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Refeeding oedema in anorexia nervosa

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ABSTRACT

Refeeding oedema in patients with anorexia nervosa is a known but yet under-reported and poorly-understood condition. We illustrate this condition in a 19-year-old girl with anorexia nervosa who developed bipedal oedema after she was started on nutritional therapy. It is important to be aware of the differential diagnoses of oedema in such cases, which includes heart failure and previous diuretic abuse. Refeeding oedema generally resolves spontaneously but some individuals may require treatment.

Keywords: anorexia nervosa, eating disorder, oedema, refeeding oedema

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INTRODUCTION

The occurrence of pedal oedema in patients with anorexia nervosa undergoing refeeding therapy is known to psychiatrists[1] but to our knowledge, there are no preceding case reports written on it and little is known of the incidence, pathology and possible treatment of this condition. Very often, few investigations are performed to elucidate the cause when the patients are seen in psychiatric units because the oedema often resolves spontaneously as refeeding continues. We would like to illustrate the condition with a case, and to review the existing literature on the current understanding of the possible pathology and management of such cases.

CASE REPORT

A 19-year-old girl studying in a local university was known to have the restricting form of anorexia nervosa for which she had been on follow-up with a psychiatrist. She had no history of other medical problems and was not on any medication. She was referred to the medical unit for nutritional rehabilitation and medical stabilisation. Her weight had steadily fallen from 48 kg to 36.6 kg over a year. She had asymptomatic sinus bradycardia with a heart rate of 40 beats per minute.

She was started on nutritional rehabilitation and developed bipedal oedema about six days later. Her jugular venous pressure was not raised and there were no signs of pulmonary oedema, pleural effusion, or ascites. The oedema became moderately severe, and the patient experienced emotional upset due to physical discomfort and inability to walk properly.

Investigations performed ruled out hypoalbuminaemia, renal failure, liver failure, cardiac failure, proteinuria, hypothyroidism, and obstruction to venous drainage due to an abdominal mass. Total protein was 82g/L, and albumin was 43g/L (not low on repeated samples). Liver enzymes were within normal range. Urine total protein was 0.01 g/L. Urea was 2.4 mmol/L, creatinine was 60 umol/L, potassium was 4 mmol/L, sodium 135 mmol/L, chloride was 97 mmol/L, bicarbonate was 26 mmol/L, calcium was 2.21 mmol/L, phosphate was 1.25 mmol/L, and magnesium was 0.92 mmol/L (all within the normal ranges). The urinary pH was 7.0.

Thyroid stimulating hormone level was 4.5 mU/L, and free thyroxine level was 12.3 pmol/L. Serum levels of antibodies against thyroid peroxidase, thyroglobulin, and thyroid hormone receptors were all low. Her chest radiographs were normal. Ultrasonography of both lower limbs did not reveal any deep vein thrombosis. D-dimer level was normal. Computed tomography of the abdomen and pelvis did not reveal any masses. Two-dimensional echocardiography was normal and the ejection fraction was 66%.

Investigations for her secondary amenorrhoea revealed deficient gonadotrophins with low levels of oestradiol (24.9 IU/L), luteinising hormone (0.1 IU/L), and follicular stimulating hormone (0.5 IU/L). Global hypopituituarism was considered unlikely, given that investigations revealed no disturbance to the other hypothalamic-pituitary hormonal axes – urine 24 hour cortisol was 191 nmol/day and prolactin was 115 mlU/L (both within normal ranges).

Empirical treatment consisting of multivitamins and thiamine was given without significant resolution. Frusemide and elevation of her legs were tried

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but improvement was transient. Her nutritional rehabilitation was continued and she began to gain weight slowly but progressively. Her oedema eventually resolved spontaneously about one month after it began.

DISCUSSION

The pathogenesis of refeeding oedema is complex. In general, two basic mechanisms are involved in oedema formation, namely: an alteration in capillary haemodynamics that favours the movement of fluid from the vascular space into the interstitium, and the retention of sodium and water by the kidneys. As shown in the above case, the pathogenesis is not that of hypoalbuminaemia, cardiac failure, renal failure, chronic liver disease, hypothyroidism, obstruction to venous outflow, or thiamine deficiency.

During refeeding, there is increased secretion of insulin and it has been proposed that insulin release can result in significant oedema[2]. Insulin can promote sodium and potassium reabsorption in the diluting segment of the distal nephron and this effect is largely attributed to hypokalaemia[3,4]. The role of glucagon has also been implicated - increased levels of glucagons during starvation exhibit a natriuretic effect[5], whereas decreased levels during refeeding enhances anti-natriuresis in the distal tubule[6].

Secondary amenorrhoea occurs in anorexia nervosa due to the deficiency of gonadotrophins. During refeeding, production of gonadotrophins, oestrogens and progestogens increase with occasional development of acne and breast tenderness and the eventual resumption of menstruation. In recent years, the multiple vasoactive functions of oestrogens have gained increasing recognition. For instance, oestrogen has been shown to induce pronounce non-genomic endothelial dependent nitric oxide mediated vasodilation[7]. Refeeding oedema may be related to these humoral changes, and this has been supported by the observation of hypothalamic disturbances in cyclical oedema[8]. The hormonal changes may result in an increase in capillary permeability, and this is enhanced by gravity during standing. This is supported by the observation that the oedema is confined to the lower limbs of patients who are ambulating and there is no evidence of pleural effusion or ascites.

It is also important to rule out other causes of oedema in an anorexic patient undergoing treatment. Prolonged periods of diuretic abuse for the purpose of weight loss are common in anorexia nervosa, and the resultant hypovolaemia activates the renin-angiotensin-aldosterone system. This humoral adaptation may not reverse as quickly when diuretics are ceased abruptly, and can result in initial oedema with spontaneous resolution over a period of time. An important differential diagnosis to rule out in refeeding oedema is cardiac failure. Patients with anorexia nervosa lose a significant amount of body mass during starvation and coupled with the reduced demand, this can lead to reduced ventricular mass and myofibrillar atrophy[9,10]. During refeeding, the sudden ingestion of relatively large amounts of nutrients can overwhelm the diminished capacity of the cardiovascular system and result in heart failure.

It is also prudent to exclude general causes of oedema, which are hypoalbuminaemia (occurring in chronic liver disease, nephrotic syndrome, protein losing enteropathy), renal failure, heart failure, and hypothyroidism, especially in patients with risk factors. Less common causes to consider are thiamine deficiency and the use of insulin with oral hypoglycaemic agents (especially the thiazolidinediones)[2]. As refeeding oedema usually resolves spontaneously, most patients do not need treatment. However, in cases where the oedema is severe, low dose diuretics can be given in the early morning (since the oedema primarily accumulates during the day when the patient is erect). Another benefit of treatment is that it confers psychological assistance to patients who are already finding it difficult to cope with the changes in their body shape.

Using an angiotensin converting enzyme (ACE) inhibitor may help in reducing the degree of oedema. The mechanism is via the inhibition of secondary hyperaldosteronism which is induced by standing[11]. ACE inhibitors, however, do not prevent capillary leak and the intravascular volume depletion can cause significant hypotension. In refractory cases, increasing sympathetic activity with medications such as ephedrine may be tried. Ephedrine has been successful in cases of idiopathic oedema[12] and insulin-induced oedema[13,14]. It probably works by causing an increased precapillary sphincter tone with resultant decreased capillary leak.

In conclusion, refeeding oedema is most likely a form of vasogenic oedema. One has to be aware of the differential diagnoses of oedema in an anorexic patient undergoing nutritional rehabilitation. Refeeding oedema generally resolves spontaneously. Preparing the patients psychologically and addressing the problem will aid in the psychiatric management of patients with anorexia nervosa.

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