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Polymyalgia rheumatica and antimitochondrial antibodies

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SUMMARY Antimitochondrial antibodies (AMA) were detected in the sera of 11 of 36 patients with a clinical diagnosis of polymyalgia rheumatica (PMR) in whom comprehensive autoantibody screening had been performed. AMA did not correlate with biochemical changes of hepatic dysfunction, which are common in PMR, nor with parameters of musculoskeletal inflammation. Possible explanations are discussed.

Polymyalgia rheumatica (PMR) is a distinct clinical syndrome. It was first described by Bruce in 1888[1] as 'senile rheumatic gout', and had many other descriptive names before its present title was suggested by Barber in 1957.[2] It may be defined as a protracted generalised disease usually found in the elderly or middle aged, characterised by severe stiffness and pain in the shoulder and/or hip girdles, often accompanied by constitutional illness. These clinical features are associated with raised levels of acute-phase reactants, including erythrocyte sedimentation rate (ESR) and C-reactive proteins. A rapid and marked improvement with corticosteroid therapy is usual. An association of PMR with giant cell arteritis (GCA) in some cases is well recognised. Hepatic abnormalities have been reported frequently in PMR, especially a raised serum alkaline phosphatase (ALP) concentration, and have been reviewed by Knorring and Wasastjerna.[3] The first report of antimitochondrial antibodies (AMA) in polymyalgia rheumatica appeared in a review of AMA in subclinical liver disease by Walker *et al.*,[4] in which their case number 30 had high titres of AMA as well as abnormal biochemical liver function tests. Robertson *et al.*[5] described 3 such patients. In an addendum to the latter paper Hamblin reported a high incidence of rheumatic disorders in a group of patients selected for high titres of antimitochondrial antibodies in their serum.

These preliminary reports prompted us to look further for possible associations between PMR and primary biliary cirrhosis (PBC), abnormal hepatic function, and AMA.

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Patients and methods

We reviewed the clinical records of 36 hospital patients under treatment for a documented diagnosis of PMR, which was based on the typical presentation of pain and stiffness of the limb girdles, marked morning stiffness, and muscle tenderness in the absence of polyarthritis, myopathy, or polymyositis. No other cause of hepatic dysfunction such as excessive alcohol intake, exposure to hepatotoxic agents, viral hepatitis, previous jaundice, or blood transfusion was found. There was no family history of liver disease or recognised autoimmune disorder.

These patients were derived from 2 sources: (1) patients attending rheumatology clinics with a diagnosis of polymyalgia rheumatica and/or cranial arteritis (23 cases); (2) patients referred for routine autoantibody screening, and in whom other hospital physicians had diagnosed PMR (13 cases).

The following investigations had been carried out: (*a*) full bood count and ESR at time of diagnosis; (*b*) hepatic biochemical function tests, including serum bilirubin, aspartate transaminase (AST), Alanine transaminase (ALT), alkaline phosphatase (ALP), 5-nucleotidase (5NT), serum proteins (albumin, globulin, and electrophoretic profile); (*c*) circulating autoantibodies were detected by immunofluorescence, using the conventional sandwich technique and a multitissue substrate; (*d*) histology–needle

Table 1 *Clinical and laboratory data from 36 patients*

Name	*Age*	*Sex*	*ESR (mm/h)*	*ALP IU/l*	*5NT IU/l*	*AMA*	*Diagnosis*
* 1	64	F	60	720	69	1:1280	PMR
* 2	60	F	49	190	17	1:8000	PMR
3	60	F	74	260	16	−ve	PMR+OA
4	80	F	50	290	18	−ve	PMR+OA
5	62	F	120	120		−ve	GCA+PMR
6	66	F	80	90		−ve	PMR
7	75	F	134	90		−ve	GCA+PMR
8	68	M	62	96		−ve	PMR
9	72	F	78	187	15	−ve	PMR
10	62	F	80	91		−ve	PMR
11	71	M	98	858	80	−ve	GCA+PMR
12	75	F	120	190	19	−ve	PMR
13	64	M	70	120		−ve	GCA
14	66	M	65	175	15	−ve	PMR
15	70	F	67	131		−ve	PMR+OA
16	66	M	75	96		−ve	PMR
17	66	F	55	671	38	−ve	PMR
*18	70	F	81	285	16	1:160	PMR
*19	60	M	61	150		1:40	PMR
*20	78	F	54	156		1:100	PMR+OA
21	64	F	80	75		−ve	PMR
22	67	F	80	84		−ve	PMR
23	79	F	60	107		−ve	PMR+OA
24	70	F	61	85		−ve	PMR
25	69	M	52	110		−ve	PMR
26	70	M	54	95		−ve	PMR
*27	78	F	34	85		1:320	PMR+OA
*28	73	F	110	688	100	1:2500	PMR+OA
29	73	F	80	99		−ve	PMR+OA
30	73	F	82	135		−ve	PMR+OA
31	68	M	51	59		−ve	PMR
32	76	F	55	79		−ve	PMR+OA
*33	65	F	52	85		1:20	PMR+OA
*34	73	F	64	95		1:40	PMR+Myxoedema
*35	64	F	87	365		1:160	PMR
*36	76	F	65	110		1:20	GCA+Sjögren's syndrome

OA=osteoarthrosis.
* Patients positive for antimitochondrial antibodies.

liver biopsy had been carried out in 3 patients and temporal artery biopsy in 4 patients.

Results

Of the 36 patients there were 9 males and 27 females aged between 60 and 80 years, mean age 67. The ESR ranged from 49 to 134 mm in the first hour. In all patients studied the serum bilirubin, AST, ALT, and plasma proteins were within normal limits. Twenty patients (55%) had raised alkaline phosphatase, and, of these, 11 (55%) had a raised 5-nucleotidase. Eleven of the 36 patients (31%) had circulating antimitochondrial antibodies (AMA) in titres ranging from 1/20 to 1/8000. In the 3 liver biopsies nonspecific histological changes were seen, denoting a mild hepatitis. However, as only one of these patients had circulating AMA (titre 1:2500), no conclusions can be drawn. Four patients had cranial arteritis, confirmed by biopsy, of whom only one had AMA in a low titre of 1:20.

There was no correlation between any of the hepatic changes and either the ESR or the clinical state, nor between the titres of AMA and other features (Table 1). There was also no significant difference in hepatic abnormality between AMA-positive and AMA-negative polymyalgia rheumatica patients.

Discussion

Boersma and Kerst[6] first reported raised levels of alkaline phosphatase and increased bromsulph-

thalein retention in patients with 'anarthritic rheumatoid arthritis (polymyalgia rheumatica)', and since then there have been several reports of disordered liver function in PMR, most commonly a raised serum ALP level. Our finding of raised ALP in 55% of patients is in general agreement with other reports.[3, 7] The rise in ALP is thought to denote a mild nonspecific involvement of the liver, and may be accompanied by nonspecific histological changes, such as were found in the 3 liver biopsies referred to above.

Glick[8] also noticed an unexpected incidence of antimitochondrial antibodies in patients with polymyalgia rheumatica. In our 11 AMA-positive patients with PMR the titre of AMA varied widely and was greater than 1/40 in 7 cases. The titres of AMA did not correlate with the ESR or ALP. AMA are considered to be strongly suggestive of PBC,[9] and they occur in less than 0·1% of the general population.[10] However, AMA are also found in about 20% of patients with chronic active hepatitis and in some with cryptogenic cirrhosis.[11] In our hands between 2 and 3% of routine autoantibody examinations requested by clinicians show AMA, and apart from hepatic disease the incidence has been highest in rheumatoid arthritis and Hashimoto's thyroiditis.[12]

Overlap between different autoimmune disorders is known to exist clinically. Serological overlap is more common. The relationship between PMR and PBC may be similar. While occasional unequivocal cases of the 2 disorders may coexist, serological and subclinical overlap may be more common. This is suggested by our study, which shows a high prevalence of serological and biochemical features of PBC in a selected group of patients with PMR. The interpretation of these findings is complicated by the lack of precise criteria for a diagnosis of PBC in the absence of characteristic histological changes, since biopsy tissue is often not available, and the diagnosis then rests on clinical judgment.[11] Theoretically AMA production could also be provoked by damage to mitochondria in cells of nonhepatic origin. It is of interest that Fassbender and Simmling-Annefeld[13] reported electron microscopic evidence of mitochondrial damage in skeletal muscle cells obtained by biopsy from patients with PMR.

It is clear that further investigation is required to answer these questions, especially into the epidemiological and pathological relationships between PMR and PBC. It appears that the incidence of PBC varies geographically within the UK, and at least ranges from 5·8 to 12·7 per million,[14] but the incidence of PMR is not known with any certainty. Rheumatic symptoms may draw attention to subclinical but potentially serious liver disease, and for this as well as other reasons careful investigation and follow-up of patients with the polymyalgia rheumatica syndrome are necessary.

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