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Candida Diarrhoea in a Patient of Nephrotic Syndrome

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Abstract:

Nephrotic syndrome is considered to be an immunosuppressive condition and hence, is associated with increased prevalence of superimposed infections. We report a case of 7 year old child suffering from nephrotic syndrome who presented with fever, swelling all over the body and pain abdomen. The child contracted diarrhoea after 3 days of stay in hospital. On stool examination, eggs of *Hymenolepis nana*, cysts of *Giardia lamblia* and budding yeast cells along with pseudohyphae were seen. Culture grew *Candida albicans*. Since the diarrhoea was not relieved even after treating the parasitic infection, *Candida* was considered to be the pathogen. The child was administered fluconazole for 2 weeks which helped in recovery from the diarrhoea. *Candida sp*. is considered to be frequent commensal of the gastrointestinal tract. However, since our patient was empirically started on multiple antibiotics, which is a known risk factor for Candida diarrhea, the probability of Candida being the enteropathogen was high, considering that antibiotic therapy facilitates proliferation of Candida in the intestine. Hence, the significance of Candida in stool sample should always be assessed by correlating with other relevant history and it should not always be dismissed as being a commensal.

Key words: Candida, Candida albicans, Cysts, Fluconazole, Nephrotic Syndrome, Giardia lamblia, Humans.

Introduction

Nephrotic syndrome is recognized as a common chronic illness in childhood. The constellation of signs and symptoms that characterize nephrotic syndrome namely proteinuria, hypoalbuminemia and oedema, develop due to alterations of the permeability barrier of the glomerular capillary wall [1]. Nephrotic syndrome is considered to be an immunosuppressive condition [2,3] and hence, is associated with increased prevalence of superimposed infections. However, there is limited knowledge on the intestinal parasitic infestation and fungal invasions among the patients with nephrotic syndrome.

Case Report

A 7 year old male patient presented to the pediatric OPD of our hospital with complains of swelling around eyes for 8 days which progressed to involve the whole body within a day. However,

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the facial puffiness decreased over a period of time. This was accompanied by low grade fever, swelling around external genitalia and pain during micturition, pain abdomen on and off for 8 days. Also, he had constipation for 3 days. He was admitted to the hospital and started initially on furosemide, ceftriaxone and cloxacillin. The child started complaining of watery diarrhea after 3 days of stay in the hospital. And hence, suspecting it to be antibiotic associated diarrhea, ceftriaxone and cloxacillin were stopped and he was started on amikacin, piperacillin-tazobactam, vancomycin and metronidazole. On examination, puffiness could be appreciated all over the body. Bilateral pitting pedal oedema was noted. There was no history of skin rash. The respiratory, cardiac and neurological examination was within normal limits. The child was immunized as for his age. The milestones had been achieved on time.

The kidney function tests were slightly deranged (urea 15 mg/dL, creatinine 0.5 mg/dL, and uric acid 2.0 mg/dL). The serum proteins of the patient were also found to be low (Total proteins: 4.0 gm/dL, albumin 2.0 gm/dL, globulin 2.0 gm/dL). Patient's hemoglobin was 10 gm%. The iron profile of the patient was within reference ranges (Total iron 88 µg/dL, TIBC 280 µg/dL, saturation 25%). The other biochemistry investigations like serum electrolytes and blood sugar were within normal limits except alkaline phosphatase which was 413 U/L.

Since the patient's diarrhea was not controlled with the antibiotics, a stool sample was sent in the microbiology laboratory for microscopy and culture. Routine examination of the sample was done with wet mount in normal saline and Lugol's iodine. On examination, oval, around 40 µm x 30 µm structures were seen. 4-5 polar filaments were spread out between the inner and outer membranes at the poles. 4-6 hooklets could be seen in the oncosphere suggesting a diagnosis of eggs of Hymenolepis nana. Cysts of *Giardia lamblia* could be seen. They were oval in shape, around 12-14 µm long, with four nuclei and a longitudinal axoneme. Also, budding yeast cells along with pseudohyphae formation were seen in the wet mount. Since yeast cells were seen in the wet mount, a Grams stain was also prepared. The sample was inoculated on blood agar, MacConkey agar and Sabouraud's dextrose agar with chloramphenicol. On blood and MacConkey agar, along with the normal flora of stool sample, growth of few white coloured, 0.2-0.5 mm, convex, dry colonies with entire edges was appreciated. Also, on Sabouraud's dextrose agar with chloramphenicol, creamish white coloured 1-2 mm convex colonies were seen. On Grams stain, these colonies showed yeast cells. Germ tube test showed formation of germ tube hence, making the probable diagnosis to be Candida albicans. Although Candida is a normal commensal of the gastrointestinal tract, it was a suspected pathogen in this case since the patient was on high load of antibiotics which is a risk factor for fungal diarrhea. A urine microscopy and culture showed no significant results, however, proteinuria (3+) could be demonstrated using dipstick method.

The immunoglobulin profile was performed for the patient in our laboratory using Diffu-Plate Radial Immunodiffusion method. The levels of IgG were 444.1 mg/dL (normal range for age 610-1380 mg/dL), IgM were 154.1 mg/dL (normal range for age 20-134 mg/dL) and IgA were 168.1 mg/dL (normal range for age 30-240 mg/dL). The serum complement levels, i.e, of C3 were 79.2 mg/dL (normal range for age 80-160 mg/dL) and of C4 were 24.2 mg/dL (normal range for age 20-40 mg/dL). The patient was non-reactive for HIV, hepatitis B and hepatitis C infections.

The patient was initially started on metronidazole. The diarrhea still continued and hence, mebendazole 100 mg twice daily for 3 days was started after stopping all other antibiotics and metronidazole. However, the diarrhea still persisted. Candida was

considered to be a commensal and its presence in the sample was initially ignored by the clinician. But on repeated isolation of Candida from the stool sample later, the patient was started on fluconazole 6 mg/kg/day x 2 weeks which helped him recover from the diarrhea.

Discussion

Candida albicans has been found to be the most common yeast species isolated from human faeces, being identified in 65% of stool samples from healthy adults. In a study done by Forbes *et al*. although higher concentrations of Candida were found in patients with diarrhea, a causative relation between the yeasts and diarrhea could not be made [4]. However, there are reports to suggest that it may cause diarrhoea. Studies have identified Candida as the sole pathogen in the stool samples of patients with diarrhoea and also reported symptom recovery following treatment [5-7]. Candida has been identified in high concentrations in the stools of malnourished children, frequently with associated diarrhea [8,9]. Also, it has been suggested as a cause of antibiotic associated diarrhoea in infants [10].

As has been mentioned earlier, nephrotic syndrome is a state of immunosuppression which makes the patient susceptible to a variety of infections [1]. This complication of the disease is not only because of the disease pathophysiology per se but also due to the administration of corticosteroids, which are the treatment of choice. Although our patient was suffering from idiopathic nephrotic syndrome, he was neither highly immuno-compromised as can be seen through the immunoglobulin and complement profile nor he was started on corticosteroids. The patient was not put on steroids as the guidelines suggest that all the infections should be first treated before starting steroids. This is because of the observation that appropriate therapy for an infection might rarely lead to spontaneous remission of the episode, thereby avoiding the need for treatment with steroids [1].

The reason for the multiparasitic infestation in our patient may be the poor hygiene in this low socioeconomic group of population. Although the patient was treated in order to cure the parasitic infections, the diarrhea was not resolved. The isolation of *Candida spp*. in the stool sample was initially ignored considering that it is a part of the normal gastrointestinal flora and despite the high concentration of *Candida spp*. in the lower gastrointestinal tract, infection does not occur under normal circumstances, owing to innate defense mechanisms [11]. However, since our patient was empirically started on multiple antibiotics, which is a known risk factor for Candida diarrhea, the probability of Candida being the enteropathogen was high, considering that antibiotic therapy facilitates proliferation of candida in the intestine [12]. Our finding of the infection being multiparasitic along with high faecal counts of Candida is also consistent with other reports showing identification of another pathogen being strongly associated with higher counts of faecal candida [8,9,13]. Hence, after repeated isolation from the stool samples, an antifungal was started which cured the diarrhea.

Conclusion

Even in the era of molecular testing and advent of new microbiological techniques, the importance of microscopy cannot be undermined since culture methods cannot be employed for all parasitic diseases. The significance of Candida in stool sample should always be assessed by correlating with other relevant history like in this case, the patient being on multiple empirical antibiotics was a known risk factor. In cases of Nephrotic syndrome, even though urine examination plays an important part in diagnosis, stool examination should also be performed especially in pediatric cases of diarrhea.

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