Case Report

Prolonged acute renal failure after i.v. immunoglobulin therapy in the refeeding phase of anorexia nervosa

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Introduction

Anorexia nervosa is a chronic disorder with a possible genetic susceptibility [1] characterized by self-induced weight loss due to body-image disturbance. The cardiovascular system adapts to starvation, e.g. reducing maximal work capacity and attenuating the blood pressure response to exercise [2]. The kidney is privileged compared to other organs, e.g. heart and brain, in that its workload is reduced in proportion to starvation. Glomerular filtration rate and hence the reabsorptive work of tubular cells decrease [3].

Much emphasis has been given to maintain patients with anorexia nervosa in an adequate state of nutrition. But since psychiatric intervention is frequently not sufficient and since ethical and social considerations delay nutritional intervention, undernutrition is often the dominant feature of the disease. Voluntary forced feeding implies that patients agree to tube feeding in order to prevent further deterioration and death. This manoeuvre has been used in many clinical settings. However, particular care must be taken to avoid complications of refeeding. Too vigorous nutritional repletion may lead to fluid and electrolyte imbalance, and to cardiovascular and neurological symptoms. The refeeding syndrome potentially causes considerable morbidity and mortality [4,5].

We report a case in which the refeeding syndrome was not initially recognized with the neurological symptoms having been mistaken for an acute Guillain–Barré syndrome. The patient received intravenous immunoglobulin (i.v.Ig) treatment and developed severe and prolonged acute renal failure.
Heart failure and acute areflexic paralysis are classical signs of the refeeding syndrome \cite{4,5} causing considerable morbidity and mortality. During and after World War II starving prisoners and victims were found to have markedly increased cardiac insufficiency, hypertension, peripheral oedema, convulsions, and coma after restoration of normal food and liquid intake \cite{6}.

In the late 1940s, the adverse consequences of refeeding were described in a now classical study, the Minnesota Experiment, in which in previously healthy subjects the effects of drastic food restriction and subsequent oral refeeding were studied \cite{7}. In its usual definition, the refeeding syndrome is the severe hypophosphataemia and its attendant complications involving the cardiac, pulmonary, neuromuscular, and haematological organ systems in patients being refed with total parenteral nutrition after significant weight loss \cite{8}. In a broader, more complete definition it includes other electrolyte abnormalities, vitamin deficiencies, fluid and glucose intolerance, and secondary complications \cite{5}.

Under conditions of starvation, the decrease in basal metabolic rate corresponds to an overall decline in liver gluconeogenesis and adipose tissue mobilization, together with a reduction in insulin secretion. The brain adapts to this situation by using fatty acids and fat substitutes as energy sources in addition to glucose. Various organs, e.g. the heart and intestine, decrease in size and function. Abrupt refeeding, particularly with carbohydrates, creates an anabolic state with hyperinsulinaemia, an increased need for electrolytes, e.g. potassium, magnesium, and phosphate, and results in a decreased sodium and water excretion. This leads to a sudden and rapid expansion of the extracellular fluid volume, precipitating heart failure in a heart not prepared to such an increase in function (reduced contractility, decreased left ventricular mass) \cite{4}.

Today, the clinical picture of the refeeding syndrome is seen only rarely in Europe. Therefore, in our patient the probability of a Guillain–Barré syndrome was overestimated and an unnecessary i.v.Ig treatment was started. The improvement in heart function and neuropathy followed the usual course described in this syndrome after having corrected the generalized fluid and electrolyte imbalance \cite{5}.

However, the refeeding syndrome is not known to induce renal damage, except for the sequelae of hypokalaemia (decreased urinary concentrating ability and decreased glomerular filtration rate), and of myoglobinuria secondary to rhabdomyolysis \cite{4,5,9}. Prerenal failure may occur at the time of severe heart failure. But in the patient presented here the blood pressure never decreased, creatine kinase never increased, and there was no myoglobinuria and no hypokalaemia. The heart failure was reversible after a short time as seen by a normal cardiac index as well as an improving ejection fraction. It did not lead to acute tubular necrosis as proven by the renal histology. The fact that the oligoanuria started 24 h after the start of high-dose...
failure in adults, mainly related to tubular dysfunction [11,12]. I.v.Ig produce aminoaciduria and proximal tubular cell proteinuria even without changing the creatinine clearance [13]. Interestingly, to our knowledge this problem has mainly been observed with i.v.Ig preparations containing sucrose, including Sandoglobulin. Experimental studies performed in animals many years ago have shown that hypertonic sucrose produces a marked degree of proximal tubular cell swelling and vacuolization which might be related not only to the hypertonicity of the solution, but also to a toxic effect of the sucrose itself as suggested by others [11,14,15].

In our patient the very early onset (24 h) and the prolonged duration of the renal failure were atypical. In most published cases renal failure associated with i.v.Ig therapy started only after 2–3 days and resolved within 14 days after discontinuing the treatment [11]. Also in contrast to many other cases, this patient was young and did not have an underlying renal disease. Thus, it must be speculated that other factors such as the refeeding syndrome, the anorexic state, and/or the hypophosphataemia [9] have contributed to the prolonged but reversible renal failure. An attractive explanation would be that the undernutrition potentiated the i.v.Ig toxicity. In particular the sucrose

\[ \text{Fig. 3. Marked swelling and vacuolization of the tubular cells without tubular necrosis and without glomerular damage ('osmotic nephrosis') H&E stain.} \]
load may have led to immediate and severe cellular dysfunction in nutrient-deficient proximal tubular cells.

References


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