Klebsiella pneumoniae Bacteraemia Complicating Rotavirus Gastroenteritis in Two Infants with Glucocorticoid Deficiency

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ABSTRACT

Rotavirus gastroenteritis was complicated by Klebsiella pneumoniae bacteraemia in two infants with glucocorticoid deficient conditions who were treated with ‘stress dose’ hydrocortisone during their illness. Delayed healing in the context of glucocorticoid administration combined with damage from rotavirus infection may result in increased risk of mucosal invasion by gastrointestinal bacteria and subsequent enteric gram-negative bacteraemia.

KEY WORDS

glucocorticoid deficiency, rotavirus, gastroenteritis, enteric gram-negative bacteraemia, corticosteroids, congenital adrenal hyperplasia

INTRODUCTION

Klebsiella pneumoniae bacteraemia complicated rotavirus gastroenteritis in two infants with glucocorticoid deficient conditions who were treated with stress-dose hydrocortisone during their illness. Enteric gram-negative (EGN) bacteraemia is an infrequently recognised complication of rotavirus infection. Rotavirus has not been shown to cause significant gastrointestinal mucosal changes; however, it has been shown to increase epithelial permeability and enhance the ability of bacteria to invade enterocytes¹. Glucocorticoids are thought to cause delay in gastroduodenal healing, most likely due to inhibition of prostaglandin synthesis². There have been no reports of secondary EGN bacteraemia in infants or children with rotavirus infection on corticosteroids. It is hypothesised that high dose glucocorticoids may increase the risk of EGN bacteraemia in rotavirus gastroenteritis.

PATIENT 1

An 8 month-old male infant with congenital adrenal hyperplasia secondary to 21-hydroxylase deficiency was admitted with rotavirus gastroenteritis. His regular medication included oral hydrocortisone (10.5 mg/m²/day) and oral fludrocortisone (100 μg twice daily). He presented with a one-day history of vomiting and watery diarrhoea with no history of fever. Rotavirus infection was confirmed via immunoassay antigen detection (VIKIA® Rota-Adeno by bioMerieux). He was commenced on hydrocortisone at a dose of 2 mg/kg intravenously every 6 hours on admission, in addition to intravenous fluids. On admission his C-reactive protein (CRP) was <1.0 mg/L, white blood cell count 19.3 x 10³/mm³ with a neutrophil count of 7.3 x 10³/mm³. His gastroenteritis was complicated by concurrent Norovirus enteric infection. He was hospitalised for six days and then discharged on oral hydrocortisone (triple his oral maintenance dose) after his symptoms settled. However, he required readmission due to recurrence of vomiting and large volume diarrhoea. Previously afebrile, his temperature increased to 39°C 11 days after readmission. Blood cultures revealed a pure growth of Klebsiella pneumoniae after 5.9 hours. Haematological testing revealed anaemia, lymphopenia and thrombocytopenia. He was commenced on ceftriaxone and gentamicin, continuing on gentamicin (7.5 mg/kg daily) for seven days after sensitivities were available. Resolution of fever...
occurred within 48 hours of antibiotic commence-
ment with subsequent decline of inflammatory
markers, improvement in haematological markers
and ultimately full recovery.

PATIENT 2

A male infant aged 8 months with bilateral
optic nerve hypoplasia and panhypopituitarism
(including ACTH deficiency) was admitted with
gastroenteritis. His regular medication included
oral hydrocortisone (10.1 mg/m²/day), oral des-
mopressin (20 μg three times daily) and oral
thyroxine (50 μg daily). He had a two-day history of
vomiting with no history of diarrhoea. His
temperature was 37.8°C on admission. He was
commenced on intravenous hydrocortisone at a
dose of 2 mg/kg six hourly. An initial blood
culture collected at the time of admission was
negative. His white cell count on admission was
9.2 x 10⁹/mm³. He was managed with oral fluids
initially. Rotavirus testing on stool (VIKIA®
Rota-Adeno by bioMerieux) was positive on day
two of admission and culture of stool from the
day of admission was negative. He deteriorated
clinically on day 3 of his admission with fever up
to 39.4°C and signs consistent with sepsis. A
blood culture subsequently grew Klebsiella
pneumoniae after 10 hours. His white cell count
was initially normal; however, it became elevated
to 24.1 x 10⁹/mm³ and his CRP peaked at 213
mg/L 32 hours after the initial fever. He also
developed anaemia, neutrophilia and thrombo-
cytopenia during the illness. He completed an 11
day course of intravenous antibiotics. He had
resolution of fever and improvement in clinical
state within 48 hours of starting antibiotics. He
subsequently made a complete recovery.

DISCUSSION

Rotavirus is the commonest cause of gastro-
enteritis worldwide and it has been recognised as
the cause of 20% of diarrhoeal deaths in children
aged less than 5 years¹. Rotavirus infects the
enterocytes and it has been demonstrated that
rotavirus infection increased enterocyte interna-
lation and replication of bacteria, including
Listeria monocytogenes, Yersinia enterocolitica
and Y. pseudotuberculosis². These mechanisms
are thought to contribute to the pathogenesis of
EGN bacteraemia, a recognised complication of
rotavirus infection. Secondary EGN bacteraemia
complicating rotavirus infection has been de-
scribed in 12 cases in children ranging in age
from two weeks to 18 months⁶⁻¹². Recrudescence
of fever in infants with rotavirus infection has
been identified as the clinical sign that should
raise suspicion of secondary EGN bacteraemia
and prompt further assessment and investiga-
tion⁶⁻¹¹.

Unlike other reported cases the patients
discussed here both received ‘stress dose’ glucoc-
corticoid steroids after admission to hospital.
Patients with adrenal insufficiency require
maintenance glucocorticoid replacement when
well. It is recognised that circulating levels of
cortisol normally increase during stress, such as
illness or surgery; therefore increased doses of
glucocorticoids are required in these states and in
some cases may need to be administered parenterally¹¹. The nature of the effect of high
dose corticosteroids on the gastrointestinal tract is
controversial and the pathophysiology is not
clearly understood. However, studies have shown
delayed epithelial healing is most likely due to
inhibition of prostaglandin synthesis². Experi-
mental studies have shown that dexamethasone
inhibits epidermal growth factor (EGF)-stimu-
lated gastric epithelial cell proliferation and basic
fibroblast growth factor¹⁴,¹⁵, which are essential
for mucosal healing via the prostaglandin path-
way. These research findings suggest a patho-
physiological basis for impaired healing of
‘damaged’ gastrointestinal mucosa in the setting
of glucocorticoid administration. Damage to the
gastrointestinal mucosa due to rotavirus infection
combined with delayed healing in the context of
glucocorticoid administration may increase the
risk of invasion of the mucosa by gastrointestinal
bacteria. Other potential sources of EGN infection
need to be considered, including intravenous catheter infections; however, in both cases discus-
sed here there was no clinical evidence of venous
catheter infection.

The first infection with rotavirus is often
between 3 and 36 months of age and is more
diarrhoea\textsuperscript{16}. From 1 July 2007, rotavirus vaccination has been included in the National Immunisation Program in Australia. The two infants described here did not receive the rotavirus vaccine. The impact of rotavirus vaccination on complications such as EGN bacteraemia remains uncertain. There remains a significant population of unvaccinated children within the higher risk age group. Studies have demonstrated that the rotavirus vaccination program provides protection for two years\textsuperscript{17}. The impact of vaccination after this period for those on high dose glucocorticoids, who are hypothesised to be at increased risk, remains uncertain.

These two cases of EGN bacteraemia complicating rotavirus infection in infants on high dose glucocorticoids for glucocorticoid deficient states raise concern about a potential increased risk for these children. Further research would be beneficial to clarify this possible association and the relevant pathophysiology. The impact of rotavirus vaccination on EGN bacteraemia has yet to be evaluated.

\textbf{REFERENCES}
