GASTROINTESTINAL AMYLOIDOSIS IN PSORIATIC ARTHRITIS

BY

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The aetiology of amyloidosis has long been a subject for debate. It develops in diseases associated with excessive amounts of immunoglobulins, *e.g.* chronic infections, rheumatoid arthritis, and myelomatosis. In studies on the prevalence of amyloidosis in rheumatic diseases (Missen and Taylor, 1956; Arapakis and Tribe, 1963), the rarer sero-negative arthropathies, *e.g.* Reiter's syndrome and psoriatic arthropathy, are not discussed. Since these diseases are not associated with the auto-immune phenomena and the gross immunological abnormalities found in rheumatoid arthritis, it might be assumed that they are not complicated by amyloidosis. However, Moise, Asch, and Imbs (1965) reported fatal renal amyloidosis in a young man with a 3-year history of psoriasis and arthritis, and amyloidosis has been reported as a complication of Reiter's syndrome by Bleehe, Everall, and Tighe (1966). It is of interest that Reiter's syndrome and psoriasis may occur in the same patient, and may in fact be part of the same disease spectrum (Wright and Reed, 1964; Maxwell, Greig, Boyle, Pasieczny, and Schofield, 1966).

We here report a further case of psoriatic arthropathy and amyloidosis with unusual gastrointestinal manifestations.

Case Report

A 63-year-old woman admitted to the Centre for Rheumatic Diseases in July, 1966, had had psoriasis for approximately 50 years associated with a progressively deforming arthritis for about 20 years. She had been bedridden for the last 10 years as a result of fixed flexion deformities of the elbows, hips, and knees. For one year before admission she had had watery diarrhoea, characterized by several loose bowel motions each day, not described as bulky nor offensive.

Examination.—She was frail and wasted, with a wide-

spread psoriatic rash involving her elbows, buttocks, and anterior abdominal wall. Her nails were pitted and the skin of her fingers atrophic, and she had palmar erythema, but no other stigmata of hepatic dysfunction. There were fixed flexion deformities of elbows, hips, and knees, and swan-neck deformities of the fingers. The articular index was 38 (Co-operating Clinics Committee of the American Rheumatism Association, 1965). There was no evidence of keratoconjunctivitis sicca (Williamson, Cant, Mason, Greig, and Boyle, 1967), no xerostomia, no subcutaneous nodules, and no evidence of Raynaud's phenomenon. Physical examination, apart from abdominal distension, was otherwise negative.

Laboratory Investigations: Hb 14.1g./100ml., packed cell volume 44 per cent.; mean corpuscular haemoglobin concentration 32 per cent.; white cell count 7,800 per cu. mm., normal differential white cell count; erythrocyte sedimentation rate 59 mm./1 hr (Westergren).

Electrophoresis of the serum showed a slight decrease in albumin levels.

Blood urea, thymol turbidity, alkaline phosphatase, bilirubin, serum calcium, phosphorus, and uric acid levels were within normal limits. Bromsulphthalein excretion test showed retention of 15 per cent. of the dye after 45 minutes. Urine analysis was normal and culture of mid-stream specimens of urine (including culture for myco tuberculosis) was sterile.

Chest x ray was negative and an electrocardiogram showed widespread myocardial ischaemia.

The Coombs's test was negative, as were the tests for rheumatoid factor, both by the latex-fixation and sheep cell agglutination techniques. The L.E. latex test was negative and no antibodies to thyroglobulin (Fulthorpe, Roitt, Doniach, and Couchman, 1961), thyroid microsomes (Holborow, Brown, Roitt, and Doniach, 1959), gastric parietal cells (Adams, Glen, Kennedy, Mackenzie, Morrow, Anderson, Gray, and Middleton, 1964) nor to small salivary ducts (MacSween, Goudie, Anderson, Armstrong, Murray, Mason, Jasani, Boyle, Buchanan, and Williamson, 1967) were demonstrated. The non-organic specific precipitin test (Beck, Anderson, Bloch, Buchanan, and Bunim, 1965) and immunofluorescence test for anti-nuclear factor (Beck, 1961) were also negative. Radiological survey showed gross rarefaction of

bones, and joint destruction, with "pencil and cup" deformities in the bones of the feet typical of psoriatic arthritis (Fig. 1).

Fig. 1.—X ray of feet, showing rarefaction of bones and "pencil and cup" deformities of joints.

There was no faecal blood loss, stool culture was negative, and faecal fat excretion was normal. Barium meal with follow-through was negative, but a barium enema showed gross nodular mucosal abnormality with two narrowed segments, one in the ascending, and one in the descending, colon (Fig. 2).

Sigmoidoscopy and histology of rectal biopsy were normal. Skin biopsy was also normal, but histology of gum and jejunal mucosa showed evidence of amyloid infiltration in the walls of the blood vessels, demonstrated by the specific uptake of thioflavine T (Vassar and Culling, 1959). Abnormalities in jejunal enzymes are shown in the Table, lactase, sucrase, and maltase activities being assayed by the method of Paton, Murray, and Watson (1966), while alkaline phosphatase activity was determined by the method of Ferguson, Watson, Maxwell and Fell (1968). Maltose and sucrose tolerance tests were normal.

Discussion

This patient demonstrates the features of psoriatic arthropathy of the deforming type: classical meta-

Fig. 2.—Barium enema (double contrast technique), showing colonic strictures and loss of haustrations.

tarsophalangeal "pencil and cup" deformity and gross rarefaction of bones on x ray, negative Waaler-Rose test, and absence of rheumatoid nodules (Wright, 1959). Amyloid infiltration involving the gastrointestinal tract has been unequivocally demonstrated.

Amyloidosis of the small intestine may be associated with a malabsorption syndrome (Babb, Alarcón-Segovia, Diessner, and McPherson, 1967), intestinal perforation (Akbarian and Fenton, 1964), intestinal bleeding (Jerman, 1967), or, as in the

TABLE
ENZYME DEFICIENCY AND MUCOSAL ABNORMALITY

Diagnosis	Histology	Maltase ¹	Sucrase ¹	Lactase ¹	Alkaline Phosphatase ²
Normal	Finger villi	13+	3+	1+	60+
Coeliac disease	Subtotal villous atrophy	1.2	.2	.1	20
Primary adult hypolactasia	Finger villi	15.3	3.3	0.0	120
Amyloidosis	Finger villi	5.4	1.2	5.8	108

¹Units of activity per g. mucosa.

²King Armstrong units per g. mucosa

present case, with no functional abnormality. The results of the intestinal enzyme assay deserve comment. As illustrated in the Table, widespread enzyme deficiency is usually associated with gross structural abnormality of the mucosa (as in coeliac disease). There may be an isolated enzyme deficiency in an otherwise normal mucosa, as in primary adult hypolactasia (Ferguson and Maxwell, 1967). In some patients with gastrointestinal or systemic disease, moderate, multiple, and usually asymptomatic, enzyme deficiencies may be present in a histologically normal, or slightly abnormal, mucosa (Ferguson, Maxwell, Murray, McKay, and Watson, unpublished). The present case is classified in the last of these groups, since there was reduction of mucosal maltase and sucrase activities, but maltose and sucrose tolerance tests were normal.

Diarrhoea, abdominal pain, and colonic stricture may result from colonic ischaemia (Marston, Pheils, Thomas, and Morson, 1966) or from ulcerative colitis. However, these diagnoses were considered unlikely in view of the absence of rectal bleeding, frank or occult, and the x-ray changes discussed below. The lack of rectal or ileal manifestations virtually excluded Crohn's disease. It is concluded that the gastrointestinal symptoms were the result of amyloid infiltration of the colonic muscle and mucosa.

Ritvo and Litner (1963) have described the x-ray appearances of colonic amyloidosis. An early barium enema in their case showed loss of haustra-

tions, a mucosal irregularity, but no mucosal serration; 4 years later there were multiple areas of narrowing in the colon, the descending colon was anastomotic, and the mucosal pattern was coarse and nodular. They pointed out that this differs from the appearances in ulcerative colitis in the character of the mucosal folds (irregular in amyloid, longitudinal in ulcerative colitis) and in the lack of serrations. The almost identical barium enema findings in the present case add weight to the suggestion that the above pattern is typical of colonic amyloidosis.

Summary

The case of a 63-year-old woman with psoriatic arthritis complicated by gastrointestinal amyloidosis is reported. Amyloidosis of the small bowel was associated with deficiencies of the enzymes maltase and sucrase. The significance of the barium enema findings is discussed.

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REFERENCES

- Adams, J. F., Glen, A. I. M., Kennedy, E. H., Mackenzie, I. L., Morrow, J. M., Anderson, J. R., Gray, K. G., and Middleton, D. G. (1964). *Lancet*, **1**, 401 (The histological and secretory changes in the stomach in patients with autoimmunity to gastric parietal cells).
- Akbarian, M., and Fenton, J. (1964). *Arch. intern. Med.*, **114**, 815 (Perforation of small bowel in amyloidosis).
- Arapakis, G., and Tribe, C. R. (1963). *Ann. rheum. Dis.*, **22**, 256 (Amyloidosis in rheumatoid arthritis investigated by means of rectal biopsy).
- Babb, R. R., Alarcón-Segovia, D., Diessner, G. R., and McPherson, J. R. (1967). *Arthr. and Rheum.*, **10**, 63 (Malabsorption in rheumatoid arthritis: an unusual complication caused by amyloidosis).
- Beck, J. S. (1961). *Lancet*, **1**, 1203 (Variations in the morphological patterns of "autoimmune nuclear fluorescence").
- , Anderson, J. R., Bloch, K. J., Buchanan, W. W., and Bunim, J. J. (1965). *Ann. rheum. Dis.*, **24**, 16 (Antinuclear and precipitating auto-antibodies in Sjögren's syndrome).
- Bleehen, S. S., Everall, J. D., and Tighe, J. R. (1966). *Brit. J. vener. Dis.*, **42**, 88 (Amyloidosis complicating Reiter's syndrome).
- Co-operating Clinics Committee of the American Rheumatism Association (1965). *Arthr. and Rheum.*, **8**, 302 (Revision of diagnostic criteria for rheumatoid arthritis).
- Ferguson, A., and Maxwell, J. D. (1967). *Lancet*, **2**, 188 (Genetic aetiology of lactose intolerance).
- , —, Murray, D., McKay, A. M. and Watson, W. C. (In preparation).
- , Watson, W. C., Maxwell, J. D., and Fell, G. S. (1968). *Gut*, **9**, 96 (Alkaline phosphatase levels in normal and diseased small bowel).

- Fulthorpe, A. J., Roitt, I. M., Doniach, D., and Couchman, K. (1961). *J. clin. Path.*, **14**, 654 (A stable sheep cell preparation for detecting thyroglobulin auto-antibodies and its clinical applications).
- Holborrow, E. J., Brown, P. C., Roitt, I. M., and Doniach, D. (1959). *Brit. J. exp. Path.*, **40**, 583 (Cytoplasmic localization of "complement-fixing" auto-antigen in human thyroid epithelium).
- Jerman, R. P. (1967). *Brit. J. clin. Pract.*, **21**, 521 (Haematemesis from secondary amyloidosis of the jejunum).
- MacSween, R. N. M., Goudie, R. B., Anderson, J. R., Armstrong, E., Murray, M. A., Mason, D. K., Jasani, M. K., Boyle, J. A., Buchanan, W. W., and Williamson, J. (1967). *Ann. rheum. Dis.*, **26**, 402 (Occurrence of antibody to salivary duct epithelium in Sjögren's disease, rheumatoid arthritis, and other arthritides: a clinical and laboratory study).
- Marston, A., Pheils, M. T., Thomas, M. L., and Morson, B. C. (1966). *Gut*, **7**, 1 (Ischaemic colitis).
- Maxwell, J. D., Greig, W. R., Boyle, J. A., Pasieczny, T., and Schofield, C. B. S. (1966). *Scot. med. J.*, **11**, 14 (Reiter's syndrome and psoriasis).
- Missen, G. A. K., and Taylor, J. D. (1956). *J. Path. Bact.*, **71**, 179 (Amyloidosis in rheumatoid arthritis).
- Moise, R., Asch, L., and Imbs, J. L. (1965). *Strasbourg Méd.*, **16**, 245 (Rhumatisme psoriasique et amylose).
- Paton, E., Murrar, E., and Watson, W. C. (1966). *Brit. med. J.*, **1**, 459 (Intestinal disaccharidase activity in rosacea).
- Ritvo, M., and Litner, C. (1963). *Amer. J. Roentgenol.*, **89**, 760 (Roentgen manifestations of primary amyloidosis of the colon).
- Vassar, P. S., and Culling, C. F. A. (1959). *Arch. Path.*, **68**, 487 (Fluorescent stains, with special reference to amyloid and connective tissues).
- Williamson, J., Cant, S., Mason, D. K., Greig, W. R., and Boyle, J. A. (1967). *Brit. J. Ophthalm.*, **51**, 721 (Sjögren's syndrome and thyroid disease).
- Wright, V. (1959). *Amer. J. Med.*, **27**, 454 (Rheumatism and psoriasis: a re-evaluation).
- and Reed, W. B. (1964). *Ann. rheum. Dis.*, **23**, 12 (The link between Reiter's syndrome and psoriatic arthritis).

Amyloidose atteignant le tube digestif au cours de l'arthrite psoriasique

RÉSUMÉ

On rapporte le cas d'une malade de 63 ans atteinte d'arthrite psoriasique compliquée d'amyloidose du tube digestif. L'amyloidose de l'intestin grêle était associée à un déficit en maltase et en sucrase. On discute la signification des résultats du lavement baryté.

Amiloidosis del tubo digestivo en la artritis sorriásica

SUMARIO

Se relata el caso de una enferma de 63 años con artritis sorriásica complicada de amiloidosis del tubo digestivo. La amiloidosis del intestino delgado se vió acompañada de deficiencia enzimática de maltasa y de sucrasa. Se discute la importancia de los resultados del enema de bario.