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Non-antibiotic Associated *C. difficile* Diarrhea in a 7-week-old Infant

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We describe a rare case of non-antibiotic associated severe C. difficile diarrhea in a 7-weekold boy. He had massive fluid loss and electrolyte imbalance. He required total parentral nutrition for 10 days and eventually recovered with oral metronidazole. Most of the reported cases in literature are associated with prior antibiotic exposure or in hospitalized patients.

Keywords: Clostridium difficile, Diarrhea.

Clostridium difficile associated diarrhea (CDAD) is a serious nosocomial illness, mostly seen in hospitalized adult patients. According to a recent review article, 2% of healthy individuals are colonized with *Clostridium difficile* bacilli; colonization rates are higher in hospitalized individuals and neonates. However, carriage of this organism

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A previously healthy 7-week-old male infant presented to emergency department with a one day history of profuse bilious vomiting and lethargy, with the background of a ten day history of loose stools and faltering weight. His weight had been just above 9th percentile from birth and had fallen to the 2nd percentile. The antenatal history was uneventful, born in hospital at term by normal delivery. He passed meconium on day 1 and did not receive antibiotics in the neonatal period. He had been exclusively breast-fed and his mother was not on antibiotics.

On presentation, he was afebrile, looked wasted and dehydrated. He required fluid resuscitation and a third generation cephalosporin was commenced after a full sepsis screen. Differential diagnosis at this stage included sepsis and surgical gastrointestinal pathology.

Initial complete blood count and

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biochemistry including serum albumin was within normal limits. Cerebrospinal fluid, blood and urine cultures (suprapubic aspirate) were sterile as were stool specimens for bacteriology, virology and ova and cyst examination. Abdominal *X*-ray, USG and upper GI contrast study were done and reported as normal.

In view of the severity of his initial presentation, the negative cultures and normal gastrointestinal tract radiology, metabolic, endocrine and immunologic disorders were considered. His blood pH, glucose, lactate and ammonia were normal: urine amino acid and organic acids profile were normal. His serum cortisol and 17-hydroxyprogesterone were normal as were his immunoglobins, his lymphocyte phenotypes T cell -CD3+, CD4+, CD8+ and B cell CD19+ were marginally low, but judged not to be very significant by our immunologist as the total lymphocyte count was always normal. His chest X-ray showed a normal thymus. His repeat full blood work showed leukocytosis with white blood count of 21.05×10^9 /L, and an elevated C-reactive protein of CRP 45 mg/L.

He was kept nil orally and full intravenous fluid maintenance started. He continued to have massive gastrointestinal losses, frequently requiring a fluid bolus immediately after a voluminous stool. He also required careful monitoring and correction of serum electrolytes.

Clostridium difficile toxin A and B (ELISA) was identified from a stool sample sent 30 hours after he had received the first dose of antibiotics. This stool specimen was negative for other enteric pathogens, viruses and parasites.

Intravenous antibiotics were discontinued, oral metronidazole commenced and continued for 7 days. His stool frequency started decreasing within 48 hours, but required total parental nutrition a further 10 days to improve his nutritional status. After six days, diarrhea gradually settled and breast-feeds were started. Repeat stool sample for *C. difficile* toxin was negative on day 7, 10 and 14, blood leukocyte count also returned to normal.

His course was complicated by upper respiratory tract infection with parainfluenza virus type 3 in the 3rd week of hospital stay. He finally gained weight and was discharged after a total of 22 days of hospital stay. Sixteen weeks after discharge he remains well and is thriving.

Discussion

Clostridium difficile is a widely distributed obligate anerobe, gram-positive, sporeforming bacillus which produces two toxins, Toxin A and toxin B. Toxin A causes fluid secretion and mucosal damage while toxin B appears to have greater cytopathic effects in tissue culture but both are believed to play a role in the pathogenesis of disease(5).

Although there is a high carriage rate in neonates and young infants, symptomatic disease is uncommon(2). There are several theories to explain why they do not exhibit symptoms, despite high colonization rates. The absence of disease may be related to the immaturity of the toxin receptor sites, which are not able to bind the toxins(2). Neutralizing effect of maternal antibodies and immaturity of the neonatal immune system may play a role(2,3). The manifestations of C. difficile infection in children may range from asymptomatic colonization or mild selflimited diarrhea to toxic megacolon and severe colitis. In symptomatic cases, systemic symptoms and signs are usually present, which include malaise, anorexia, nausea, lowgrade fever and leukocytosis(6). The diagnosis of CDAD is based on a combination

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of clinical symptoms, history, laboratory testing, and occasionally endoscopic evaluation. Due to asymptomatic carriage of *C. difficile*, the mere presence of the organism is not adequate to diagnose CDAD; toxin A and B identification is essential, the gold standard being tissue culture cytotoxin assay.

Although, majority of the cases are antibiotic related, occasionally, patients develop disease due to C. difficile in the absence of recent exposure to antibiotics. This most commonly occurs in patients with malignancies on antineoplastic drugs and hypogammaglobinemia(4). In this case no risk factor could be identified, it may be argued that C. difficile toxins was identified 30 hours after commencing on antibiotics. Usual time of presentation of illness is 4-8 days after first dose of antibiotic, but may be delayed as long as 21 days after antibiotics have been discontinued(7); this case had the symptoms of diarrhea and faltering weight 10 days before presentation and prior to antibiotics being commenced.

Literature does emphasis on leukocytosis as a marker of *C.difficile* colitis(6) and low albumin levels as an indicator of severe illness(8). Our case had leukocytosis for initial 6 days and a normal albumin level.

This case responded very well to oral metronidazole with no relapse, the other alternative is oral vancomycin, which is equally effective. The major problem with treatment of *C. difficile* disease is recurrence following initial therapy. Prospective trials have demonstrated recurrence of symptomatic associated diarrhea of 20% in patients, and can be managed effectively by repeating treatment(9). The use of steroids with good effect has been reported in refractory cases of colitis(10). Surgical therapy is rarely required

for patients with *C. difficile*-associated disease.

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Neonatal Lupus Erythematosus

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We describe case report of a 45 days old male baby with neonatal lupus erythematosus, who presented with 3rd degree congenital heart block and depigmented skin lesions on face and upper part of body. Diagnosis of the baby was confirmed by anti nuclear levels and skin biopsy.

Keywords: Congenital heart block, Neonatal lupus erythematosus.

Neonatal lupus erythematosus (NLE) is a rare form of lupus erythematosus first described in 1954(1). It is characterized by the presence of cutaneous lesions or congenital heart block or both, in an infant whose mother has connective tissue disease or auto antibodies to extractable nuclear antigens Anti-Ro (SSA), Anti-La (SSB) or ribonucleoproteins (RNP)(2).

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Case Report

A 45-days-old male delivered to a 22-year-old, primigravida by caesarean section at 35 weeks of gestation due to fetal bradycardia. There was no history of fever, rash, lymphadenopathy or drug intake during pregnancy. The natal and postnatal periods were uneventful. At presentation the infant weighed 3.8 kg, with length of 51.5 cm and head circumference 34.2 cm. The heart rate was 76/min, regular and had no pulse deficit. All peripheral pulses were palpable. There were areas of depigmentation (with no erythema or scaling) over the nose, cheeks, around the eves, scapular region and lower back. There was no significant lymphadenopathy, bleeding spots, rash or hepatosplenomegaly. Laboratory investigations showed Hg of 12g% (PCV was 40%). Total Leukocyte Count was 6800/mm³, differential leukocyte count was P60, L40, E0, M0 and platelet count of 22,000/mm³. Liver function tests were within normal limits. Anti-nuclear antibody (ANA) by immunoflorescence was strongly positive (1:640), Anti Ro and Anti La were negative. Electrocardiogram of the baby revealed type 3 congenital heart block The echocardiography showed a structurally normal heart. Skin biopsy revealed scattered lymphocytic infiltration in the dermis with few lymphocytes seen clustered around dermal appendages features compatible with NLE. Immunoflorescence studies could not be done. ANA was positive at 1:640 with speckled pattern in mother's serum. Anti-Ro

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