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Edwardsiella ictaluri, an unusual cause of bacteraemia in a Nigerian child with acute bloody diarrhoea

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Abstract

Enteric septicaemia of catfish was first detected in 1976 as an economically significant disease associated with commercial catfish production. Initially, *Edwardsiella ictaluri* was a host specific pathogen of catfish species but has also been reported from other hosts other than the catfish such as the zebrafish. *E. ictaluri* has not been isolated in humans hence it is not a zoonotic infection. There has been no previous report of isolation of this organism in humans. This was a case report of a 5 year old boy who presented with fever, vomiting, passage of bloody stool of 6 days and abdominal pain of a day duration. In the case of this 5 year old boy who presented with features of dysentery, blood culture using BACTEC™ grew *E. ictaluri. E. ictaluri* may be a pathogen which can infect humans just like another closely related species, *Edwardsiella tarda.* Although, *E. ictaluri* has not been reported in humans, could this be the first case? Non availability of diagnostic technique appropriate for its diagnosis may explain the rare incidence of the organism in humans, hence many cases would have been treated without isolating the organism.

Keywords

Dysentery; Zoonotic; Septicaemia; Pleomorphic; Species

INTRODUCTION

Acute diarrhoea disease is a major health issue that affects children in both developed and developing countries, although simple measures can be used to prevent and treat it.[1] While diarrheal deaths of under five are significantly decreasing globally (from 1.2 million in 2000

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to 0.5 million in 2016), it is still the second largest cause of under-five deaths in the world.[2] Diarrhoea kills approximately 525,000 children under five years of age and Nigeria is among the countries with high burden of diarrhoea diseases in children.[1] The latest national population health survey (NDHS) in 2018 revealed that 13% of children under five years of age were reported to have had diarrhoea within 2 weeks preceding the survey. It reflects a rise of 10% from 2008 to 2013. No data was reported on bloody diarrhoea among children suggesting the rarity of the condition.

Diarrhoea is often a symptom of infections caused by a host of bacterial, viral and parasitic microbes, most of which are spread by drinking of contaminated water. Diarrhoea of infectious origin is more common in households with inadequate sanitation and hygiene and lack of safe drinking, cooking and cleaning water.[1] It is often characterized by the passage of loose stools with rare blood or blood stains. Acute bloody diarrhoea (also known as dysentery) is defined as an acute bout of diarrhoea lasting less than 14 days in which patients pass bloody or blood-stained stools.[2] The causes of bloody diarrhoea were well studied and the common aetiology and pathogens have described in several studies which have been summarised in a systematic review.[3] Studies have shown that bloody diarrhoea is frequently associated with intestinal damage and loss of nutrients in children, many of which have been attributed to the pathogen.[4,5] A study reported that 5-15 percent of all deaths from diarrhoea in children 0-59 months of age in seven countries including Bangladesh, Ethiopia, Ghana, India, Pakistan, Uganda and the United Republic of Tanzania have acute bloody diarrhoea.[6]

Acute bloody diarrhoea is often caused by infectious agents ranging from bacteria to protozoa. However, *Shigella* species, *Salmonella* species or enterohemorrhagic *Escherichia coli* and *Entamoeba histolytica* are commonly reported in literature.[3,7] Most of these organisms are transmitted via faeco-oral route through contaminated water. In a similar manner some other rare organisms in the *Enterobacteriaceae* family such as *E. tarda* which transmission is water related have been reported.[8,9] This bacterium can cause gastroenteritis and can infect open wounds in humans.[10] Human infections due to *E. tarda* usually manifests as acute secretory enteritis associated with consumption of raw seafood, snake flesh or aquatic exposure. Apart from *E. tarda,* no other species from the genus of *Edwardsiella* has been reported to cause intestinal infection in man. In this article, we presented a case of septicaemia attributable to *E. ictaluri* in a 5 year old child with acute bloody diarrhea and suspected septicaemia.

CASE REPORT

A 5 year old boy presented at the children emergency ward of the university college hospital, Ibadan, Nigeria with complaints of high-grade fever, vomiting, passage of bloody stool of 6 days duration. The fever was insidious in onset and occurred intermittently. No respiratory or urinary symptoms. No eye, ear or nasal discharge. He had 4 to 5 episodes of non-bilious vomiting daily which occurred post-prandial. He passed loose stool, about 8 episodes on each day. The stool appeared mucoid and later became bloody after 3 days. There was associated generalised abdominal pain and loss of appetite. There was a recent history of consumption of catfish by the patient and other members of the family, however, no history

of similar presentation in them. No history of consumption of food prepared outside the home.

He was initially managed at a private health facility for 6 days where investigations showed positive malaria parasite, white blood cell (WBC) count, 3,300/mm^3, serum electrolytes: sodium 149 mol/l, potassium 3.1 mol/l, bicarbonate 27.5 mol/l, urea 14.5 mg/dl, creatinine 0.85 mg/dl. Stool culture and sensitivity yielded *Streptococcal spp.* Patient was sensitive to cefuroxime, augmentin, nitrofurantoin, gentamycin and ofloxacin. He was managed with intravenous amoxicillin and metronidazole, intravenous Ringer's lactate, intravenous artesunate and loperamide. He was referred to our facility for expert management due to persistence of symptoms.

At presentation, he looked acutely ill, temperature 38.1 °C, not pale with generalised abdominal tenderness and guarding but no rebound tenderness. He had hepatomegaly of 4 cm below the right costal margin, bowel sound was normoactive. He weighed 16 kgs, 89% of expected weight for age (EWA), height 113 cm, 105% of EWA and mid arm circumference of 14 cm (normal) The examination of other systems was normal.

Initial diagnosis of acute dysentery with a differential diagnosis of typhoid fever was made. Packed cell volume was 31%, rapid diagnostic test for malaria was negative, WBC 4.81×103/ul, neutrophils 48%, lymphocytes 24.1%, monocytes 25.6%, eosinophils 1.9% and basophils 0.4%. Serum electrolytes were sodium 134 mmol/l, potassium 3.6 mmol/l, chloride 95 mmol/l, bicarbonate 27 mmol/l, urea 6 mmol/l and creatinine 0.4 mmol/l. Stool microscopy showed no ova, cyst or trophozoite of parasite and culture yielded no *Salmonella* or *Shigella*. Urine culture showed WBC 0-1 and yielded no growth. Blood culture grew *E. ictaluri*, sensitive to gentamycin, levofloxacin, ceftriaxone, cefuroxime, ceftazidime and augmentin. He had 1 week of intravenous ceftriaxone one gram 12 hourly. The symptoms resolved on the 5th day of treatment.

Repeat blood culture taken after completion of antibiotics was sterile after 5 days of incubation. He was seen twice in the outpatient's clinic and he remained well.

Method of laboratory bacterial isolation

Blood sample was collected into BACTEC™ blood culture bottle (Becton, Dickson UK) and incubated at 35°C for 72 hours. The culture blood sample was subcultured on both blood agar plate with 5% sheep blood (BA) and MacConkey agar, for maintenance of stock culture prior to biochemical and colonial morphology identification.

Biochemical identification of the isolate

The isolate was presumptively identified using Gram stain reaction, catalase test, cytochrome oxidase test strip, Simmons citrate utilization test, Christensen's urea test, glucose fermentation test in broth, Kligler's iron agar slant, indole test, esculin hydrolysis on bile esculin broth. Also, the motility was assessed using standard bacteriological test method called hanging drop method. The isolate was further inoculated into API 20E strip (Biomerieux diagnostics) for species identification and the strip was incubated at 35 °C

for 48 hours. The results were interpreted according to manufacturer's instructions for *Enterobacteriaceae* species.

Antibiotic-susceptibility testing

Antibiotic susceptibility was determined by disc diffusion technique using quality control methods outlined in the M02, M07 and M11 documents of the CLSI 2019 (clinical and laboratory standards institute). The inoculum suspensions equivalents to a 0.5 McFarland turbidity standard were made from the blood agar cultured plate to be tested in 5 ml of sterile 0.85% saline. Kirby-Bauer disc diffusion susceptibility test protocol was done using a sterile cotton-tipped applicator saturated with the bacterial suspension to lawn the entire surface of Mueller-Hinton agar plates.

Paper disc impregnated with the antibiotic (Oxoid) such as augmentine (AMC), levofloxacine (LEV), ceftriazone, cefuroxime (CXM), gentamycine (CN) and ceftrazidime were placed evenly within equal distances from other discs on surface of 90 mm diameter MHA plates after it was inoculated. A control plate was inoculated with *E. coli* ATCC 25922 to serve as quality control standard for the antibiotics. The plates were inoculated at 28 °C and zones of inhibition were measured at 24 hours.

DISCUSSION

In this paper, *E. ictaluri* was reported as an unusual blood isolate of a Nigerian child with predominant features of acute diarrhoea with blood-stained stools. *E. ictaluri* is a gram-negative and oxidase-negative rod-like bacterium.[11] It is a member of the class gamma-proteobacteria, order *Enterobacteriaceae*, a group of bacteria which thrive more commonly in the intestine. This case appeared to be the first time that *Edwardsiella* species, a known cause of enteric septicaemia in fish, has been detected in human blood.[12,13] However, other species like *E. tarda* also belonging to a genus of gram-negative facultatively anaerobic bacteria of the family *Enterobacteriaceae* is an opportunistic pathogen causing diarrhoea in humans, dogs, pigs and calves.[8,11]

Our patient had a history of intake of catfish in which the organism was known to be pathogenic. However, the other members of the family who ate the fish did not develop any of the symptoms in the index case. It was therefore difficult to attribute the source of diarrhoea or aetiology of septicaemia to catfish consumption. The presence of poor immune status or immunosuppression in the patient, the only child among catfish consumers, could be a plausible reason that the child was the only one affected. However, the clinical assessment and laboratory investigation such as the complete blood count, did not suggest an immune compromise.

Although both *E. tarda* and *E. ictaluri* were closely related, MicrobactTM gram-negative system can be used to identify the exact species as was done for this index case.[8,14] The details of the laboratory bacteria isolation were as described above. The *E. ictaluri* was differentiated from *E. tarda* by the following characteristics: failure to grow at 35 degree Celsius, having weaker motility, weaker gas production in carbohydrate media, negative

hydrogen sulphide production, negative indole reaction, slower growth rate and smaller colony morphology.

The fact that the blood culture (BACTEC™) yielded *E. ictaluri* in the case of a child who presented with dysentery in this report suggests that the organism may have been translocated to blood through the intestinal mucosa, although the stool culture did not produce growth. This observation was expected because a course of oral metronidazole was given to the patient prior to referral to our facility, which may have cleared some of the intestinal bacteria.

In the present study it was shown that *E. ictaluri* was sensitive to gentamycin, levofloxacin, ceftriaxone, cefuroxime, ceftazidime and augmentin. While detailed literature examinations of *E. ictaluri's* antibiotic susceptibility patterns have not been reported, the susceptibility to a number of antibiotics identified in this study suggested that commonly available antibiotics were appropriate for the treatment of infections. This finding agreed with earlier report that demonstrated high susceptibility of *Edwardsiella* species to several antibiotics in studies with *E. tarda* and in a few studies with *E. ictaluri* and *E. hoshinae*.[10,14-17] It was expedient to carry out studies to demonstrate *in-vitro* or *in-vivo* antibacterial activities of locally available antibiotics in our setting.

Our report needed to be understood in the context of the limitation of laboratory investigations and procedures in developing countries. The fact that we were unable to apply molecular techniques to the identification could have limited the full description of the organism identified as *E. ictaluri.* In addition, the antibiotic susceptibility test was limited to antibiotics reported due to laboratory constraints in the assessment of other possible antibiotics. Thus, the resistance spectrum *of E. ictaluri* remained largely unknown.

CONCLUSION

This report has shown that *E. ictaluri* may be a pathogen that can infect humans, especially children such as other *Edwardsiella* and *Enterobacteriaceae* species. It is the *E. ictaluri* is sensitive to antibiotics that are commonly used. Paediatricians and microbiologists need to consider rare microbial causes of septicaemia in children with bloody diarrhoea, especially when catfish is part of family staple foods.

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