Hansenula anomala infections in children: from asymptomatic colonization to tissue invasion

ALLON MOSES, MD, SHLOMO MAAYAN, MD, YIGAL SHIVL, MD, ANWAR DUDIN, MD, ILANA ARIEL, MD, AMIN THALJI, MD AND ITZHACK POLACHEK PHD

Fungi that were previously regarded as nonpathogenic for man are now being reported with increasing frequency as the cause of a multitude of diseases. Species of the genus Hansenula have been implicated as the cause of interstitial lung disease,1 fungemia in a neonatal intensive care unit, endocarditis, and infection in chronic granulomatous disease.2 We report three children with Hansenula anomala infection: one with enteritis and tissue invasion; the other two with infection complicating peritoneal dialysis色调 with a symptomatic peritoneal fluid infection, and the other with an asymptomatic infection. The patient with invasive disease was treated with amphotericin B, another improved after removal of the Tenckhoff catheter and the third recovered spontaneously.

CASE 1

A 5-month-old female infant born after normal pregnancy and delivery was well until the age of 3 months, when she was referred to the Makassed Islamic Hospital with severe watery diarrhea, vomiting, and abdominal distension. On examination she was active and afebrile; her weight was 5.7 kg. Chest examination was normal. The abdomen was distended with diminished bowel sounds. Rectal examination was normal. Plain abdominal film showed generalized distention of the bowel. An initial diagnosis of septicaemia and suspected intussusception was made. Barium enema was normal. Treatment with intravenous ampicillin and gentamicin was started. During the next few days the course was complicated by pancreatitis, hypotremia, hypocalcemia, and seizures. The antibiotic treatment was changed to chloramphenicol and gentamicin.

Because no clinical improvement was observed necrotizing enterocolitis was suspected and a laparotomy was performed. The abdominal cavity was filled with 200 ml of purulent fluid. A 30 cm segment of the ileum showing patchy gangrenous areas was resected with end to end anastomosis. Postoperatively the fever persisted despite administration of amikacin and cefoxitin. On the second postoperative day a yeast was cultured from several blood specimens, from peritoneal fluid and from the resected ileum. This yeast was identified as H. anomala by virtue of its characteristic morphology on corn meal agar, the formation of ascii with hat-shaped ascospores on malt extract agar and the typical biochemical pattern in API 20C. A loop of small intestine was submitted for pathologic examination. The intestine was focally distended with multiple necrotic areas and was covered by a patchy purulent exudate. Blood was found in the lumen and the mucosa was irregular and hemorrhagic. Necrotizing enteritis with infiltration of the intestinal wall by yeasts and pseudohyphae was found on histologic examination. These fungal elements infiltrated walls of blood vessels with formation of thrombi (Fig. 1). Periodic acid Schiff stain disclosed infiltration of the intestinal wall by branching pseudohyphae and yeasts (Fig. 2).

Because of continuing deterioration in the patient’s status a second operation was performed on the fifth postoperative day. Fecal material was present in the abdominal cavity and there was a leak from the anastomosis and necrotic areas in the ileum. An additional 80 cm of intestine were resected and an ileostomy was performed. The patient was given amphotericin B intravenously in a daily dose of 1 mg/kg. For the next 4 weeks blood urine and peritoneal fluid cultures continued to be positive for H. anomala. Amphotericin B was continued for 31 days and a total dose of 130 mg was administered. Because of persistent fever amphotericin B was discontinued and ketoconazole, 5 mg/kg/day, was administered orally. After 28 days the patient gradually defervesced. Blood cultures became sterile and the patient received ketoconazole for 6 weeks more in the hospital and an additional 6 weeks...
DISCUSSION

CASE 7

Symmetric with normal development for age. The diagnosis of polycystic kidney disease was confirmed. The patient was advised to continue with medical treatment and to undergo regular follow-up appointments. The family was counseled on the importance of early intervention and the need for genetic counseling for future pregnancies.

The imaging findings were consistent with polycystic kidney disease. The kidneys were enlarged and showed multiple cysts of varying sizes. The cysts were distributed throughout both kidneys, with the right kidney appearing more involved.

The patient was referred to a nephrologist for further evaluation and management. The family was encouraged to participate in support groups and to seek counseling to cope with the diagnosis. The patient was advised to maintain a healthy lifestyle and to follow a diet that is low in sodium and protein.

Patients with polycystic kidney disease may require regular monitoring for the development of complications such as hypertension, anemia, and infection."

The data showed a significant correlation between the presence of cysts and the progression of kidney disease. The findings also highlighted the importance of early diagnosis and intervention to prevent complications.

The patient was discharged with a plan for follow-up appointments and educational materials on polycystic kidney disease. The family was provided with resources and encouraged to seek support from local organizations.

In conclusion, the findings from this study support the importance of early diagnosis and intervention for patients with polycystic kidney disease. Further research is needed to understand the genetic and environmental factors that contribute to the development of this condition. The patient was referred to a genetic counselor for further evaluation and counseling.
implicated as the causative agent of fatal interstitial pneumonia in neonates. In 1986 Murphy et al. described 32 neonates in a neonatal intensive care unit who in a period of 13 months were colonized with \textit{H. anomala}. Eight babies became infected, 5 of them had tychiasis, 2 had tychiasis and ventriculitis and 1 had only ventriculitis. In each of these babies \textit{H. anomala} was the sole pathogen. No inanimate environmental source for the organism was found. In 1980 McGinnis et al. described a case of a child with chronic granulomatous disease in whom an infection of the mediastinal lymph nodes was caused by \textit{H. anomala}. The patient was treated with amphotericin B and recovered.

Recently Mlóstoc et al. described a case of \textit{H. anomala} tychiasis. A 55 year old man with multiple sclerosis and quadriplegia developed respiratory failure and urinary tract infection caused by \textit{Pseudomonas aeruginosa}. After treatment with antibacterial antibiotic his condition deteriorated again and \textit{H. anomala} was recovered from blood cultures. The patient received intravenous amphotericin B therapy for 10 days and recovered from the infection.

Nobile et al. reported a case of \textit{H. anomala} endocarditis on a bioprosthetic aortic valve. The patient was an intravenous drug addict. On amphotericin B the aortic valve dehisced and the patient consequently underwent aortic valve replacement. He received a total dose of 2 g of amphotericin B and recovered from the infection.

Haron et al. and Dickensheets recently reported on two different cases in which catheter-related sepsis occurred secondary to \textit{H. anomala}; the first one in an acute leukemia patient and the second in an immunocompetent one. In both cases therapy was successful with catheter removal and a short course of amphotericin B.

Our report of the isolation of \textit{H. anomala} from 3 patients from 2 hospitals with a total of 1300 beds, during a period of 1 year, is an example of the changing virulence of microorganisms which in the past have not caused disease in man. Although none of the patients had a malignant disease, in 2 cases infection was preceded by treatment with broad spectrum antibiotics. In the third case \textit{H. anomala} was isolated repeatedly from the peritoneal fluid without causing any clinical symptoms. This may represent asymptomatic infection or colonization of the peritoneal fluid or Tenckhoff catheter.

The optimal treatment of infection with \textit{H. anomala} is not well defined. Murphy et al. treated the neonates infected with \textit{H. anomala} with amphotericin B and fluconazole but did not treat those considered to be colonized. In other reports of \textit{H. anomala} recovered from blood cultures the patients were treated with amphotericin B. Our patient in whom tissue invasion was demonstrated was treated initially with amphotericin B and later it was necessary to change to ketoconazole because of a poor clinical response. Our other two patients did not receive antifungal therapy. One responded to the removal of the peritoneal catheter and the other recovered without intervention. There have been no controlled studies of the treatment of \textit{H. anomala} infections with ketoconazole, but our experience might suggest such therapy in the advent of failure with amphotericin B.

In recent reports of isolation of \textit{H. anomala} or \textit{H. polymorpha} from blood cultures, cerebrospinal fluid, and hilar, posterior mediastinal and paratracheal nodes, the fungus was not seen in histopathologic specimens obtained from these areas.

Thus the present description of a patient with invasive \textit{H. anomala} of the intestinal wall is the first case in which this pathogen has been visualized in tissue. To the list of well recognized tissue invasive fungi, such as species belong to the genera \textit{Aspergillus}, \textit{Candida}, \textit{Cryptococcus}, \textit{Mucor} and \textit{Fusarium}, we may now add \textit{H. anomala}.

A recent review of the world literature on \textit{Hansenula} infection\(^1\) suggests that the predisposing circumstances for infection by \textit{Hansenula} are similar to those for \textit{Candida} species.

As treatment of malignant disease becomes more aggressive, we may expect to see more infections with organisms not previously recognized as human pathogens.

REFERENCES