

Nutritionally Acquired Immune Deficiency Syndromes (NAIDS): common but often not diagnosed early.

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Case Summary:

It has been the perception in some pacific island countries that the textbook presentation of kwashiorkor has decreased in incidence possibly due to improved public health services and economic development of the country. However, the diagnosis and treatment is nonetheless crucial to child survival. This paper discusses the clinical courses of 2 children with kwashiorkor whose presentation were not of that taught to medical students or even junior doctors. Their presentation together with their subsequent nutritionally acquired immune deficiency syndrome (NAIDS) is illustrated to raise awareness of the complexities in diagnosis and management of such patients.

Introduction

Childhood infections, coupled with underlying malnutrition are major contributors to childhood mortality which account to some 10 million deaths globally each year¹. The majority of these deaths are preventable and occur in developing countries with scarce resources. Although the diagnosis of malnutrition per se may not be listed as a primary cause of death in children aged 0 to 5 years, it is the underlying cause of death of 53% of deaths in this age group². The World Health Organization (WHO) has developed a set of criteria for the classification of malnutrition³ which is used in the developing countries. Severe malnutrition is also described as "severe wasting, severe stunting OR oedematous malnutrition"⁴. Oedematous malnutrition, the presence of bilateral pitting oedema of nutritional origin, is one type of the severe acute malnutrition (SAM) with an associated case fatality rate of up to 50 to 60% in some developing countries, these being complicated by concurrent infections, and gram negative septicaemia⁵.

In a majority of cases, the causes of malnutrition include poverty and poor socio-economic circumstances. These then lead to poor access to health facilities which can be prevented through economic development and improved public health measures. To this end, global programmes such as the Infant and Young Child Feeding programme and the Integrated Management of Childhood Illnesses had been developed by the World Health Organisation (WHO) and UNICEF to address these issues⁶.

Kwashiorkor (oedematous malnutrition) is typically seen in children between 2 to 3 years of age and its management, once diagnosed, is well described in several books of guidelines developed by WHO (7). However, non-typical presentations in patients admitted for other more obvious problems may be overlooked. The management of this severe underlying disease may then be delayed or even neglected.



The case histories of two such cases are presented and discussed below to raise awareness of a different perspective to the same disease and to illustrate the complexities of management if diagnosed late. This is especially so where treatment options beyond that described in treatment protocols for developing countries is limited.

Case History

Patient 1

The first patient was diagnosed with probable Hirshsprung's Disease at birth. The parents had refused consent for a rectal biopsy and colostomy. He was not brought for follow-up clinics and was admitted at 8 months of age for an entero-colitis. After only five days of antibiotics, his mother removed him from hospital. The child was readmitted at 13 months of age with a 2 day history of fever, irritability and a distended abdomen. He was diagnosed with bowel obstruction and probable septicaemia and was started on antibiotics whilst awaiting investigations. His weight on admission was 9.5 kg but decreased to 8.5kg five days later. His initial Full blood count was: Haemoglobin- 8.1g/dL; White Cell Count $10.6 \times 10^6/\mu\text{L}$ with left shift; platelet count of $367 \times 10^3/\mu\text{L}$. Urea and electrolyte measurements were normal and blood cultures were negative. Surgery for a de-functioning colostomy was again refused. He improved over the next few days but was noted to have peripheral oedema by a different team. Serum levels were then taken which showed a total protein of 29g/L (66 – 87 g/L); s/albumin of 12g/L (34-46g/L);s/globulin 17g/L (15-30g/L). (On questioning, his mother stated that the child's hands and feet were 'like that' before admission i.e. swollen. This was queried by the referring doctor but not noted by the admitting doctors) The parents later consented for surgical intervention but whilst awaiting further investigations the patient developed seizures and was found to be hypoglycaemic (Random Blood Sugar of 0 mMol/L), hypokalaemic (serum potassium of 1.7mMol/L) with deranged coagulation profile. He was in shock and was resuscitated. Over the course of the next few days, he developed signs of full blown kwashiorkor and despite intensive treatment for septic shock went into multi-organ failure and succumbed a week later.

Patient 2

The second patient was a term 3.6 kg neonate born normally with normal Apgar scores who presented with poor feeding with dehydration at 5 days of age. Ensuing investigations revealed small bowel atresia with malrotation. The first laparotomy with small bowel resection performed at 12 days of life was complicated by leakage from the anastamotic site and infection, despite being on triple antibiotics. A second operation followed a similar course. Over the next two months, the infant underwent a cycle of bowel anastamosis, post-operative infection; triple antibiotic therapy, breakdown of anastamosis with subsequent repair; leakage from the site and further severe infections with multi resistant Klebsiella. Nutritional deficiency was a concern but parenteral nutritional supplement was unavailable. When it was feasible the infant was fed enterally. Despite these attempts at feeding, little was absorbed and the weight decreased as low as 2.7kg before the onset of obvious oedema. Over the course of 3 weeks, the infant had a serum protein of 33 g/L with s/albumin being 17 g/L. He developed signs of full blown kwashiorkor a few weeks later and succumbed from a combination of overwhelming sepsis and end organ failure at 2 months of age.



Discussion

The earliest sign of Kwashiorkor is bilateral pedal oedema in the absence of another definitive diagnosis such as nephrotic syndrome. However, this sign in the absence of any other, is often unrecognised especially in inpatients who have had several intravenous infusions that have gone into tissue. This may therefore delay an early diagnosis. When this state progresses and kwashiorkor becomes full-blown as shown in the picture (figure 1) below, the diagnosis is not difficult.

Figure 1: Photograph showing swelling of both feet, dark peeling hyper-pigmented skin with areas of hypo-pigmentation typical of kwashiorkor.



Even in the early stage, normal physiological mechanisms are reduced and are unable to respond to stresses such as infection. Biochemical derangements such as hypoglycaemia and hypokalaemia as seen in the first patient are common causes of morbidity with hypo-albuminaemia being a hallmark of this condition. The physiological adaptations of worsening malnutrition are probably best illustrated through the understanding of normal metabolism.

In aerobic cellular metabolism, glucose is broken down for the production of ATP (energy source) with water and carbon dioxide as by-products. Caloric requirement for growth is listed as 100 to 120 kcal/kg/day⁸ with a minimum or maintenance requirement of 40kcal/kg/day for a sick child⁹. Whilst the initial response to 'starvation' is to compensate through the breakdown of glycogen stores, gluconeogenesis will utilise peripheral lipolysis and then amino acid oxidation from muscle stores¹⁰ once the glycogen stores are depleted. Thus insufficient oral intake for three to seven days in well nourished children is a trigger for supplemental feeding¹⁰.

In the first case scenario, the child had presented with severe malnutrition from chronic functional bowel obstruction (Hirschsprung's Disease). The effects of severe malnutrition are well illustrated in the article on the "physiologic basis for treatment of severe malnutrition" reproduced from a treatment manual by WHO⁴. Of particular note is the poor functioning of the immune system where the role of some micronutrients are shown to be essential to the functioning of many enzymes required for nucleic acid synthesis and cell replication¹¹.

Enterocolitis, the main presenting diagnosis, is a known severe complication of Hirschsprung's Disease and was adequately treated with the appropriate antibiotics. However, the severity of the nutritional deficiency



may not be addressed even if the diagnosis of kwashiorkor had been made earlier as a 10% dextrose solution at full maintenance volumes would only provide approximately half the required calories and nothing else. When the child manifested signs of metabolic failure, the management becomes very difficult. Hirshsprung's Disease, left uncorrected, will almost invariably lead to nutritional deficiency because of the functional malabsorptive state. For this reason, parents need to be carefully counselled as to the potential longer term complications so as to prevent such situations occurring.

In the second case scenario, the neonate had thrived on the maternal circulation in utero. However, mechanical bowel obstruction led to inadequate nutritional uptake as evidenced by a weight loss of 25% over the weeks in spite of enteral feeding of up to 100 mls/kg/day at one stage. Parenteral nutrition would have been indicated for such a neonate but was not available.

Severe malnutrition has associated micronutrient deficiencies even though this more commonly manifests as a macro-nutrient deficiency. Severe PEM results in generalised atrophy of the T-lymphocyte areas of the lymphoid tissue¹². There is a marked repression of cell mediated immunity with a loss of ability to destroy foreign tissue by killer lymphocytes¹³. When deficient, Vitamin A and zinc are micronutrients particularly linked to these defects with impaired IgG responses to protein antigens and also pathological changes to the surfaces of mucosa. The synthesis of new proteins is essential to all immunologic host defence mechanisms and is also dependent on other trace elements such as the B vitamins, iron, selenium and copper¹².

Both the case scenarios illustrated above are examples of nutritionally acquired immune deficiency syndromes (NAIDS). Both were young children with immature immune systems and small protein reserves. Both developed severe septicaemia with septic shock and were treated with triple antibiotics. Inability to absorb nutrients due to their surgical diseases complicated by recurrent infections resulted in their NAIDS. To quote: *"In fact, the combination of NAIDS and common childhood infections (...) is the leading cause of human mortality, producing more than ten million childhood deaths a year"*¹². Although NAIDS is reversible, in a situation where nutritional rehabilitation (in these patients, parenteral) is unavailable, the outcome becomes almost inevitable.

Conclusion

The case scenarios illustrated above demonstrates the challenges faced in developing countries such as the Pacific which are striving to provide optimal care in the absence of resources to support this. A better understanding of the physiological functioning of the body and pathological processes of diseases may raise the index of suspicion to early diagnoses. More importantly, this may create greater awareness for prevention of complications where health care providers may be more pre-emptive rather than be reactionary.

If diagnosed early and where available, there is a role for the use of parenteral nutrition as a nutritional supplementation even if this cannot be given as total parenteral nutrition (TPN). A basic pre-package formula such as G19 could be used over 48 hours before it has to be discarded. The basic principles for the management of severe malnutrition also need to be implemented conjointly. These include treating for possible underlying infection; hypoglycaemia and hypothermia with careful monitoring of electrolyte



balance and micronutrient supplementation. A comprehensive protocol is given in the WHO pocket book of Hospital care for children⁷.

The cases illustrated demonstrate scenarios where the development of kwashiorkor is to be expected given the clinical course. Awareness of such situations may hopefully lead to their prevention in the future.

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*“One’s first step in wisdom is to question everything
– and one’s last is to come to terms with everything.”*

Georg Christoph Lichtenberg

