We thank Dr L. Y. Y. Fong for the serum zinc analysis.

References

- Al-Rashid, R. A., and Spangler, J. (1971). Neonatal copper deficiency. *New England Journal of Medicine*, **285**, 841–843.
- Ashkenazi, A., Levin, S., Djaldetti, M., Fishel, E., and Benvenisti, D. (1973). The syndrome of neonatal copper deficiency. *Pediatrics*, **52**, 525–533.
- Griscom, N. T., Craig, J. N., and Neuhauser, E. B. D. (1971). Systemic bone disease developing in small premature infants. *Pediatrics*, **48**, 883–895.
- Heller, R. M., Kirchner, S. G., O'Neill, J. A., Jr, Hough, A. J., Jr, Howard, L., Kramer, S. S., and Green, H. L. (1978). Skeletal changes of copper deficiency in infants receiving prolonged total parenteral nutrition. *Journal of Pediatrics*, **92**, 947–949.
- Karpel, J. T., and Peden, V. H. (1972). Copper deficiency in long-term parenteral nutrition. *Journal of Pediatrics*, **80**, 32–36.
- Sann, L., David, L., Galy, G., and Romand-Monier, M. (1978). Copper deficiency and hypocalcaemic rickets in a small-for-date infant. *Acta paediatrica Scandinavica*, **67**, 303–307.
- Shaw, J. C. L. (1973). Parenteral nutrition in the management of sick low birthweight infants. *Pediatric Clinics of North America*, **20**, 333–358.
- Willoughby, M. L. N. (1977). *Paediatric Haematology*, p. 149, Churchill-Livingstone: Edinburgh.

Correspondence to Professor J. H. Hutchison, Queen Mary Hospital, Department of Paediatrics, Hong Kong.

Pulmonary candidiasis in cystic fibrosis

B. M. JENNER, L. I. LANDAU, AND P. D. PHELAN

Royal Children's Hospital, Melbourne, Australia

SUMMARY A child with cystic fibrosis and asthma developed pulmonary candidiasis. Predisposing factors in this patient were prolonged antibiotic therapy, high-dose corticosteroids, and intravenous catheterisation. A diagnosis was made by lung puncture and confirmed by rapid response to 5-fluorocytosine.

Pulmonary candidiasis is an invasion of viable lung tissue by *Candida* species. It has long been known that this occurs in patients with impaired host resistance—such as those with Hodgkin's disease or leukaemia, and those on cytotoxic therapy. In 1844 Bennett commented: 'it is indicative of great depression of the vital powers and impairment of the nutritive functions of the economy' (Winner and Hurley, 1966).

Candida colonisation is seen in the tracheo-bronchial tree of children with cystic fibrosis on long-term antibiotics. Pulmonary candidiasis, however, has not been reported in such children.

This is a report of a child with cystic fibrosis and asthma requiring corticosteroids, who developed pulmonary candidiasis and responded to treatment with 5-fluorocytosine.

Case report

A 6½-year-old girl had cystic fibrosis diagnosed in the first year of life and associated bronchial asthma. She was initially well maintained on standard antibiotic and physical therapy for cystic fibrosis

lung disease, with intermittent bronchodilator treatment for the asthma.

At age 5 years she required continuous bronchodilators and, subsequently, three intermittent courses of corticosteroids to control the wheeze. At 6 years more prolonged courses of high-dose prednisolone were necessary to control quite severe airways obstruction but these were reduced to a maintenance dose of 4 mg daily. During a course of high-dose prednisolone for an acute exacerbation of airways obstruction she became increasingly lethargic, lost weight, and developed a fever which reached 39°C daily. She developed rapid shallow breathing with fine inspiratory crepitations. Chest x-rays showed increased reticulonodular markings (Figure).

Intravenous cloxacillin and gentamicin, and later chloramphenicol and carbenicillin, were given for nearly 4 weeks without response. On several occasions sputum cultures grew *Escherichia coli*, *Streptococcus* species, *Haemophilus influenzae*, and *Achromobacter* species, but moderate to profuse growth of *Candida* species, not *C. albicans*, was always present. Multiple blood cultures were negative. Immune function tests were normal. Tuberculosis, autoimmune disease, and sepsis elsewhere were excluded.

A lung puncture was performed with instillation of 2 ml saline into the lung and aspiration of alveolar fluid. This fluid was smeared and cultured. A pure growth of *Candida* species, not *C. albicans*, was obtained.

She was started on 5-fluorocytosine orally; within

Figure Chest x-ray at the onset of the febrile illness. The lungs are overinflated. There is patchy nodular consolidation throughout both lung fields with prominent peripheral parenchymal opacities. The hilar vessels are prominent.

4 days her condition had improved, her appetite had returned, and she became ambulant for the first time in 2 months. She was afebrile within 10 days. Chest x-ray one month later showed significant clearing. 5-Fluorocytosine was continued for 6 weeks. She developed mild diarrhoea during the last week of this regimen.

Discussion

The rarity of pulmonary candidiasis is attributed to a natural resistance of columnar epithelium to invasion by the *Candida*, which is particularly prone to attack stratified epithelium. Pulmonary candidiasis occurs when there are impaired host defence mechanisms. It has been known to present as severe tracheobronchitis, bronchopneumonia, or pulmonary abscess. Although not usually seen in cystic fibrosis, predisposing factors in this child were a debilitating disease, prolonged antibiotic and corticosteroid therapy, and prolonged intravenous catheterisation (Hurley *et al.*, 1975).

Establishing a diagnosis can be difficult as was shown in this child. The clinical findings of tachypnoea and fever, with crepitations and rhonchi in the chest, are nonspecific and the radiological findings are not characteristic (Goldstein and Hoeprich, 1972). Candidaemia may not be associated with tissue invasion and, on the other hand, a negative

blood culture does not exclude invasive candidiasis (Mirsky and Cuttner, 1972). Sputum culture does not indicate invasion. The most reliable method of diagnosis is demonstration of the fungus in lung tissue histologically. Lung puncture is next best, but even so, *Candida* can be cultured from lung fluid without invasion (Klein, 1969; Bandt *et al.*, 1972).

Treatment of pulmonary candidiasis with 5-fluorocytosine appears to be effective (Kohlschütter and Pelet, 1974). There are few side effects with this drug, those described being predominantly anorexia, nausea, vomiting, and diarrhoea. There have been some reports of haemopoietic depression as well as renal and hepatic toxicity. *Candida* has been noted to develop resistance to 5-fluorocytosine. Amphotericin B has also been used for the treatment of candidiasis but it was not used in this instance because of its known toxicity. The combination of these two drugs in extremely ill patients has been recommended (Montgomerie *et al.*, 1975).

Pulmonary candidiasis, although a rare complication, should be considered in children with cystic fibrosis who develop a febrile illness not responding to antibiotics. This complication may become an increasing problem with the use of corticosteroids and long-term intravenous catheters in a small group of children with cystic fibrosis in whom this type of treatment appears warranted.

References

- Bandt, P. D., Blank, N., and Castellino, R. A. (1972). Needle diagnosis of pneumonitis. Value in high-risk patients. *Journal of the American Medical Association*, **220**, 1578-1580.
- Goldstein, E., and Hoeprich, P. D. (1972). Problems in the diagnosis and treatment of systemic candidiasis. *Journal of Infectious Diseases*, **125**, 190-193.
- Hurley, D. L., Balow, J. E., and Fauci, A. S. (1975). Experimental disseminated candidiasis. II. Administration of glucocorticosteroids, susceptibility to infection, and immunity. *Journal of Infectious Diseases*, **132**, 393-398.
- Klein, J. O. (1969). Diagnostic lung puncture in pneumonias of infants and children. *Pediatrics*, **44**, 486-492.
- Kohlschütter, A., and Pelet, B. (1974). Pulmonary candidiasis treated with 5-fluorocytosine. *Archives of Disease in Childhood*, **49**, 154-156.
- Mirsky, H. S., and Cuttner, J. (1972). Fungal infection in acute leukemia. *Cancer*, **30**, 348-352.
- Montgomerie, J. Z., Edwards, J. E., Jr, and Guze, L. B. (1975). Synergism of amphotericin B and 5-fluorocytosine for *Candida* species. *Journal of Infectious Diseases*, **132**, 82-86.
- Winner, H. I., and Hurley, R., editors (1966). *Proceedings of a Symposium on Candida infections*, London, May 1965, p. 87. Livingstone: Edinburgh.

Correspondence to Dr B. M. Jenner, Royal Children's Hospital, Flemington Road, Parkville, Melbourne, Victoria 3052, Australia.

Reprints from Dr L. I. Landau, Department of Thoracic Medicine, Royal Children's Hospital.