

Scurvy and vitamin C deficiency in Crohn's disease

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Summary

A case of scurvy presenting in a patient with Crohn's disease is reported. A normal response to replacement therapy is seen. Vitamin C (ascorbic acid) deficiency was found in 7 out of 10 patients with clinically quiescent Crohn's disease, 4 of whom had an adequate oral intake of vitamin C. There was no significant difference in oral intake between patients with Crohn's disease and matched controls but there was a significant difference ($P < 0.001$) in leucocyte ascorbic acid levels. It is recommended that patients with Crohn's disease be screened for vitamin C deficiency and receive prophylactic vitamin C supplements daily.

Introduction

Several vitamin deficiencies have been described in association with Crohn's disease, including the B complex, B₁₂, D and K. Other deficiencies may include iron, folic acid, calcium, magnesium, sodium, potassium or zinc (Avery Jones, Gummer and Lennard-Jones, 1968; Donaldson, 1973; Bockus, 1976).

As recommended treatment may include low residue diets or parenteral nutrition, both of which have a low vitamin C content, and the disease itself often causes malabsorption, it seems possible that vitamin C deficiency may be relatively common in Crohn's disease. It has been shown by Gerson and Fabry (1974) that vitamin C (ascorbic acid) concentrations in patients with Crohn's disease are decreased compared to normal controls. They postulated that fistula formation could be due to local ascorbate deficiency. Hughes and Williams (1978) have recently reported low concentrations of leucocyte ascorbic acid (LAA) in Crohn's disease. There are no reports in the literature of scurvy in association with Crohn's disease. The following case is thus reported.

Case report

A 28-year-old female with small bowel and colonic Crohn's disease (radiological and histological evidence) of 3 years' duration attended out-patients with a 3-month history of malaise, aching

joints and general weakness and a 2-month history of spontaneous painful bruises on the thighs and lower legs. Clinically the Crohn's disease was quiescent and she had received no drug therapy for approximately one year. On examination she was well nourished. There were some petechiae and ecchymoses on the lower limbs only. The remainder of the skin was normal and she was edentulous with normal gum appearance. These skin appearances suggested early scurvy.

The following investigations were normal: full blood count, platelets, prothrombin time, partial thromboplastin time, fibrinogen concentration, fibrinogen degradation product titre, ESR, urea, electrolytes, serum proteins, serum and red cell folate, vitamin B₁₂ and calcium. However, leucocyte ascorbic acid concentration was 25 nmol/10⁸ white blood cells (normal 119-301 nmol/10⁸ WBC). The safe antiscorbutic level is 85 nmol/10⁸ WBC (Hughes and Williams, 1978).

Oral vitamin C, 600 mg daily for one week rapidly led to resolution of the skin lesions and non-specific complaints of malaise, joint ache and weakness. The treatment was continued at a lower dose of 100 mg/day. Subsequent dietary assessment showed a very low daily intake of ascorbic acid of less than 10 mg daily. This was due to a self-imposed low residue diet adopted by the patient because of occasional colicky abdominal pains.

In view of this experience, it was decided to examine the next 9 out-patients with proved Crohn's disease for evidence of scurvy. Assessment of the ascorbic acid status, dietary intake of vitamin C and the macroscopic extent of the disease was also done, in order to establish whether subclinical ascorbic acid deficiency was as common in this group of Crohn's cases as in other series.

Methods

Leucocyte ascorbic acid, which most reliably reflects the state of tissue saturation (Burns, 1975), was measured by the method of Denson and Bowers (1961). The normal range of this method measures the ascorbic acid content of the buffy coat, i.e. leucocytes and platelets and is referred to as the

TABLE 1. Details of vitamin C studies in Crohn's disease and age- and sex-matched controls

Patient	Sex	Age (years)	Leucocyte ascorbic acid (nmol/10 ⁸ WBC (normal 119-301))		Ascorbic acid intake in mg/24 hr	Current drug therapy in Crohn's patients		Site of macroscopic bowel involvement including resections in Crohn's patients
			Crohn's	Controls		Crohn's	Controls	
1*	F	28	25	190	5	41	Nil	Terminal ileum, colon
2	M	26	34	294	5	117	Nil	Small bowel (extensive)
3	F	36	101	257	78	114	Codeine, loperamide	Ileum
4	M	33	57	233	7	74	Sulphasalazine, prednisolone	Terminal ileum, colon
5	F	35	81	226	104	83	Codeine, prednisolone, vitamin B ₁₂ , iron	Terminal ileum, colon
5	F	27	46	139	30	30.5	Codeine, oral disodium cromoglycate	colon
7	F	25	180	228	95	85	Prednisolone, pentazocine, oral disodium cromoglycate	Terminal ileum, anal
8	M	27	156	203	23	41	Nil	Terminal ileum, caecum, anal
9	F	28	92	259	81	62	Oral disodium cromoglycate, iron	Terminal ileum, colon, and hemicolectomy
10	M	35	157	226	80	45	Codeine, oral disodium cromoglycate	Colon
Mean			92.9	225.5	50.8	69.3		
Standard deviation			± 55.2	± 42.32	± 40.3	± 30.7		
Unpaired 't' test			t = 60.3	P < 0.001	t = 1.15	P > 0.1		
			Degrees of freedom = 18	Highly significant	Degrees of freedom = 18	< 0.5		
						Not significant		

*Patient with scurvy

'leucocyte ascorbic acid'. This range was used. However, later work by Gibson, Moore and Goldberg (1966) altered the normal range by measuring ascorbic acid in leucocytes only. Conversion factors based on leucocyte and platelet counts can be applied to results obtained by Denson and Bowers' method for specific leucocyte ascorbic acid levels.

The dietary intake of vitamin C was estimated by trained dieticians using McCance and Widdowson food composition tables. A control group of healthy adults with no evidence of bowel disease and matched for age and sex was included, and dietary assessment and LAA measurement was performed in them. Comparisons between controls and patients were performed with the unpaired 't' test.

Results

The results are shown in Table 1.

No clinical evidence of scurvy was detected in any of the 9 patients examined. The Crohn's disease was clinically quiescent in all patients apart from patient 7, who had colicky abdominal pain requiring intermittent pentazocine.

Seven of 10 patients had low LAA levels. Of these, 4 had a low dietary intake by any criteria. Two of the patients had LAA levels below the safe antiscorbutic concentration of 85 nmol/10⁸ WBC despite an adequate diet.

Overall, the concentration of LAA in Crohn's patients was significantly lower ($P < 0.001$) than in matched signals. There was no significant difference ($P > 0.1$, < 0.5) in oral intake of vitamin C between controls and patients with Crohn's disease.

Discussion

James Lind (1753) has probably recorded the best clinical description of scurvy. He stated that the first sign of cutaneous bleeding was often to be found in the lower thighs just above the knees. Large spontaneous bruises almost always appear first on the legs. This was the case in the present patient who also exhibited the early non-specific symptoms of scurvy, namely fatigue, malaise, lassitude and joint aching. Oral lesions occur almost exclusively in patients who have retained their own teeth (Van Itallie, 1977). As the patient was edentulous it is not surprising that she had no oral lesions and none of the gum changes often seen in this condition. It has been said that the LAA level falls to zero just before scurvy develops (Herman, Stibel and Greene, 1976) and in this, the present patient was not typical although the level of 25 nmol/10⁸ WBC was far below the 'safe' antiscorbutic level of 85 nmol/10⁸ WBC (Hughes and Williams, 1978).

Vitamin C deficiency can lead to malaise, anorexia weakness, lassitude, bone and joint aching and psychological changes. It causes poor collagen for-

mation due to failure to convert proline to hydroxyproline and failure of synthesis of chondroitin sulphate, an important constituent of ground substance. Wounds therefore heal poorly. There is a failure to utilize iron and convert folic acid to folinic acid with the potential to develop folate deficiency and anaemia (Schrimshaw, 1975). Some of these features are seen in Crohn's disease and it is possible that deficiency of vitamin C may be a factor in their aetiology.

However, it should be noted that vitamin C deficiency is not specific to Crohn's disease and is well recognized in conditions which damage the body, such as burns, fractures or surgical operations. These lead to rapid disappearance of the reduced vitamin (Davidson *et al.*, 1975). Deficiency is also seen in a wide variety of chronic illnesses, especially sepsis, neoplastic disease, etc., and is thought to be due to increased utilization of the vitamin (Burns, 1975; Latner, 1975).

Vitamin C is a simple sugar with a molecular weight of 176. It is water soluble and an acid. It has been thought to be absorbed throughout the small intestine by passive diffusion (Nicholson and Charnock, 1942), but recent work by Stevenson (1974) and confirmed by Mellors, Nahrwold and Rose (1977) shows an active transport mechanism of absorption by the ileum. Even after major resections of the small intestine resulting in a state resembling starvation, absorption of vitamin C is still maintained and deficiency is not usually a problem (Stewart and Booth, 1964; Preston and Ascuncheon, 1968). However, LAA levels have been found to be decreased in steatorrhoea and clinical evidence of vitamin C deficiency has been reported (Williamson, Goldberg and Moore, 1967). The present patients had not had small bowel resections and radiology had not shown internal fistulae. There was nothing to suggest steatorrhoea clinically, although faecal fats were not measured.

Gerson and Fabry (1974) suggested that low LAA concentration in Crohn's cases could be related to low dietary intake. There is controversy over the adequate minimum daily LAA intake for an adult. The United Kingdom recommended daily intake is 30 mg or more, while the Food and Nutrition Board of the National Research Council, U.S.A., has progressively decreased the recommended daily intake from 75 mg in 1943 to 45 mg in 1974. On the latest criteria, therefore, only 5 cases were having an inadequate dietary intake of vitamin C. Although the lowest LAA results correlated with the lowest dietary intake, there were 3 patients with low LAA concentrations on an adequate dietary intake by all standards, and 4 patients with low LAA concentrations on adequate dietary intake by United Kingdom standards.

Patients with colonic involvement alone are unlikely to develop vitamin C deficiency due to malabsorption. However, patient 6 had colonic involvement only, an adequate dietary intake by United Kingdom standards and a low LAA. It is interesting that the site of the Crohn's disease apparently bears no relation to the low LAA levels observed. However, malabsorption can occur in apparently normal bowel and thus the site of macroscopic Crohn's disease involvement is probably not relevant.

It is possible that there is an increased demand for vitamin C in Crohn's disease rather than malabsorption. It may be possible to correlate activity or severity of the disease to vitamin C levels, but this will require more study. There is no evidence that codeine phosphate, sulphasalazine, disodium cromoglycate or steroids affect LAA levels. Large doses of vitamin C are said to have no deleterious side effects (Burns, 1970).

In view of the findings of vitamin C deficiency in this and other studies, it is recommended that regular vitamin C supplements (50–100 mg daily) should be given to all patients with Crohn's disease to prevent overt or subclinical vitamin C deficiency and possibly improve their sense of well being. In proved deficiency a dose of 200–1000 mg daily initially should be satisfactory (Losowsky, Walker and Kelleher, 1974).

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