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Clinical and Autopsy Findings of a Nine-month-old Girl with Malnutrition and Pneumonia

Postmortem Study Case - 15/91

PRESENTATION OF THE CASE

A nine-month-old girl was admitted to the ICDDR,B Clinical Research Centre with a history of intermittent fever, watery diarrhoea and reluctance to take food for 10 days. The patient came from a family with low socioeconomic status; the father is a rickshawpuller earning $40 per month.

She was born at term in the hospital, but her birth-weight was not known. The girl had no major illnesses in the past and had received BCG and one dose of DPT and polio vaccines. She was breastfed and at the same time was given diluted formula milk and some rice curry.

The history given by the mother was that the child was well some 10 days previous to admission when she developed watery stools 4-5 times per day and intermittent fever, without chill or rigour. The child was severely anorectic, but had no vomiting and was treated at home with some unspecified medicines. No medical document was available.

On physical examination the patient was found to be lethargic, moderately dehydrated, and weighing 3.4 kg. Her weight for age was 36% of the NCHS median (1). The radial pulse of the child was 120/min. regular and of a moderate volume. The rectal temperature was 37.5°C and her respiration was 40/min. and regular. Oedema, jaundice, cyanosis and lymphadenopathy were absent. Her abdomen was distended, but soft; bowel sounds were present and active. The liver and spleen were not palpable. There was discharge from her left ear and she had scabies. Examination of other systems revealed no abnormality. A provisional diagnosis of watery diarrhoea with marasmus and acute suppurative otitis media was made on admission.

A routine blood count showed a total leukocyte count of 11800/mm^3 with 60% neutrophil, 39% lymphocyte, and a haematocrit of 31%. Serum electrolyte profile showed Na^+ 134.8 mmol/l, K^+ 2.34 mmol/l, Cl^- 120 mmol/l and TCO_2 8.0 mmol/l. Rectal swab culture yielded no growth. Dehydration, hypokalaemia and acidosis of the patient were treated initially with intravenous acetate solution (Na^+ 133 mmol/l, K^+ 13 mmol/l, Cl^- 90 mmol/l, HCO_3 48 mmol/l) supplemented with KCl and $NaHCO_3$, followed by ORS. Oral amoxicillin (50 mg/kg.d) and benzyl benzoate for local application was given for ear infection and scabies respectively. The child was also given vitamin A, zinc acetate and multivitamins.

On the 12th day after admission, the child's diarrhoea improved and she was transferred to the Nutrition Rehabilitation Unit (NRU). In the NRU the patient was offered halwa (a porridge containing rice, bengal gram, cane sugar and oil providing 2.4 kcal/g) along with breastmilk to increase caloric intake. But after 24 hours the watery diarrhoea recurred, and she was transferred back to the diarrhoea treatment unit where she was given a milk-cereal-based diet (milk powder 40 g, rice powder 40 g, sugar 25 g, soya oil 25 g, magnesium chloride 0.5 g, and kcl 1.5 g providing 67 kcal/100 ml).

On the 17th hospital day the patient developed fever and cough. At that time her lungs were clear clinically, but a chest radiograph showed bilateral infiltration. Since the patient had received amoxicillin earlier for the ear infection, erythromycin (75 mg/kg.d) was given to cover *Staphylococcus aureus* infection or atypical pneumonia. On the 24th hospital day the patient was highly febrile despite erythromycin therapy for 7 days, had bilateral rales on auscultation and the chest x-ray showed further deterioration. The blood count showed a total leukocyte count of 15,100/mm^3 with 60% neutrophil. The repeat serum electrolyte profile was normal. On suspicion of nosocomial pneumonia, after drawing blood for culture, ampicillin (200 mg/kg.d) and gentamicin (6mg/kg.d) were added to cover infection with probable Gram-negative organisms. However, the blood culture showed no growth. Over the next 7 days the patient deteriorated further both clinically and radiologically, but she had no diarrhoea.

At this stage, based on a positive Mantoux skin reaction (19x18 mm) and radiological and clinical deterioration despite adequate antibiotic therapy, pulmonary tuberculosis was diagnosed and antitubercular therapy was started. The therapy included INH (10 mg/kg.d), rifampicin (10 mg/kg.d), and pyrazinamide (30 mg/kg.d). On the 34th hospital day, the patient developed signs of heart failure and digoxin was started given. Finally, the patient died on the 35th day of hospitalisation. The cause of death as described by the attending physician was pulmonary tuberculosis with hospital acquired pneumonia and suspected septicaemia.

Clinical Case Discussion. During the long 35 days stay in the hospital, the clinical problems

encountered in this patient were: (a) diarrhoea, (b) hypokalaemia and acidosis, (c) acute suppurative otitis media, (d) pneumonia, and (e) terminal heart failure.

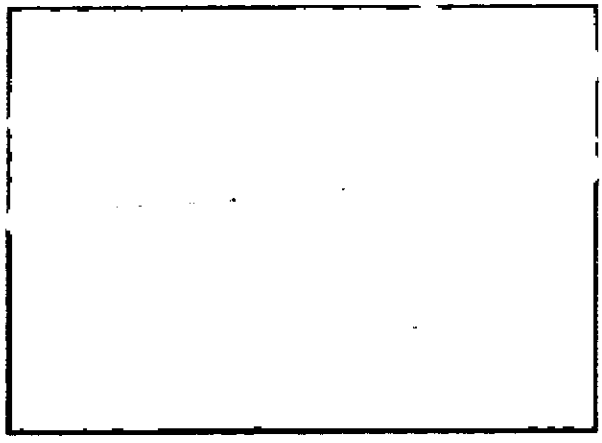

Fig. 1. Necrotising bronchitis with pneumonia in adjoining lung. H & E stain; original magnification X 13.2

The patient came to the hospital with watery diarrhoea of 10 days duration which continued for 22 hospital days. Pre-existing malnutrition in this child probably caused the persistence of diarrhoea in this case (2).

It is well established that infectious diseases run a more severe course in nutritionally deprived children (3,4) and septicaemia or respiratory infections due to Gram-negative organisms frequently complicate moderate to severe protein energy malnutrition (PEM) (5). In our patient, severe pneumonia can be explained by the severe PEM. It is more likely that the poor nutritional status of the child contributed to the immunodepression (4) which permitted the offending organisms to colonise and invade the respiratory epithelium to cause severe bronchopneumonia.

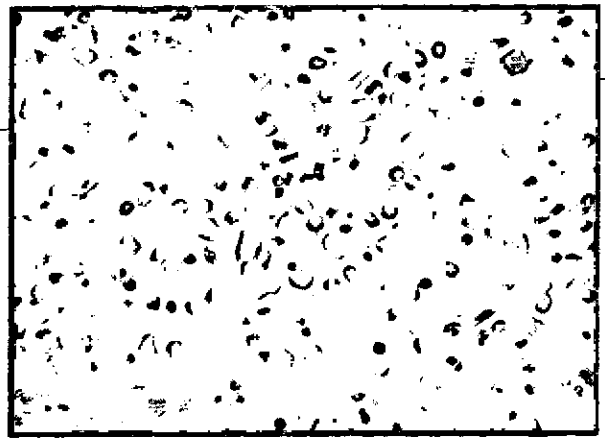

Fig. 2. Mononuclear infiltrate in lung lesions, also showing cells with "smudge nuclei" and an occasional cell with Cowdry type A intranuclear inclusion. H & E stain; original magnification X 133.

Despite adequate treatment with a proper antibiotic, the pneumonia did not resolve, rather it became worse. The cause of this unresolved pneumonia could be infection with viruses including *Cytomegalovirus*, respiratory syncisitial virus or systemic candidiasis or any other opportunistic microorganism. We failed to isolate any organism from the blood culture; however, we did not culture the lung aspirate.

The child was treated with antitubercular drugs without any improvement. The reasons might be that the poor nutritional status of the child did not permit her to fight against the organism or there was miliary dissemination. On the other hand, absence of any radiological evidence of miliary dissemination of the organisms and a strongly positive Mantoux reaction eliminate the possibility of miliary tuberculosis. The reason for terminal heart failure could be due either to severe bronchopneumonia producing anoxaemia and shock, or septicaemic shock.

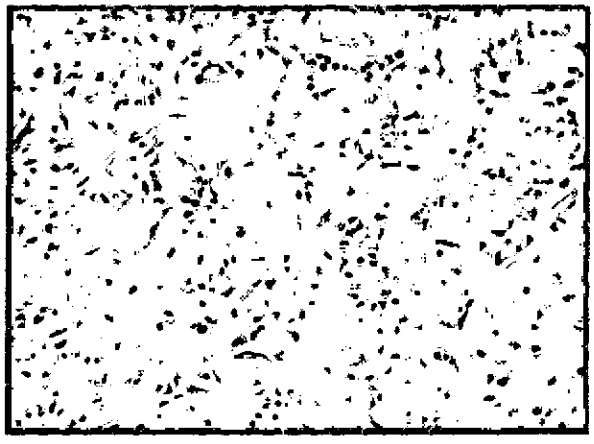

Fig. 3. Aggregation of multinucleated giant cells in alveolar exudate in lung. H & E stain; original magnification X 133.

Finally, the causes of death in this case can be summarised as follows:

Underlying cause	Immediate cause	Associated cause
PEM	Pneumonia	Persistent diarrhoea Tuberculosis

Clinical diagnosis:

1. Marasmus
2. Bronchopneumonia

Discussion On Postmortem Findings. An autopsy was performed five-and-one-half hours after death on this malnourished female infant. On opening the abdomen, distended loops of small intestine were seen. Other abdominal organs appeared unremarkable. The right lung showed consolidation of the apical part of the upper lobe, the whole middle lobe and the posterior part of the lower lobe. The cut

surface revealed scattered greyish white indurated patches in these areas of consolidation. The left lung also showed similar changes in the whole of the lower lobe and the medial aspect of the upper lobe. The heart was unremarkable. Microscopic examination of both lungs showed patches of necrotising pneumonia, interstitial pneumonia, necrotising bronchitis and bronchiolitis and oedema in adjoining lung parenchyma. The inflammatory infiltrate in these consolidated areas were predominantly mononuclear cells, among which Cowdry type A nuclear inclusions were present, and many "smudge cells" with indistinct nuclear membrane were seen. Scattered aggregates of giant cells were also present, but tuberculous granulomas or caseation were not seen. Acid-fast bacilli were not seen in Zeihl-Neelsen stained sections. The ileum and caecum showed focal superficial mucosal necrosis. Microscopy of other organs revealed no significant abnormality. Cultures of postmortem aspirates from both lungs were sterile. The pulmonary pathology in this patient is suggestive of viral pneumonia. The presence of necrosis "smudge cells' and Cowdry type nuclear inclusions are features of adenovirus pneumonia, which is possibly the cause of death in this infant. We have not been able to ascertain the etiology of the persistent diarrhoea.

Anatomical diagnosis

1. Bilateral adenovirus pneumonia
2. Severe malnutrition

Question – answer session:

Q. **Dr Kabir.** Did you think of amoebiasis or giardiasis as a cause of persistent diarrhoea in this case?

A. **Dr Mujib.** Yes, these may cause persistent diarrhoea. However, in a 9-month-old child, giardiasis and amoebiasis are not so common. Moreover, the absence of *Giardia* and *E. histolytica* on two subsequent stool microscopy limited their possibility.

Q. **Dr Serajul Islam.** I have two comments. First, as you have suggested that Gram-negative infection is a cause of pneumonia at the age of 9 months, I would really think first of a Gram-positive organism, because Gram-negative infections come first in children below the age of 3 months. So, *Staphylococcus* and *Streptococcus* come first, then *Pseudomonas*, *E. coli* and other organisms. The second point is, since this was a malnourished child, did you think of hypothermia, hypokalae-mia, or hypoglycaemia as likely complications?

A. **Dr Mujib.** Yes, nosocomial infection by either Gram-positive or Gram-negative organisms could have occurred. But as this patient was already treated with amoxicillin and erythromycin, we thought infection by resistant Gram-negative organisms was more likely. Nosocomial infection with Gram-negative organisms have been more common in our centre.

Regarding your second comment, I would agree that hypothermia, hypoglycaemia, and hypokalaemia could have occurred. However, the patient was not hypothermic as shown by the two hourly recording of her temperature. The blood glucose of the patient was found to be normal, and the serum electrolyte profile was also normal. So, I think these were not causes of death in our patient.

Q. **Dr Samiul.** To what extent does BCG protect against tuberculosis?

A. **Dr Mujib.** BCG prevents the haematogenous spread of the tubercle bacillus. In a country like ours where there are so many open cases, the time schedule of the BCG vaccination is very important, because, when we vaccinate, the child may already have developed a primary complex. So, it is very difficult to measure the protective role of BCG in this situation. Unfortunately, there is no case-control study in our country. The possibilities of disease also depend on the doses of exposure to acid fast bacilli only. One thing is sure, that it protects from haemotogenous spread.

Q. **Dr Samiul.** What could be the explanation of a strongly positive Mantoux reaction in a severely malnourished child?

A. **Dr Mujib.** Usually, in malnourished children the Mantoux reaction is low or negative. On the other hand, a strong positive reaction indicates that the child had a normal cellular immune response; this goes against our hypothesis that as a malnourished child our patient was immunocompromised. In this case it could be that the cellular response was normal, but the child had another immune deficiency, like opsonisation and humoral immune systems. Another possibility could be the error in measuring the diameter of the induration.

Q. **Dr Habte.** What do you think about the cause of such a severe degree of malnutrition (wt/age 36%) in a 9-month-old child?

A. **Dr Mujib.** It is most likely the malnutrition started before birth. Though we do not know the nutritional status of the mother, it can be postulated that undernutrition in the mother might have contributed to low birth-weight, followed by inadequate breast milk and finally diluted formula feed due to ignorance and poverty of the family.

Q. **Dr Kabir.** You were not able to identify acid-fast bacilli in the lung lesions. Do you think this could be due to the effect of anti-tubercular therapy which was given to this patient for quite some time?

A. **Dr M. Islam.** Although I do not know exactly

how long it takes to eradicate tubercle bacilli from tubercular lesions, I do not think it can be achieved after only twelve days therapy as in this infant. It may be possible to eradicate tubercle bacilli from the lesions after a full course of treatment, but even then the healed and fibrotic scars of tubercular lesions would persist which we have not seen in this patient.

Q. **Dr Nahrina.** Heart failure was mentioned as a cause of death in this case. What findings do you expect at postmortem in case of heart failure?

A. **Dr M. Islam.** In congestive heart failure of short duration, as in this patient, one would expect to find fluid in the pleural and peritoneal cavities, gross oedema in the lungs and centrilobular sinusoidal congestion and fatty change in the liver. However, storage of cadavers in a supine position results in pooling of blood in dependent areas of liver and mimics centrilobular congestion. In chronic heart failure a "nutmeg" appearance and centrilobular fibrosis in the liver are more characteristic.

Comment. **Dr MS Akbar.** I am not convinced that this infant had really developed heart failure. She had widespread interstitial pneumonia with consequent impairment of diffusion and hypoxaemia causing tachypnea and tachycardia which were thought to be due to heart failure.

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Errata: *Please refer to Clinicopathological Conference of the ICDDR,B.* A 1-Year Old Girl with Severe Malnutrition, Bloody-Mucoid Diarrhoea and Fever. Postmortem Study Case-2 of 1992. *J Diarrhoeal Dis Res* 1992;10(3):164-70.

On page 169. **Comments by Maj Gen M R Choudhury.** This is an interesting case of PEM complicated by fatal *Ascaris* infection. Ascariasis is an important public health problem in this country. More than 90% of children in rural Bangladesh have ascariasis. In the privileged class of our society including the army about 50% of the individuals have intestinal parasites. I think the role of ascariasis in childhood malnutrition should be adequately assessed.