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Life-threatening Folic Acid Deficiency: Diogenes Syndrome in a Young Woman?

To the Editor:

Profound anemia due to dietary restriction is uncommon in the United Kingdom. If it does occur, it may be an indicator of severe malnutrition and concurrent risk of provoking refeeding syndrome. Screening for the risk of refeeding syndrome in patients with profound anemia secondary to nutritional restriction is strongly advised.

A clinical presentation of extreme self-neglect in elderly individuals with multiple nutritional deficiencies and life-threatening illness was described in patients with a high intelligence quotient, often with successful careers, but who latterly tended to live in squalid surroundings and neglect their personal hygiene and nutrition. Patients had mild deficiencies of iron and folate often with anemia. The authors referred to this constellation of circumstances as Diogenes syndrome.[1] This presentation is not uncommon in elderly patients who are seen in acute medical admission units in the United Kingdom, but it is rarely seen in young women except perhaps in the context of alcohol excess or drug misuse. We describe a case consistent with Diogenes syndrome but with much more profound upsets in clinical parameters and posing substantial treatment associated risks.

CASE REPORT

A 28-year-old white woman was referred to the hospital emergency department in an obtunded state. She was unable to give any history, but her partner stated that she had experienced intermittent abdominal pain and diarrhea for 6 weeks, had stopped eating and drinking, and had become socially withdrawn and uncommunicative. There was a history of opioid use, although this had reduced dramatically in the preceding 2 weeks. She was profoundly pale with mild jaundice, cachexia, tachycardia, and hypotension with cool peripheries but afebrile. Investigations are listed in Table.

She was transferred to the intensive care unit and commenced intravenous thiamine, folinic acid, vitamin K, and hydroxocobalamin on the basis that her cachexia and profound macrocytic anemia were likely to indicate an underlying nutritional deficiency. Subsequently, absolute folic acid deficiency was confirmed, and intravenous thiamine and folinic acid were continued.

She received nasogastric feeding (initially at a rate of 400 kcal/24 hours) and was prescribed intravenous potassium replacement. Eight hours later, she had a primary

Table Laboratory Parameters at Presentation, During Refeeding, and 6 Weeks After Presentation

	Admission	Day 3 After Admission	Day 42 After Admission
Hemoglobin (g/L) NR (115-160)	15	42	124
Mean corpuscular volume (fl) NR (78-98)	110	92	8
White cell count (×109/L) NR (4.0-11.0)	4.2	3.4	6.1
Platelets (×109/L) NR (150-400)	29	30	352
Lactate (mmol/L) NR (0.6-2.4)	20.1	6.5	1.1
Albumin (g/L) NR (30-45)	24	32	38
Bilirubin (μmol/L) NR (3-21)	69	56	13
ALT (U/L) NR (10-50)	754	773	31
Alkaline phosphatase (μ/L) NR (40-125)	74	75	41
Phosphate (mmol/L) NR (0.8-1.4)	0.58	0.21	1.03
Potassium (mmol/L) NR (3.4-5.0)	4.5	3.3	4.9
Calcium (mmol/L) NR (2.1-2.6)	2.21	1.96	2.31
Magnesium (mmol/L) NR (0.70-1.00)	0.91	0.72	0.96
Folic acid (μg/L) NR (2.8-20)	0.3		
Vitamin B12 (ng/L) NR (180-2000)	459		
Ferritin (μg/L) NR (15-200)	388		

NR = normal range.

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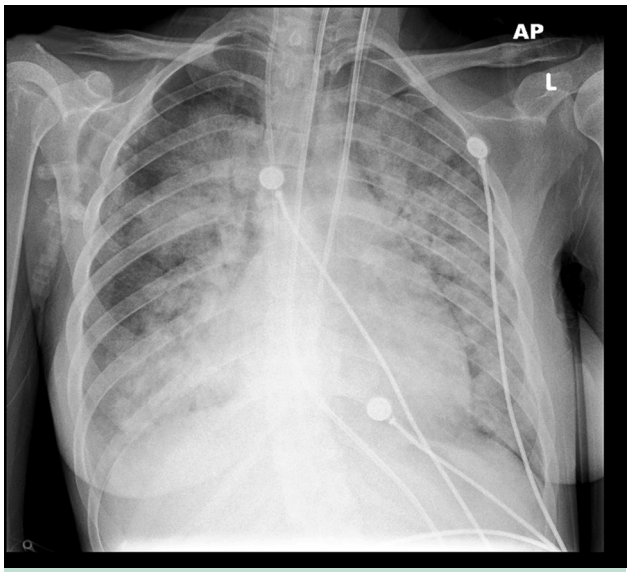

Figure Chest radiograph after intubation demonstrating intra-alveolar shadowing in keeping with acute pulmonary edema. AP = anteroposterior; L = left.

generalized seizure that terminated after administration of intravenous diazepam. Significant hypophosphatemia was detected (**Table**), and intravenous phosphate replacement was administered. She received a single unit of red cell concentrate and developed acute pulmonary edema requiring intravenous diuretic therapy and transient intubation and ventilation (**Figure**). An echocardiogram confirmed mild impairment of left ventricular systolic function without evidence of valvular heart disease, Takotsubo cardiomyopathy, or pericardial effusion.

Her treatment was simplified to oral folic acid, phosphate, potassium, and multivitamin replacement. She made a full recovery with restoration of all clinical and laboratory parameters to normal (**Table**).

DISCUSSION

This patient presented with profound macrocytic anemia due to profound folic acid deficiency and exhibited features consistent with thiamine deficiency-related cardiac failure as a consequence of a general malnourished state. The malnourished state occurred in the context of a more generalized state of self-neglect akin to that described in the so-called Diogenes syndrome.[1] Such profound nutritional anemia is uncommon in our local area, even in patients with severe restrictive anorexia nervosa (A. Jamieson, unpublished observations, March 2015).

This patient received pretreatment with oral thiamine to avoid the neurologic consequences of refeeding syndrome and improve the features of beri-beri. However, despite cautious nasogastric feeding, she still developed profound refeeding syndrome, exacerbated by the administration of a single unit of packed red cells. In retrospect, the need to administer red cells was probably driven by anxiety surrounding the extremely low hemoglobin level rather than the absolute risk associated with her concurrent cardiovascular state.

The rapid onset of the biochemical and clinical features reinforces the need for extreme clinical vigilance in dealing with patients at high risk of refeeding syndrome.[2] Patients with a body mass index less than 16 kg/m^2, recent dietary restriction for more than 10 days, or abnormal electrolyte levels (potassium, phosphate, magnesium) before refeeding are at high risk of developing refeeding syndrome, and the presence of profound nutritional anemia also should indicate that elevated risk is present.[3,4]

CONCLUSIONS

This case demonstrates the ability of the human body to function at extreme limits but also highlights the potential for significant harm to occur in these circumstances, even when performing the least possible intervention. Clinicians must be vigilant regarding the risk of refeeding syndrome and its extreme consequences when confronted with patients who exhibit features of extreme nutritional anemia, and ensure that a full assessment of that risk is undertaken with the initial assessment of the patient before instituting therapy that may provoke rapid and profound changes in clinical parameters.

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