A CASE OF POLYSEROSITIS (CONCATO'S DISEASE)

A DISCUSSION OF ITS POSSIBLE RELATIONSHIP TO COLLAGEN DISEASES

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My purpose in reporting the following case is not only to describe a comparatively rare condition but also to review the aetiology and the possible relationship of a group of similar cases to the collagen diseases.

CASE HISTORY

A European male, a metallurgist, aged 28 years, referred by Dr. N. K. Cath of Welkom, O.F.S., was admitted to a nursing home under my care on 14 December 1958 for bilateral pleural effusions, a pericarditis and a hectic temperature. The history was of insidious onset: The patient, a healthy young man, found that he was losing weight and energy from about March 1958. About the middle of November a left pleural effusion was followed very soon by signs of bilateral pleural effusions and a pericarditis. Intensive antituberculous treatment was commenced towards the end of November 1958. Accompanying X-ray films and an electrocardiogram confirmed the diagnosis of bilateral pleural effusions and a pericarditis. There was also a history of recurrent attacks of dysentery during the previous 3 years—diagnosed as mild ulcerative colitis although sigmoidoscopy was reported as negative. At the time of his admission under my care the dysentery had been temporarily controlled with salicylazosulphapyridine. During the next 2 or 3 weeks a very persistent intermittent temperature with tachycardia continued. Dyspnoea, sweating, anorexia and slight loss of weight were noted.

From mid-December 1958, repeated examinations confirmed the persistence of pleural effusions. The pericarditis was recognized by the ECG changes and X-rays. No pleural or pericardial rub was audible. The only additional feature, which became more evident towards the end of December, was ascites. Negative features were the absence of any significant rash, adenopathy, enlargement of spleen, or albuminuria. The joints were not involved; there was no pain; there were no superficial lumps, no history of asthma, and the reflexes were all present. The X-ray showed some enlargement of the liver.

Pending investigations, active antitubercular therapy was continued. Because of the uncertain aetiology and the suspicion that other organisms besides the tubercle bacillus may be responsible for a polyserositis, additional treatment with a full course of anti-amoebic therapy (emetine and aralen) and of broad-spectra antibiotics, including an intensive course of chloromycetin, was also administered.

Routine Investigations

Tuberculosis has always been stressed in the past as a possible cause of polyserositis, often resulting in a constrictive pericarditis (Pick's disease). Tests for tuberculosis were predominant in the routine investigations in this case.

Investigations cover a period of about 3 months—from early December 1958 to April 1959. The results were as follows (the figures in brackets indicate the number of times the examinations were carried out):

Blood examinations. Haemoglobin (7): 15·3 - 16·5 g.%. Leucocytes (per c.mm.): December 14·1; January—5·2, 9·5, 7·6, 10·1; February 17·4; March 14·1 and April 11·0 (neutrophils 62-75%, monocytes, 2-10%, lymphocytes 6-25%, eosinophils—4·5, 11·5, 8·0, 16·5, 11·0, 1·0, 1·0 and 0%). Sedimentation rate —5, 10, 2, 6 and 2 minutes per hour. *Comment:* The raised leucocyte count in February may have been due to a gluteal abscess. At no time was there a monocytosis or a raised sedimentation rate. An eosinophilia persisted till the end of January.

X-rays of chest. December 1958 to January 1959 (6+), bilateral pleural effusions and pericardial effusion (Figs. 1 and 2). February to April 1959 (3), pleural effusions absorbed (Fig. 3). No evidence of pulmonary tuberculosis, hydatid disease or other pathology.

Tuberculosis. Mantoux test 1 in 1,000 (1) negative after 48 hours. Sputa (6) negative. Pleural fluid: direct examination (3) negative; culture (3) negative; biological test (2) negative; microscopic examination showed lymphocytes, polymorphonuclear leucocytes, and clumps of mesothelial cells; total proteins 4·2 g.%; specific gravity 1,017. Pleural biopsy negative.

Hydatid and bilharzia. Hydatid complement-fixation test (2) positive. Casoni test (1) negative. Bilharzia C.F.T. (1) negative. No clinical or radiological evidence to suggest hydatid disease.

Stools (3), parasites, pathogenic bacteria and pus cells; negative.

Sigmoidoscopy (15 cm.), no ulceration.

Widal test (1) for typhoid, melitensis and proteus, negative.

Liver function tests (1), showed marked hepato-cellular changes: thymol turbidity test, 5·0 units; thymol flocculation, 3+; colloidal red, 4+; cephalin cholesterol flocculation, negative (24 hr.); Takata Ara reaction, 1+; zinc sulphate turbidity, 20·6; total lipid, 491; alkaline phosphates, 6·7; Van der Bergh reaction, negative; bilirubin (direct), 0·2 mg.%, (total), 0·4 mg.%; total protein, 7·6 g.%; albumin, 3·0 g.%; globulin, 4·6 g.%; gamma globulin, 2·20 g.%; cholinesterase, 100% of average normal activity; and mucoprotein, 240 mg.%.

Electrolytes (4), showed a hypokalaemia (before and after steroids were prescribed).

Electrocardiogram. December 1958 to January 1959, changes compatible with pericarditis. February 1959 to April 1959, pattern reverted to normal.

Additional Investigations for Collagen Disease

The possibility of this being a collagen disease was considered from the time of the admission of the patient. Involvement of the serous cavities, pericardial, pleural, and peritoneal, offered a suggestion of the disease being in some way related to systemic lupus erythematosus or, perhaps, periarteritis nodosa, notwithstanding the absence of many clinical features associated with these diseases. It has become fashionable to suggest the use of steroids in many conditions which await further clarification regarding aetiology. It is not surprising, therefore, that one should think along these lines—as was the case here. However, since in the

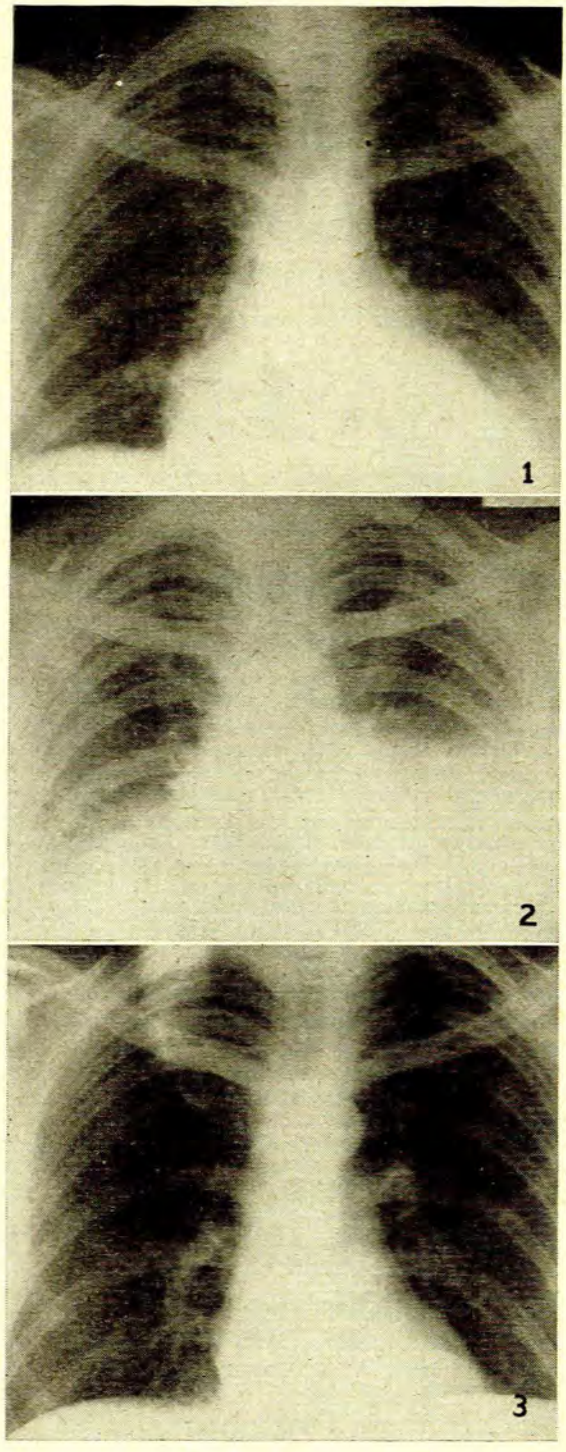

Fig. 1. 24 November 1958. Onset with pericardial effusion and left-sided pleural effusion.

Fig. 2. 11 December 1958. Bilateral pleural effusion which persisted to the end of January 1959.

Fig. 3. 16 February 1959. 14 Days after steroid therapy both pleural and pericardial effusions have disappeared.

past tuberculosis has always been stressed as a possible cause of polyserositis, caution had to be exercised in the administration of steroids even though the patient was having streptomycin and isoniazid in full doses (24 November—4 March 1959).

Whilst active antitubercular therapy was being pursued, the following investigations for collagen disease were carried out:

Lupus erythematosus cells (5), negative.

Pleural biopsy (1) on 20 January 1959 by Mr. D. Adler. Dr. J. C. Wagner of the South African Institute for Medical Research, Johannesburg, reports: 'Sections . . . show the presence of two fragments of parietal pleura in which there is a non-specific chronic inflammatory change.'

A personal request to Dr. Wagner to review slides for any evidence of collagen disease confirmed his previous impressions that there was no evidence of this in any form.

Biopsy of skin and muscle (1) on 13 February 1959 by Mr. Max Tucker. Dr. J. C. E. Kaufmann, of the South African Institute for Medical Research, Johannesburg, reports: 'Histological examination of a section from this specimen of skin from the calf over the region of the gastrocnemius muscle, cut at different levels, shows the presence of some follicular plugging, an area of atrophy of the epidermis, a suggestion of slight endothelial swelling of the small vessels, one or two small foci of perivascular round-cell infiltrate, and a tendency to condensation of the peri-adnexal collagen around the pilosebaceous follicles. No significant pathological change has been observed in a section taken from the subcutaneous fibre fatty tissue. A section from the specimen from the gastrocnemius muscle shows the presence of a very occasional thin fibre but no other significant pathological change. No definite evidence of periarteritis nodosa or other collagen disease has been observed in the sections examined.'

On 20 April 1959 the mucoprotein was 263 mg.%. C-reactive protein was 4+ positive. The paper-electrophoretic pattern was: Total proteins, 7·6 g.%; albumin, 45·2%—3½ g.%; alpha 1 globulin, 7·2%—0·55 g.%; alpha 2 globulin, 16·2%—1·24 g.%; beta globulin, 17·8%—1·35 g.%; and gamma globulin, 13·6%—1·03 g.%. Macroglobulin estimations were not available. *Comment.* No definite evidence of collagen disease was found.

Progress on Steroid Therapy

This was begun on 27 January 1959 with 60 mg. of prednisone (Delta Stab) daily. The general condition of the patient improved and the pleural effusions diminished rapidly. An X-ray of the chest on 16 February 1959 (Fig. 3) showed complete absorption of the fluid after about a fortnight. The dosage of steroid was gradually reduced. All antitubercular treatment was discontinued on 4 March 1959.

The patient was discharged from the nursing home on 14 March 1959, 3 months after admission, feeling comparatively well again. The pleural effusions had disappeared and there was no evidence of residual pericarditis or ascites.

On 20 April 1959, about 5 weeks after discharge from hospital, the patient was seen again. He reported fair progress. He felt tired and complained of some pain in the right shoulder joint, aggravated by deep breathing. There was no undue breathlessness or oedema. There was no history of cough or pyrexia. He had a mild cushinoid appearance. His temperature was 98° and his blood pressure was 120/90 mm. Hg. Clinically, his heart was not enlarged—no rub, no murmurs and no gallop were heard. There was no evidence of fluid in the pleural cavities and no definite evidence of ascites, although the abdomen looked slightly distended. The liver and spleen were not palpable.

Clinically, therefore, there had been no return, thus far, of serous effusions whilst a daily maintenance dose of 5 mg. of prednisone was continued and antitubercular treatment had been discontinued for about 6 weeks.

DISCUSSION

What is meant by the term polyserositis?

A review of the literature shows that there is a tendency to discuss polyserositis in relation to constrictive pericarditis, particularly of tuberculous origin.

In 1896, Pick (quoted by White[6]) described 3 cases of constrictive pericarditis with 'pseudocirrhosis of the liver resulting from chronic adhesive pericarditis involving the

mediastinum'. Two cases were due to tuberculosis and the third was of unknown aetiology.

Osler[5] (1920) says: 'In all forms of chronic peritonitis . . . polyorrhymenitis, general chronic inflammation of the serous membranes, Concato's disease (as the Italians call it) may occur in this form as well as in the tuberculous variety. The pericardium and both pleurae may be involved.'

In 1942, Harrison and White[3] reviewed a series of 37 cases of constrictive pericarditis; 5 of them were ascribed to tuberculosis and 3 to other infections and in 29 the cause was either 'unknown' or 'questionable'.

In 1944, Paul Dudley White[6] writes that 'ascites may also be a part of polyserositis (Concato's disease) which forms the background for constrictive pericarditis (Pick's disease)'. He then makes the significant statement that although polyserositis may eventually be responsible for constrictive pericarditis 'these two conditions have often been confused in the past'.

In 1948, Andrews, Pickering and Sellors[1] reviewed the subject of constrictive pericarditis. In 18 cases the cause was tuberculosis and in 14 of these cases one or more of the other serous cavities (pleural or peritoneal) were involved. Although they apply the term 'polyserositis' to these cases of tuberculous pericarditis with involvement of the adjacent pleurae, these authors later make the following statement: 'Constrictive pericarditis is a clinical entity which should be differentiated . . . from polyserositis'.

Paul Wood[7] (1957) described polyserositis as follows: 'Whilst tuberculosis may affect the pleura and peritoneum as well as the pericardium, the term polyserositis (Concato's disease) is usually reserved for a somewhat similar inflammatory process of unknown origin. Large effusions collect in the serous sacs, the fluid being a clear or opalescent, straw-coloured, sterile exudate . . . When the pericardium is involved, resorption of fluid is followed by total obliteration of the pericardial cavity, and constriction may ensue. The course and prognosis are similar to those of tuberculous pericardial effusion.' In the absence of a known cause of polyserositis as described by Wood, the possibility of a constrictive pericarditis following at a later date again introduces the likelihood of a tuberculous or other infective process as the cause.

Comment. Most of the authors to whom reference was made here, as well as other authors, admit there is confusion in the terminology. It would appear that no clear line of distinction is drawn between the generalized acute type of polyserositis, where all the serous cavities become affected almost simultaneously or in rapid succession, and those cases which commence with a pericarditis, frequently tuberculous, with spread of infection to the neighbouring pleurae and, in some cases, to the peritoneum. If this latter group were referred to as *infective pericarditis* (tuberculous, pneumococcal, etc.) and the term *acute generalized polyserositis* was reserved for the former group—the acute disease in which all the serous cavities are involved almost simultaneously and in which group the aetiology is unknown—it would assist in eliminating a good deal of the confused terminology. The case described here would fall under the heading of acute generalized polyserositis.

Is this type of acute generalized polyserositis a protean manifestation of connective-tissue diseases (collagen diseases)?

In a large number of cases of polyserositis discussed by the authors referred to in the preceding section, no aetiological factor was found. The tubercle bacillus and other organisms have not been found except in those cases which presented originally as acute pericarditis. The possibility of this condition—acute generalized polyserositis—being due to a collagen disease was, therefore, considered on the following lines:

Clinical

Serous effusions are frequently found in systemic lupus erythematosus and, at times, in periarteritis nodosa.[2] However, the effusions are not, as a rule, massive or generalized in these conditions. No other clinical features such as skin lesions, enlargement of spleen, renal involvement, neurological lesions, asthma or gastro-intestinal pathology, except mild ulcerative colitis, were present. It must be admitted that apart from the serous effusions the resemblance to these collagen diseases is remote.

Laboratory Tests

Nothing specific was found in the blood examinations and biopsies. Lupus erythematosus cells were repeatedly negative. The alpha 2 globulin and gamma globulin were not specific. The liver-function tests were not significant. On the other hand, the numerous investigations for tuberculosis and other infections proved to be negative. Again no evidence to suggest a collagen disease can be drawn from this source.

Recent Additions to the Collagen Diseases

The scope of these diseases is being extended and, among the more recently proved conditions now accepted as being different forms of lupus erythematosus, are Sjögren's syndrome, Mikulicz's disease and Felty's syndrome. There are features in common between Sjögren's syndrome and lymphadenoid goitre (Hashimoto's disease), suggesting a common aetiological basis, although lupus erythematosus has not been proved in lymphadenoid goitre.[4] Is it possible that a similar relationship may exist between lupus erythematosus and acute generalized polyserositis?

Response to Treatment

This is the most significant feature suggesting that generalized polyserositis may be a protean manifestation of a collagen disease. The response to steroid therapy was immediate and, thus far, has been sustained in spite of discontinuing antitubercular and other therapy. Steroids are used in acute tuberculosis with antitubercular drugs to control toxic manifestations. There is, however, no evidence that the steroids accelerate the healing of tuberculosis or influence the absorption of tuberculous effusions, which may take many months to disappear. In this case the effusions disappeared about 2 weeks after commencing steroid therapy.

SUMMARY

A case of polyserositis is described. Routine investigations gave no definite clue to the aetiology. There was no response to antitubercular therapy, penicillin, broad-spectra antibiotics and anti-amoebic therapy.

Additional investigations for collagen disease, such as a repeated search for lupus erythematosus cells, pleural biopsy, and skin-muscle biopsy, likewise gave no indication as to the aetiology. However, there was a dramatic response to steroid therapy, with the disappearance of the bilateral pleural

effusions, the pericardial effusion, and the ascites. The terminology of polyserositis is considered and a suggestion is made that the term 'acute generalized polyserositis' be reserved for a group of these cases in which simultaneous multiple serous effusions of unproved aetiology occur. There is some evidence, but no proof, of a link between polyserositis as defined here and the collagen diseases in view of the serous effusions resembling those found in systemic lupus erythematosus and the immediate (perhaps temporary) response to steroids.

ADDENDUM

The patient was re-examined on 20 July 1959, 6 months after steroid therapy was commenced and antituberculous treatment discontinued. He was feeling very well, was able to do a full day's work, and had discontinued the 'tapered' dose of cortisone a fortnight previously. There was no evidence of any recurrence of fluid in the serous cavities on clinical, X-ray and ECG examinations. Lupus erythematosus cells and the indirect Coomb's test remained negative.

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