CASE REPORT

Kwashiorkor: an unexpected complication to anorexia nervosa

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SUMMARY

We present the case of a woman aged 48 years, diagnosed with anorexia nervosa (AN) at the age of 12. She was admitted to a highly specialised eating disorder facility with distended abdomen, muscular atrophy, ulcerative dermatitis, electrolyte derangements and low serum albumin. Her weight was 53.1 kg, corresponding to a body mass index (BMI) of 17.9 kg/m². After initial stabilisation, a therapeutic ascites puncture relieved the patient from 6500 mL of ascites. After 6 weeks of nutritional and diuretic treatment, the patient was discharged with a weight of 46.8 kg (BMI 15.7 kg/m²), without ascites and with healed ulcerations. The condition was consistent with kwashiorkor, a complication to malnutrition rarely seen in AN.

BACKGROUND

Kwashiorkor is a nutritional syndrome caused by protein deficiency in the diet, meaning 'the disease of the displaced child'. Kwashiorkor is seen almost exclusively in the non-industrialised world, and reflects the condition in an older child who has been weaned from breast milk, replaced with a diet high in carbohydrates.¹ Although an authoritative definition of kwashiorkor is lacking, the syndrome is characterised by growth retardation, changes in the pigmentation of the skin and hair, oedema, hepatomegaly and distended abdomen. This is not only due to the enlarged liver, but also due to ascites, presumably explained by hypoalbuminaemia and low oncotic pressure.

Anorexia nervosa (AN) is a psychiatric disease characterised by refusal to maintain normal weight, fear of gaining weight, disturbed perception of body image, ambivalence, perfectionism and, according to the Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition (DSM-IV), amenorrhoea.

Although multiple malnutrition-related manifestations are well described in AN,² the presentation differs somewhat from that of kwashiorkor. Cardiovascular features include bradycardia, hypotension and oedema and gastrointestinal findings are, among others, dysphagia and constipation due to gastroparesis and impairment of colonic function. Hepatic transaminase levels can be elevated, and may be explained by a combination of starvation-induced hepatocyte autophagy and decreased perfusion of the liver, resulting in ischaemia. Common dermatological manifestations include the presence of hypopigmentation of hair in face and body and acrocyanosis. Ulcerations,

however, are not common. Finally, even with prolonged protein energy malnutrition, hypoalbuminaemia is rarely seen in AN.^{3 4}

We report the case of kwashiorkor as a complication to malnutrition in a patient with long-standing AN.

To the best of our knowledge, kwashiorkor in the absence of alcohol abuse or other comorbidities has not previously been described in relation to AN.

CASE PRESENTATION

A woman aged 48 years was admitted to our specialised nutrition unit in poor nutritional condition with impaired general well-being, and electrolyte derangement. She had a history of AN for more than 30 years with a total of three prior admissions with dehydration and electrolyte derangement. There was no history or evidence of abuse of laxatives, diuretics nor alcohol. She had been bedridden for about 3 months prior to the admission nursed by her husband. At admission, she was extremely weakened and unable to stand on her feet without support. Her weight and height was 53.1 kg and 1.72 m, corresponding to a body mass index (BMI) of 17.9 kg/m².

Initial workup revealed high diastolic blood pressure (134/101 mm Hg) and increased heart rate (127 bpm).

Physical examination showed a distended and diffuse tender abdomen (figure 1). The extremities presented with atrophy of the muscles, dry skin and multiple small ulcerations (figure 2).

INVESTIGATIONS

Blood samples are shown in figure 3. On admission, anaemia, decreased albumin, hypernatraemia

Figure 1 Distended and diffuse tender abdomen at admission.

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Figure 2 Extremities with atrophy of the muscles, dry skin and multiple small ulcerations.

and a small increase in C reactive protein was noted. An ECG revealed sinus tachycardia, otherwise normal. Urine analysis showed no sign of albuminuria. Ultrasonic assessment of the abdomen revealed ascites and an enlarged liver. Liver biopsy was considered; however, we abstained from it in the light of the ultrasound without focal pathology, ascites without tumour cells and the fact that the patient clearly improved during the nutrition therapy.

Urine cultures showed a significant count of *Escherichia coli*, and a swab from the ulcerations of the lower legs showed a significant count of *Staphylococcus aureus* on culture. Blood cultures yielded negative results.

DIFFERENTIAL DIAGNOSIS

- ▶ Alcohol abuse
- ▶ Diuretic abuse
- ▶ Malignancy
- ▶ Bacterial infection

TREATMENT

The initial refeeding was carried out in accordance with the *Management of Really Sick Patients with Anorexia Nervosa* (MARSIPAN) guideline on nutrition,⁵ starting at 4700 kJ/day for this patient. A commercial available nutritional solution with 50% carbohydrate, 15% protein and 35% fat (Resource Complete Nutrition, Nestle Healthcare Nutrition) was used. The energy content in the diet was gradually increased, to attain full demands after 10 days of hospitalisation.

Figure 3 Biochemistry. Asterisk indicates deviation from references. ALT, alanine transaminase; LDH, lactate dehydrogenase; GGT, γ -glutamyl transpeptidase; KFNT, coagulation factor II, VII, X; HbA1C, glycated haemoglobin; T3, triiodothyronine; T4, thyroxine.

Parameter	References	Admission	1 week	2 weeks	3 weeks	4 weeks	6 weeks
Hgb (mmol/L)	7.3-9.5	5.5*	5.5*	6.0*	6.6*	6.9*	7.2*
WBC (10E9/L)	3.5-8.8	8.62	8.65	9.11*	10.2*	9.04*	
Albumin (g/L)	36-48	20*	19*	25*	32*	33*	36
Phosphate (mmol/L)	0.76-1.41	1.05	1.23	1.49*	1.53*	1.7*	1.37
Potassium (mmol/L)	3.5-4.4	4.3	3.8	4.1	4.1	4.1	3.6
Creatinine (μ mol/L)	45-90	57	44*	42*	42*	45	54
Magnesium (mmol/L)	0.71-0.94	0.71		0.75	0.72	0.77	0.66*
Sodium (mmol/L)	137-145	134*	134*	138	136*	136*	141
Bicarbonate (mmol/L)	22.0-26.0	22.0	23.3	22.6	23.2		24.5
KFNT (U/L)	0.70-1.30			0.76	0.77		0.9
ALT (U/L)	10-45	<6*	15	13	7*		9*
Alkaline phosphatase (U/L)	35-105	104	235*	161*	131*		83
GGT (U/L)	10-75	56		239*	185*		
LDH (U/L)	105-205		261*			237*	
Myoglobin (μ g/L)	<61					21	
CRP (mg/L)	<6	18*	38*	16*	8.4*		
TSH (10E-3IU/L)	0.3-4.0	1.3		4.8*	3.3		
Thyroxine (mmol/L)	60-130	78		80	72		
Triiodothyronine (mmol/L)	1.3-2.2	1.0		2.1	1.7		
Zinc (μ mol/L)	10.0-19.0			7.0*			

Vitamin supplement with a vitamin B preparation (including thiamine, B2 and B6 vitamins), zinc and multivitamins as well as thrombosis prophylaxis were prescribed. The anaemia was corrected with a single blood transfusion. Based on the antibiotic resistance pattern, the bacterial infection in the ulcerations was treated with oral dicloxacillin. Ultimately, 6500 mL of ascites was drained, followed by infusion of 250 mL (12.5 g, CSL Behring, Marburg, Germany) human albumin. A normal cell count and no bacteria or tumour cells were found in the cultures from the ascites fluid.

OUTCOME AND FOLLOW-UP

As a result of ascites drainage and diuretic treatment, and under continued antithrombotic treatment, her weight was reduced by 10 kg over a period of 3 weeks. With intense physiotherapy, she was gradually mobilised to an extent where no assistive facilities were necessary in order to take the stairways.

The patient was discharged after 6 weeks of treatment with a weight of 46.8 kg equalling BMI 15.7 kg/m², and further follow-up in the outpatient clinic. At discharge, the ulcerations on the lower extremities were dry and healed.

In continuation of the admissions, she was offered psychiatric treatment, but declined. The cause of this is unknown, but it is well known that there are a high dropout rate and resistance to psychotherapy among patients with AN.⁶

DISCUSSION

We report the case of an AN patient referred to our nutritional unit with enlarged liver, ascites and skin ulcerations, a clinical presentation consistent with the kwashiorkor syndrome. Although effects of malnutrition on the gastrointestinal and dermatological systems are common in AN, kwashiorkor is a rare complication to AN, and almost exclusively seen among the paediatric population in developing countries. This case provides information about the approach in a rare case of kwashiorkor in AN.

Our patient presented with ascites, most likely attributed to hypoalbuminaemia. The association between malnutrition, albumin metabolism and ascites is by no means straightforward, and even with severe malnutrition, hypoalbuminaemia is not common in AN,^{3 4 7} and does not serve as a predictor of nutritional status. Why patients with chronic malnutrition unrelated to AN develop hypoalbuminaemia, and AN patients do not, is not known. A possible explanation in our case could be the combination of decreased supply of amino acids, and infection,

as inflammation is known to decrease albumin mRNA levels.⁸ In addition to hypoalbuminaemia, vitamin deficiencies and oxidative stress have been proposed as part of link between malnutrition and ascites, but any definitive explanation remains to be found.⁹

In terms of hypoalbuminaemia and oedema, kwashiorkor share several features with the nephrotic syndrome. As our patient had no protein loss through the kidneys, the explanation must be decreased intake of amino acids and/or impaired albumin synthesis in the liver, although levels of coagulation factors and alanine transaminase (ALT) were normal. During renutrition, the s-albumin of the patient slowly increased and reached normal values within 6 weeks, supporting the diet as the key factor.

In addition to ascites, an enlarged liver contributed to the abdominal swelling observed at admission. The mechanism leading to fatty liver in kwashiorkor is believed to be decreased production of lipoproteins, leading to accumulation of lipids in the liver.¹⁰ Indeed, the ultrasonography was consistent with hepatic steatosis rather than cirrhosis.

As part of the kwashiorkor syndrome, our patient presented with ulcerations on the lower extremities. Although ulcerations per se are not common in relation to AN, dermatological manifestations of poor nutrition in eating disorders have been described. Escá et al¹¹ reported a dermatological case concerning a woman aged 26 years with kwashiorkor and acrodermatitis. This patient's eating disorder was disclosed by psychiatric examination in the period of hospitalisation. During substitution with zinc, the ulcers on the lower extremities healed. Later, Abbott et al¹² described a woman aged 28 years with eating disorder and a 6-month history of rash on the lower extremities. At examination, she had ascites and peripheral oedemas. The BMI was 15 kg/m². She admitted to an alcohol intake of 100 units/week, contributing to an early development of cirrhosis as well as failure in hepatic albumin synthesis causing oedemas.

These two cases outline the eczematous rashes as a result of zinc deficiency and moreover describe how excess intake of alcohol can result in a kwashiorkor-like condition. Since ulcerations typically not are associated with zinc deficiency, the subnormal levels of zinc (7.0 µmol/L) in our case seemed not to be the cause of her ulcerations, which most likely can be ascribed as part of the kwashiorkor syndrome. Nevertheless, it has been described as a result of zinc deficiency in vegetarian patients with AN.¹³

Zinc binds to albumin and zinc deficiency is thereby associated with hypoalbuminaemia. This relationship could be the cause of the low zinc concentration seen in our patient.

In regard to the role of alcohol, our patient did not report excess intake of alcohol, and we had no reason to suspect otherwise.

Over the years, there have been several speculations regarding the pathogenesis of kwashiorkor, especially in regard to inadequate protein intake and/or excessive oxidative stress.¹⁴ However, there is still no substantial evidence for any of those hypotheses. A recent breakthrough study by Smith et al¹⁵ implicates the gut microbiota as a central factor in the cause of kwashiorkor. To investigate the role of the gut microbiota, faecal microbiota samples from monozygotic and dizygotic Malawian twin pairs discordant for kwashiorkor were transplanted into gnotobiotic mice, allowing them to get insight of the pathogenesis of kwashiorkor. Results from subsequent dietary experiments implicated certain gut microbiome profiles combined with the Malawian diet, as a causal factor in kwashiorkor.

Trehan et al¹⁶ later supported the hypothesis in their randomised, double-blinded, placebo-controlled trial. They randomly assigned Malawian children with severe acute malnutrition amoxicillin, cefdinir or placebo for 7 days, in addition to therapeutic food. The results showed a significant improvement in recovery and mortality rates.

Our patient was treated with dicloxacillin because of her ulcerations and consistent to the aforementioned theory of microbiota, this might have been contributing to her recovery.

At present, the gut microbiota from patients with AN has only been sparsely studied. A case report by Gouba et al¹⁷ investigated the eukaryote communities in the gut of an anorexic woman with a BMI of 10.4 kg/m² finding four microeukaryotes not previously described. In a recent study, Kleiman et al¹⁸ found an association between levels of depression and eating disorder symptoms and the diversity and composition in intestinal microbiota. The clinical significance of these findings, as well as the pathophysiological link, is yet to be uncovered, and further investigation is much needed.

In summary, our case demonstrates kwashiorkor as a very rare condition secondary to AN. To the best of our knowledge, this is the first report of kwashiorkor secondary to known AN, in patients with no abuse of alcohol. The case raises important questions concerning how the individual AN patient is affected by malnutrition with implications on diagnostics and treatment. Analysis of gut microbiota from patients with AN¹⁹ may potentially play a role in future studies in order to determine the pathogenesis of different forms of malnutrition. The role of antibiotics in the treatment of malnutrition in the Western world is yet to be assessed, and clearly an area for future research.

Learning points

- ▶ Kwashiorkor is a nutritional syndrome not exclusively found in children in tropical areas.
- ▶ Anorexia nervosa (AN) is a syndrome of unknown aetiology with multifaceted clinical manifestations.
- ▶ Kwashiorkor can be seen in AN patients.
- ▶ Severe hypoalbuminaemia is not common in AN, and should be thoroughly investigated.

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Competing interests None declared.

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REFERENCES

- 1 Kwashiorkor. A nutritional disease of children associated with a maize diet by Cicely D. Williams from the Lancet, Nov. 16, 1935, p. 1151. *Nutr Rev* 1973;31:350–1.
- 2 Mehler PS, Brown C. Anorexia nervosa—medical complications. *J Eat Disord* 2015;3:11.
- 3 Huysentruyt K, De Schepper J, Vanbesien J, et al. Albumin and prealbumin levels do not reflect the nutritional status of female adolescents with restrictive eating disorders. *Acta Paediatr* 2016;105:e167–9.
- 4 Narayanan V, Gaudiani JL, Mehler PS. Serum albumin levels may not correlate with weight status in severe anorexia nervosa. *Eating Disord* 2009;17:322–6.

- 5 MARSIPAN: Management of Really Sick Patients with Anorexia Nervosa Royal College of Psychiatrist 2014 Contract No: College Report 189.
- 6 Dejong H, Broadbent H, Schmidt U. A systematic review of dropout from treatment in outpatients with anorexia nervosa. *Int J Eat Disord* 2012;45:635–47.
- 7 Krantz MJ, Lee D, Donahoo WT, *et al.* The paradox of normal serum albumin in anorexia nervosa: a case report. *Int J Eat Disord* 2005;37:278–80.
- 8 Moshage HJ, Janssen JA, Franssen JH, *et al.* Study of the molecular mechanism of decreased liver synthesis of albumin in inflammation. *J Clin Invest* 1987;79:1635–41.
- 9 Golden MH. Nutritional and other types of oedema, albumin, complex carbohydrates and the interstitium—a response to Malcolm Coulthard's hypothesis: oedema in kwashiorkor is caused by hypo-albuminaemia. *Paediatr Int Child Health* 2015;35:90–109.
- 10 Onitiri AC, Boyo AE. Serum lipids and lipoproteins in children with kwashiorkor. *BMJ* 1975;3:630–1.
- 11 Esca SA, Brenner W, Mach K, *et al.* Kwashiorkor-like zinc deficiency syndrome in anorexia nervosa. *Acta Derm Venereol* 1979;59:361–4.
- 12 Abbott RA, Robson A, O'Donoghue N. Acquired loss of hair pigment associated with a flexural dermatosis. *Clin Exp Dermatol* 2009;34:735–6.
- 13 Bakan R, Birmingham CL, Aeberhardt L, *et al.* Dietary zinc intake of vegetarian and nonvegetarian patients with anorexia nervosa. *Int J Eat Disord* 1993;13:229–33.
- 14 Golden MH, Ramdath D. Free radicals in the pathogenesis of kwashiorkor. *Proc Nutr Soc* 1987;46:53–68.
- 15 Smith MJ, Yatsunenko T, Manary MJ, *et al.* Gut microbiomes of Malawian twin pairs discordant for kwashiorkor. *Science* 2013;339:548–54.
- 16 Trehan I, Goldbach HS, LaGrone LN, *et al.* Antibiotics as part of the management of severe acute malnutrition. *N Engl J Med* 2013;368:425–35.
- 17 Gouba N, Raoult D, Drancourt M. Gut microeukaryotes during anorexia nervosa: a case report. *BMC Res Notes* 2014;7:33.
- 18 Kleiman SC, Watson HJ, Bulik-Sullivan EC, *et al.* The intestinal microbiota in acute anorexia nervosa and during renourishment: relationship to depression, anxiety, and eating disorder psychopathology. *Psychosom Med* 2015;77:969–81.
- 19 Kleiman SC, Carroll IM, Tarantino LM, *et al.* Gut feelings: a role for the intestinal microbiota in anorexia nervosa? *Int J Eat Disord* 2015;48:449–51.

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