case report

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Abstract

Nalidixic acid is a commonly prescribed treatment for suspected dysentery in Middle Eastern populations. We describe a case of convulsions resulting from a single dose of nalidixic acid in a previously healthy two-month-old child in Northern Iraq who was being treated for a diarrhoeal illness. The child presented to us with new onset seizures, irritability, and acidaemia. Nalidixic acid was thought to be responsible after the exclusion of other potential causes of seizures. Symptoms resolved by treatment with intravenous (IV) diazepam, and cessation of nalidixic acid, and the child recovered fully and was discharged home neurologically intact after two days of observation. In regions where it is commonly prescribed, such as Northern Iraq, nalidixic acid should be considered as a cause of convulsions in any seizing child who has been exposed to the drug. Furthermore, quinolones such as nalidixic acid are contraindicated in children < 3 months of age.

INTRODUCTION

A 2-month-old boy presented to our Emergency Room (ER) with convulsions and abnormal cry. His mother also noticed apnoeic episodes prior to arrival. The infant had a history of 3 days of non-bloody diarrhoea. No vomiting, fever, rash, coughing or respiratory distress were reported. The child was exclusively breastfed and had been feeding well prior to his illness. He had been seen by a community healthcare practitioner who prescribed simethicone, and nalidixic acid 55 mg/kg/day, and was administered one dose of each drug that morning ~2 hours before presentation. The nalidixic acid was in the form of a 250 mg/5 ml suspension for oral use. His mother reported that she followed the dosing instructions and did not administer any extra of either drug, although it was unclear what exact dose she gave as she did not have the dosage spoon with her. An overdose of nalidixic acid was certainly possible if the full 55 mg/kg/day was given in a single dose, as it is typically recommended to be administered in four equally divided doses.

Of note, in our Humanitarian and Resource-Limited Setting (HRLS) in post-conflict Northern Iraq, primary healthcare is limited, and the gap has been filled by practitioners who may be operating outside their usual scope of practice. Inappropriate drug prescription is a common occurrence, and children may be prescribed antibiotics empirically for what in most cases is viral gastroenteritis.

PATIENT INFORMATION

The infant was born at full term by uncomplicated vaginal delivery 2 months previously at our hospital. He had been developing

Received: June 4, 2020; **Revised:** August 29, 2020; **Accepted:** October 14, 2020

- Heart rate 156 bpm
- Respiratory rate 51 rpm
- O_2 saturations 99 %
- Temperature 36.6°C
- Height 57 cm
- Weight 4.5 kg
- Capillary glucose 132 mg/dl (7.3 mmol/L)

Figure 1: Vital signs upon presentation.

normally since birth. There was no known family history of seizure disorders, and no maternal illnesses or congenitally transmitted infections were reported during the pregnancy.

CLINICAL FINDINGS

The child's weight and vital signs upon arrival are presented in Fig. 1.

Initial assessment revealed a well-developed but mildly dehydrated infant with abnormal cry. His anterior fontanelle had subtle bulging. He had tachypnoea and efforts suggestive of acidotic breathing, and he was making sounds that resembled grunting. The child was not responding appropriately to stimulation, and his gaze was deviated to the left. His pupils were 1 mm and sluggish. He had some repetitive puckering of his lips, plus rhythmic jerking motions of his right arm and leg, similar to those seen earlier by his mother. All four limbs appeared to periodically stiffen. IV diazepam 0.2 mg/kg was administered, which quickly aborted the suspected seizure. An hour later, the convulsions recurred, and he received another 0.2 mg/kg dose of diazepam, again effectively terminating the seizure.

DIAGNOSTIC ASSESSMENT

The child's laboratory results (taken on initial assessment) are shown in Fig. 2. Differential diagnosis considered at the time is shown in Fig. 3 [1].

THERAPEUTIC INTERVENTION

Therapeutic approach included supportive care and cessation of nalidixic acid. Due to his high white cell count, the child received empiric IV ceftriaxone 100 mg/kg initially until we could rule out meningoencephalitis as the cause of seizures. He also received IV hydration during his post-ictal phase, and later oral zinc for his diarrhoea. The child was discharged home neurologically intact after remaining seizure-free during his 48 hours of observation on the paediatric ward.

DISCUSSION

Venous blood gas (VBG) revealed an overall acidaemia from mixed anion- and non-anion gap metabolic acidosis, plus an element of respiratory alkalosis. We did not have a lactic acid assay available so we were unable to assess its contributions to the anion gap. Note that nalidixic acid, through its interference with lactate metabolism, is a recognized cause of anion gap metabolic acidosis [2]. Presumably, the non-anion gap acidosis component of the VBG was from bicarbonate loss in diarrhoea.

Nalidixic acid is a bactericidal antimicrobial of the synthetic quinolone class, and its use is contraindicated in children <3 months old. It is known to lower the seizure threshold in patients with predisposition to seizures [3].

Nalidixic acid has been traditionally used in the treatment of urinary tract infections (UTI) and shigellosis. The recommended therapeutic dose for children is 55 mg/kg/day in four equally divided doses [3].

Prescription of quinolones is declining worldwide due to safety concerns [4], along with increasing antimicrobial resistance [5]. However, nalidixic acid is still seen in some resource-limited settings.

Case reports exist of seizures and acidosis from nalidixic acid at therapeutic dose and in overdose [6, 7]. Idiopathic intracranial hypertension (IIH) has also been reported from therapeutic doses of nalidixic acid [8], and it is listed as a potential adverse effect by its manufacturers [4].

Idiopathic intracranial hypertension is a rare neurological disorder in children characterized by raised intracranial pressure in the absence of hydrocephalus, structural or vascular malformations, or brain parenchymal masses or infections.

IIH is not typically associated with seizures but can present as unexplained irritability in a young child [8, 9].

In our HRLS setting, we do not have consistent access to complete blood count, lumbar puncture (LP), lactate, extended electrolytes (including calcium), liver function testing, neuroimaging or electroencephalogram. Thus, without opening pressures by LP, we cannot conclusively state that this was a case of IIH. However, upon exclusion of other causes by clinical suspicion and the limited blood tests in our setting, we believe that nalidixic acid was the cause of this child's seizures by direct toxic effects in overdose (as implied by the metabolic acidosis), or from nalidixic acid-induced IIH or reduced seizure threshold at therapeutic dose. While simethicone was also given to the patient at the same time, there are no reported drug interactions with simethicone and nalidixic acid, and simethicone is not noted to cause convulsions [10].

Nalidixic acid continues to be prescribed as an antibiotic for diarrhoea and UTI in resource-limited settings, and as our case in Northern Iraq demonstrates, it should be considered

White Cell Count (WCC) 20.4 x10^3 cells/mm^3
Haematocrit 28%
Haemoglobin 9.5 g/dL
Sodium (Na^+) 141 mmol/L
Potassium (K^+) 3.2 mmol/L
Chloride (Cl^-) 117 mmol/L
Bicarbonate (HCO_3^-) 5.4 mmol/L
Glucose 7.3 mmol/L
pH 7.088
pCO_2 17.8 mmHg
Anion Gap 18.6
Base Excess 24 mmol/L
Blood urea nitrogen (BUN) < 20 mg/dL
Creatinine < 18 µmol/L

Figure 2: Patient's laboratory results upon presentation.

- metabolic disturbance (hypoglycaemia, hypocalcaemia, hypomagnesaemia)
- febrile seizures
- seizure disorder (benign familial neonatal epilepsy, early myoclonic epilepsy, infantile spasms, epilepsy of infancy, myoclonic encephalopathy)
- tetanus
- sepsis
- central nervous system infection (meningitis, encephalitis, cerebritis, cerebral abscess etc.)
- electrolyte/metabolic disturbance (Ca, Na, K etc.)
- inborn error of metabolism
- medications and toxins

Figure 3: Differential diagnosis considered.

as a cause of convulsions in any seizing child who has been exposed to it. Furthermore quinolones, including nalidixic acid, should be used with caution in young children and should never be prescribed to children under the age of 3 months.

INFORMED CONSENT

Written informed consent for the publication of this case was obtained from the child's father. We have purposefully removed the name of the town and of the hospital in Northern Iraq from the body of the text so as to remove any potential identifiers from this case report.

ACKNOWLEDGEMENTS

We acknowledge the medical writing services of Dr Marta A. Balinska, Médecins Sans Frontières Austria, Taborstrasse 10, 1020 Vienna, Austria.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

FUNDING

This study was entirely funded by Médecins Sans Frontières Operational Centre Geneva.

ETHICAL APPROVAL

No ethical approval was required since we received written consent from the patient's father.

GUARANTOR

Dr Michael Galvin.

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