CASE REPORT

Multiple vitamin deficiencies in a patient with a history of chronic alcohol excess and self-neglect in the UK

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SUMMARY

We report a case of inadequate diet (caused by extreme self-neglect and alcohol excess) which led to chronic severe deficiencies of vitamins A, D and E. At presentation the patient had widespread follicular hyperkeratosis of the skin, keratomalacia of both eyes and a severe cognitive impairment. He responded well to treatment including high dose parenteral vitamins, but lasting impairments in his vision and cognition have caused permanent disability.

BACKGROUND

To the best of our knowledge, combined severe deficiencies of fat-soluble vitamins have not been reported in the UK. Undernutrition associated with chronic alcohol consumption is well documented¹ and although water-soluble vitamin deficiencies are most commonly reported, it is well known that alcohol consumption can interfere with vitamin A metabolism.² The literature associating alcohol abuse with vitamin D or E deficiency is limited and inconsistent. The fat-soluble vitamins have a diversity of roles in metabolism, and inadequacy can have serious clinical sequelae. Most complications of vitamin deficiency are likely to respond well to treatment, but early treatment gives the best chance of a full recovery. Late treatment can cause significant irreversible morbidity. Parenteral and oral vitamins can be easily and cheaply administered with very few side effects.

CASE PRESENTATION

Presenting complaint

A 48-year-old man of no fixed abode was admitted to a hospital in England in 2009. He was confused (Glasgow Coma Scale 14/15), agitated and unable to give any history (and there was no collaborative history). He was very thin and he was in extremely poor general condition with striking abnormalities of his eyes and skin. His body mass index (BMI) was 14.2 (height 178 cm and weight 44.7 kg), he was hypotensive (blood pressure 75/50, with a normal heart rate) and hypothermic (33.8°C).

Dermatological problems

The clinical picture was complex with several distinct cutaneous signs. There was widespread follicular hyperkeratosis that was most florid on the lower abdomen and the anterior aspect of the thighs (figure 1). The changes on the thighs were accompanied by crusting and boggy inflammation that

probably represented areas of discoid eczema. The facial skin, including the forehead and neck, harboured tumid inflammatory lesions similar to those seen in papular rosacea (figure 2).

Ophthalmological problems

The right eye was red with a sticky discharge, there was a corneal ulcer and a hypopyon (figure 3). The left eye showed corneal stromal scarring and vascularisation at the site of a healed ulcer.

Medical history

After a few days the patient was able to provide a brief history, he described years of self-neglect, heavy alcohol use and poor diet. He was of no fixed abode for much of his life, he did not have money to buy food, he often skipped meals and did not have the means to access a balanced diet for years before his admission. He was born in the UK and has lived here all his life. His medical records documented a history of pulmonary tuberculosis, a healed left corneal ulcer and an intertrochanteric fracture of the left hip (fixed with a dynamic hip screw).

INVESTIGATIONS

Initial investigations and treatment

Initial investigations showed mild hypokalaemia, normal renal function, normal calcium and normal magnesium. He was thrombocytopenic with slightly raised inflammatory markers. His liver function tests were normal.

Vitamin status

Since the abnormalities of his eyes and skin and his history of self-neglect severe nutritional deficiency was suspected. Blood samples were taken for the measurement of fat-soluble vitamin concentrations: A, D (25-hydroxycholecalciferol) and E. The water-soluble vitamins, vitamins B and C, had already been replaced with intravenous Pabrinex so these were not measured.

TREATMENT

Initial resuscitation and preliminary treatment

Initial management on day 1 was intravenous fluids, intravenous Pabrinex, regular topical chloramphenicol in both eyes, urethral catheterisation and application of a warming device. He was initially unable to take anything by mouth because of his reduced consciousness but within a few days he was able to eat three meals a day and

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Figure 1 (A) The medial aspect of both thighs showing florid follicular hyperkeratosis. These skin changes were accompanied by crusting and boggy inflammation which probably represents discoid eczema. (B) A close-up of the medial aspect of the right thigh.

Figure 2 Tumid inflammatory lesions on the patient's forehead early in his admission. The rest of his face has been cropped out to ensure confidentiality.

Figure 3 The patient's right eye early in his admission showing signs of active infection: injected conjunctiva, sticky discharge, corneal ulcer and hypopyon.

take tablets. During the first 48 h of admission his serum electrolytes deteriorated showing a pattern consistent with refeeding syndrome (table 1). After 7 days of intravenous replacement, his electrolytes returned to normal and his platelets normalised. See table 3 for a summary of his vitamin treatments.

His initial BMI was 14.2 (weight 44.7 kg, height 1.78 m) so he was reviewed by a dietician and his energy and protein requirements were calculated at 1972 kcal and 47–55 g respectively. The dietician recommended a nutritional support menu, the patient's intake was monitored, and oral nutritional supplements were used in addition as required (as per table 3).

Dermatological treatment

His dermatological lesions were treated with vitamin supplementation (see below for details), regular application of emollients and good personal hygiene.

Ophthalmological treatment

Corneal scrapes were taken from the right eye for culture and after 5 days there was a growth of *Streptococcus pneumoniae*. Intensive topical treatment was instituted: topical antibiotics (ofloxacin 0.3% every hour) and topical atropine (1% once

Table 1 Results of routine blood test results on days 1, 3 and 10

	Ref range	Day 1	Day 3	Day 10
Full blood count				
Hb	13.5–18.0 g/dL	13.3↓	10.4↓	11.3↓
WCC	4–11×10 ⁹ /L	6.9	7.2	5.4
Platelets	135–360×10 ⁹ /L	52↓	39↓	138
Biochemistry				
Na	135–145 mmol/L	139	138	139
K	3.5–5.5 mmol/L	3.5	2.7↓	3.9
Urea	3.2–7.5 mmol/L	5.8	0.5↓	1.7↓
Creatinine	70–120 µmol/L	62↓	37↓	35↓
Corrected Ca	2.20–2.65 mmol/L	2.53	2.15↓	2.41
Mg	0.7–0.95 mmol/L	0.87	0.62↓	0.77
PO ₄	0.7–1.4 mmol/L	1.05	0.56↓	1.24
Inflammatory markers				
ESR	1–10 mm/h	45↑	–	–
CRP	<10 mg/L	35↑	–	10

CRP, C reactive protein; ESR, erythrocyte sedimentation rate; Hb, haemoglobin; WCC, white cell count.

daily). Plus oral antibiotics (doxycycline 100 mg once daily) with gradual addition of topical steroids later on.

Treatment of vitamin deficiencies

The results showed deficiency of vitamins A, D and E (table 2) plus an acquired abetalipoproteinaemia that is, low serum lipids secondary to poor nutrition. This was treated with high dose parenteral vitamins because he was unable to reliably take medications orally during the first 2 days of his admission. He was prescribed oral vitamin supplements once he had recovered.

There is no national guidance for treatment of vitamin A or D deficiency. Standard practice is to treat patients with vitamin D deficiency (definitions of this vary) with oral ergocalciferol (D2) or colecalciferol (D3). Only ergocalciferol is licensed for parenteral high-dose treatment so, in line with the British National Formulary (BNF), 300 000 units (7.5 mg) of ergocalciferol was given as a single intramuscular dose. Retinyl palmitate (vitamin A) treatment is not listed in the BNF, but based on current recommendations³ 100 000 units (30 mg) was given intramuscular on two consecutive days.

He was not given specific vitamin E replacement. The USA's Food and Nutrition Board define the RDA (Recommended Daily Allowance) of vitamin E (α -tocopherol) as 15 mg (22.4 IU) and the British National Formulary (BNF) states that the requirement is not well-defined but is probably 3–15 mg daily. His supplemented oral intake, 10 mg (15 IU) daily as part of a generic multivitamin tablet (table 3), was deemed to contain sufficient vitamin E to slowly correct his deficit.

In addition to parenteral treatment he was given daily oral preparations of multivitamins plus specific preparations of B vitamins, vitamin D (ergocalciferol 1.25 mg once daily), and iron. These are listed individually in table 3.

OUTCOME AND FOLLOW-UP

General condition and cognition

His agitation and hypothermia resolved within 2 days, and he tolerated the reintroduction of normal food, but he remained sleepy for the first week of his admission. By day 12 he was alert, could hold a rational conversation and his blood tests were essentially back to normal. His neurological examination was normal, but he was cognitively impaired. He had a significant retrograde amnesia, his ability to retain new information was impaired and he showed significant cognitive slowing. His mini-mental state examination (MMSE) on day 21 was 18/30

Table 2 Serum vitamin and lipid concentrations with reference ranges (along with reference ranges from local and regional NHS laboratories)

	Laboratory ref range	Serum concentration	Vitamin/lipid ratio (ref range)
A (μ mol/L)	>0.70	<0.1	NA
D (ng/mL)	>30	6.9	NA
E (μ mol/L)	9–28	6.1	3.35 (3.9–5.9)
Cholesterol	4.1–6.5	1.3 mmol/L	NA
Triglycerides	0.6–2.2	0.52 mmol/L	NA

It is recommended that serum vitamin E is expressed as a molar ratio to serum lipids. The population-dependent reference range is 3.9–5.9 with deficiency being defined as <2.1 μ mol/mmol lipids. However, this will overestimate vitamin E status in the presence of pathologically low lipids so uncorrected vitamin E is a more appropriate estimate of tissue levels in this case. Vitamin A=retinol, vitamin D=25-hydroxycholecalciferol, vitamin E= α -tocopherol.
NA, not applicable; NHS, National Health Service.

Table 3 The exact doses of vitamin and nutritional treatments

Name (route) and regime	Active ingredient	Dose per unit
Vitamin A (intramuscular), $\times 1$ once daily on days 1–2	Retinyl palmitate (vitamin A)	100 000 units (30 mg)
Vitamin B tablets (orally), $\times 2$ twice daily	Thiamine (B1)	5 mg
	Riboflavin (B2)	2 mg
	Nicotinamide (B3)	20 mg
	Pyridoxine (B6)	2 mg
Thiamine hydrochloride (orally), $\times 2$ twice daily	Thiamine (B1)	50 mg
Vitamin D (orally), once daily	Ergocalciferol	1.25 mg
Vitamin D (IM), $\times 1$ on day 1	Ergocalciferol	300 000 units
Pabrinex (intravenous), $\times 2$ three times a day on days 1–2	Ascorbic acid (vitamin C)	500 mg
	Anhydrous glucose	1 g
	Nicotinamide (B3)	160 mg
	Pyridoxine (B6)	50 mg
	Riboflavin (B2)	4 mg
	Thiamine (B1)	250 mg
Multivitamin tablets (orally), once daily	Vitamin A	800 μ g
	Thiamine (B1)	1.4 mg
	Riboflavin (B2)	1.6 mg
	Nicotinamide (B3)	18 mg
	Pantothenic acid (B5)	6 mg
	Pyridoxine (B6)	2 mg
	Folacin (B9)	200 μ g
	Vitamin B ₁₂	1 μ g
	Ascorbic acid (vitamin C)	60 mg
	Vitamin D	5 μ g
	Vitamin E	10 mg
Oral nutritional supplements orally PRN	Protein	6 g
	Carbohydrate	18.4 g
	Fat	5.8 g
	Energy	300 kcal
Iron (orally), $\times 1$ three times a day	Ferrous sulfate	200 mg

Dose per unit is the amount of each active ingredient in each tablet or injection. Oral nutritional supplements were of the Fortisip brand. B Vitamins were given as generic vitamin B tablets ('vitamin B tablets, compound, strong' as listed in the British National Formulary) and generic thiamine hydrochloride tablets (as listed in the British National Formulary).

so he went for a CT scan of his head that showed significant cerebral atrophy with unusually prominent cerebral sulci, especially in the frontal and temporal lobes. After 90 days his BMI was 17.2 (weight 54.8 kg) and he was discharged from dietetics.

His cognitive impairment is likely to be multifactorial. Chronic alcohol excess and the associated deficiency of B vitamins is a well-documented cause of cognitive impairment.⁴ He did not exhibit the typical confabulation of Korsokoff's psychosis, but his amnesia may well be due to the same disease process. Vitamin E deficiency causes cognitive impairment and may have contributed to his problems.

Eyes and vision

After intensive treatment the infection in the right eye resolved and the corneal ulcer healed but it left severe scarring. There is now bilateral corneal scarring and a profound visual impairment (visual acuity 6/60 in both eyes). He was able to mobilise independently on the ward but he would often get lost, could not

read signs and could not read normal print. His visual impairment is a major source of disability.

It is likely that in addition to the infectious keratitis there was also an underlying keratomalacia caused by vitamin A deficiency. His cornea did not exhibit the classical signs of vitamin A deficiency related keratomalacia such as Bitot's spots or dry eyes, however, there were advanced corneal changes to a degree rarely seen in a developed country.

Skin

With parenteral vitamin A replacement, regular application of emollients and good personal hygiene his skin returned to normal over 3–4 weeks.

Bones

Our patient had sustained a hip fracture in the past, which is unusual for a man of his age in the absence of major trauma. This injury is very suggestive of osteoporosis although his bone density was not assessed at the time of the injury and has not been assessed since.

Functional status and discharge

There are very few services in the UK for young people with chronic cognitive impairment, but after a long wait he was eventually discharged to a rehabilitation hospital which specialises in alcohol-related brain injuries. His cognitive and visual impairments mean that he is unable to self-care even with regular support from social services. He is unlikely to find employment again and will probably spend the rest of his life in some form of institution or sheltered housing.

DISCUSSION

Vitamin A deficiency

Vitamin A (retinol) is present in animal products, particularly liver, fish oil, egg yolks and milk. It can also be formed in the gut from β -carotene which is present in carrots and green vegetables.⁵ Deficiency occurring through reduced intake alone is a serious public health problem in the developing world, but it is very rare in western countries (except patients with malabsorption syndromes and in liver diseases which affect transport and storage).

Vitamin A and the eyes

Vitamin A is required for detection of light by the retina, since in the form of retinol it is present in the opsin proteins of rods and cones. Retinol is also required for normal function of epithelial cells, immune function and bone growth. Deficiency of vitamin A has a twofold effect on the eye: loss of night vision and degeneration of the cornea. Specific lesions of the conjunctiva called Bitot's spots may also be seen (foamy patches of epithelial debris, which histologically show hyperkeratosis, parakeratosis and loss of goblet cells).

The WHO categorises the progression of vitamin A related eye disease⁶ in the following order: night blindness, conjunctival dryness (xerostosis), Bitot's spots, corneal xerostosis, degrees of corneal ulceration/scarring (keratomalacia) followed finally by structural retinal damage (xerophthalmia fundus). Permanent corneal damage can be avoided by early replacement of vitamin A but keratomalacia is regarded as non-reversible.

Vitamin A and the skin

Skin lesions in vitamin A deficiency result from loss of goblet cells and excessive keratinisation. The dermatopathy, usually seen in association with eye signs of vitamin A deficiency, is called

follicular hyperkeratosis (or phrynoderma). It takes the form of red-brown follicular papules approximately 2–6 mm in diameter with central keratotic spinous plugs.

Vitamin D deficiency

Vitamin D is produced in the skin in the presence of ultraviolet light.⁷ To a lesser extent it is obtained from dietary sources, in particular oily fish and fortified fat spreads and cereals. Dietary and synthesised vitamin D undergo sequential hydroxylation in the liver and kidney to the active form 1,25-dihydroxycholecalciferol. Its primary role is in calcium metabolism and bone formation. Deficiency classically causes reduced mineralisation of bone (osteomalacia) with bone pain and fractures. These features are often associated with proximal myopathy.

Vitamin E deficiency

The principal dietary sources of vitamin E are oils of plants.⁸ It has antioxidant properties which help prevent damage to cell membranes and deficiency causes haemolytic anaemia and chronic cognitive impairment. Vitamin E absorption is dependent on the presence of dietary lipids. A rare congenital deficiency of apolipoprotein B causes several clinical problems, including night blindness, ataxia and acanthocytosis.

Learning points

- ▶ Deficiencies of the fat-soluble vitamins A and E are rare in the UK; low vitamin D status (based on serum concentration of 25(OH)D) occurs in some groups within the population especially during the winter months. To the best of our knowledge, combined frank deficiencies of these three vitamins, associated with clinical symptoms, has not been reported in the UK population.
- ▶ The prevalence of combined frank deficiencies may be underestimated because testing for deficiencies in high risk groups is rarely undertaken. Alcoholism increases the likelihood of frank nutritional deficiencies.
- ▶ Most complications of vitamin deficiency are likely to respond well to treatment and early treatment gives the best chance of a full recovery. Late treatment can cause significant irreversible morbidity.
- ▶ Vitamins A, D and E can all be easily replaced orally and parenterally.
- ▶ If vitamin deficiencies are suspected samples for their measurement should be taken prior to replacement. However, replacement should be started immediately and not be delayed until results are available, as assays usually require referral to a specialist laboratory. Liaison between the clinician and laboratory is essential.

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REFERENCES

- 1 Halsted C. Nutrition and alcoholic liver disease. *Semin Liver Dis* 2004;24:289–304.
- 2 Clugston R, Blaner W. The Adverse effects of alcohol on vitamin A metabolism. *Nutrients* 2012;4:356–71.
- 3 Carlier C, Coste J, Etchepare B, *et al*. A randomised controlled trial to test equivalence between retinyl palmitate and β carotene for vitamin A deficiency. *BMJ* 1993;307:1106–10.
- 4 World Health Organisation. *Vitamin and mineral requirements in human nutrition*. Geneva, 2004.
- 5 Sommer A. Vitamin A deficiency and clinical disease: an historical overview. *J Nutr* 2008;138:1835–9.
- 6 World Health Organisation. *Global prevalence of Vit A deficiency in populations at risk 1995–2005. WHO global database on Vitamin A deficiency*. Geneva, 2009.
- 7 Holick M. Deficiency of sunlight and vitamin D. *BMJ* 2008;336:1318–19.
- 8 Clarke M, Burnett J, Croft K. Vitamin E in human health and disease. *Crit Rev Clin Lab Sci* 2008;45:417–50.

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