SHORT REPORTS

e Antigen among male homosexual patients

Studies in the USA and UK have shown that hepatitis-B virus (HBV) infection is common among sexually promiscuous people and that male homosexuals have a particularly high frequency of past or current infection with HBV.^{1,2} We have attempted not only to determine the prevalence of HBsAg and its major subtypes among male homosexual and heterosexual patients but, in order to assess some of the risks to patients' contacts, have also conducted tests to detect such possible markers of virus infectivity as the recently described e antigen, Dane particles, and antibody to the core antigen (anti-HBc).

Patients materials and methods

Patients attending the department of genitourinary medicine at St Thomas's Hospital with such high-risk factors of HBV infection as drug abuse, past history of jaundice, tattooing, birth in countries with high HBsAg carrier rates, or homosexual practices were selected for study between January 1975 and March 1977. HBsAg was detected by solid-phase radioimmunoassay.* The major ad and ay subtypes were also detected by a radioimmunoassay technique.³ e Antigen and its antibody (anti-e) were detected by agar gel diffusion,⁴ and Dane particles by immune electron-microscopy. Anti-HBc was detected by complement fixation tests, core antigen being extracted after death from the liver of an HBsAg carrier who had been given a renal transplant but who died from cardiac infarction.

Of 1602 patients tested 58 (3.6%) were HBsAg positive. Of 360 male homosexuals 20 (5.5%) were HBsAg positive compared with 34 of 993 (3.4%) male heterosexual patients. This difference was not significant ($P>0.05$) (see table). e Antigen, however, was detected in a significantly greater proportion of male homosexual than heterosexual patients, being present in the sera of nine of 20 (45%) homosexuals but only in four of 30 (13%) heterosexual patients ($P<0.02$). Of the 20 HBsAg-positive homosexual patients, 12 (60%) did not have any other apparent risk factor and, of these patients, seven (58%) were e antigen positive. There was no significant difference in the proportion of HBsAg-positive homosexual and heterosexual patients who were anti-e positive or anti-HBc positive, and similar anti-HBc titres were present in both groups (see table). Of the 58 HBsAg-positive patients, six (10%) had acute hepatitis. Three were homosexuals, but only one was e antigen positive. The duration of e antigen responses could not be reliably determined, since many patients did not attend regularly. In one heterosexual patient who did not have jaundice, however, it had disappeared seven weeks after it was first detected, while in one homosexual patient, it was still present 38 weeks after its first detection.

Comment

e Antigen is considered to be a marker of HBV infectivity.⁵ Since HBV infection may be acquired sexually,² sexual contacts of homosexuals may be at particular risk of acquiring infection. The high proportion of e-antigen-positive sera among homosexuals emphasises the importance of handling specimens in the laboratory from such patients with particular care. The Dane particle is probably the hepatitis-B virus itself. In our study these particles were detected in 10 of 13 (77%) e-antigen-positive sera but in only two of eight (25%) which contained anti-e ($P<0.02$). Subtyping was carried out on 14 of 20 homosexual patients of whom 12 (86%) had the ad subtype.

* Austria 2, Abbott Laboratories, Chicago, Illinois, USA.

In contrast, 14 of the 21 (67%) heterosexual patients on whom subtyping was carried out had ay subtypes. These differences, however, probably reflect the countries of origin of these patients, since 10 of the 12 homosexual patients with the ad subtype were of Western European origin. (The ad subtype is generally much more commonly encountered than ay among Western European HBsAg carriers). In contrast, most of the HBsAg-positive heterosexual patients originated from West Africa and the Middle East, parts of the world in which the dominant subtype among carriers is ay.

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- ¹ Jeffries, D J, *et al*, *British Medical Journal*, 1973, **2**, 455.
² Szmuness, W, *et al*, *Annals of Internal Medicine*, 1975, **83**, 489.
³ Heathcote, J, Cameron, C H, and Dane, D S, *Lancet*, 1974, **1**, 71.
⁴ Magnus, L O, and Espmark, J A, *Journal of Immunology*, 1972, **109**, 1017.
⁵ Takahashi, K, *et al*, *Journal of Immunology*, 1976, **117**, 102.

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Pemphigoid and pernicious anaemia

Circulating antibodies reactive against the epidermal basement membrane area¹ may be found in most patients with pemphigoid. Nevertheless, it is still not certain whether these antibodies are merely secondary to the eruption, or are a primary event. An association between pemphigoid and other conditions with an autoimmune basis would support the second possibility. One of us (JAS), reviewing the clinical notes of 96 patients dying with pemphigoid, was impressed by the fact that four were being treated for pernicious anaemia. These patients were not fully documented, however. We present here details of a fifth patient at present under our care, believing her to be the first reported example of this association.

Case report

A 74-year-old woman presented in July 1976 with an eight-week history of recurrent blisters. She had no history of skin disease other than pruritus

Numbers of homosexual and heterosexual patients (percentages given in parentheses) with HBsAg, anti-HBc, e antigen, and anti-e

Patients	No	HBsAg	e Antigen	Anti-e	HBsAg subtypes		Anti-HBc		
					ad	ay	No positive/tested	Range of titres§	GMT§
Male heterosexuals	993	34†(3.4)	4(13.3)	7(23.3)	7	14	29/29	32-1024	588
Male homosexuals	360	20 (5.5)	9(45)	3(15)	12	2	17/19	128-1024	629
Females*	249	4†(1.6)	0	1	0	2	2/2	256-1024	507
Total	1602	58 (3.6)	13(24.5)	11(20.7)	19	18	48/50	32-1024	574

* Details of sexual behaviour were not obtained.

† 30 sera were tested for e antigen and anti-e.

‡ 3 sera were tested for e antigen and anti-e.

§ Reciprocal titre.

ani related to prolapsed rectal haemorrhoids, and atrophic vaginitis in August 1975, treated with dienoestrol cream and zinc sulphate tablets. For 29 years she had been receiving monthly injections of vitamin B₁₂ for a "macrocytic anaemia." She was obese and pale and had massive tense blisters on the right upper arm, left breast, trunk, and both legs, where there were some urticarial plaques as well. There were no mouth lesions and the rest of the physical examination showed normal findings.

Skin biopsy of an early lesion showed on histology a subepidermal blister consistent with the diagnosis of bullous pemphigoid. The result of the indirect immunofluorescent test was negative at that stage, but circulating IgG antibody against basement membrane was later detected. Haemoglobin concentration was 13.1 g/dl; mean corpuscular volume 87 fl; WBC 10.8 × 10⁹/l; ESR 68 mm in 1 hour (Westergren). The results of other extensive routine investigations were normal. Minor enlargement of the heart and a large hiatus hernia were seen on her chest radiograph. Serum immunoglobulins were: IgG 150 IU/ml; IgA 192 IU/ml; IgM 36 IU/ml. Schilling test without intrinsic factor was less than 1%; with intrinsic factor 2.6% (normal range 7-22%). Autoantibody test against rat gastric parietal cells was positive on two occasions and anti-intrinsic factor antibody was positive (> 10.4 ng units/ml), but no antibodies were detected against thyroid and kidney cells.

Her injections were continued for her pernicious anaemia. Her bullous pemphigoid responded to 30 mg daily of enteric-coated prednisolone, which was gradually reduced, 20 mg daily being found to keep her free of blisters. She was discharged on this dosage, but subsequently developed a compression fracture of the first lumbar vertebra. She was then readmitted for orthopaedic treatment and azathioprine started at the daily dosage of 150 mg, prednisolone being gradually reduced to 10 mg daily. She was given analgesics and a corset for her back, and she remained ambulant. There were no further blisters on this regimen. Nevertheless, three blue-red nodules have since developed on her legs. The clinical diagnosis of Kaposi's sarcoma has been confirmed histologically. This association with pemphigoid has been reported once before.²

Discussion

Bullous pemphigoid was separated from pemphigus in 1953.³ Its claim to be an entity was strengthened by finding circulating auto-antibodies of IgG, and occasionally IgM, classes to basement membrane in 80% of cases of pemphigoid.⁴ Immunoglobulins are found exactly at the lesions in both conditions, which are hence usually considered to be autoimmune; but reports of associations with other autoimmune diseases have been uncommon, and there have been no published reports of an association with pernicious anaemia.

¹ *Immunological Aspects of Skin Disease*, ed by Lionel Fry and P P Seah. Lancaster, MTP, 1974.
² Tye, M J, *Archives of Dermatology*, 1970, **101**, 690.
³ Lever, W F, *Medicine*, 1953, **32**, 1.
⁴ Greaves, M W, *Immunology in Medical Practice*, ed by Geoffrey Taylor, p 312. London, Saunders, 1975.

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Complicated polymyalgia

Classical polymyalgia rheumatica is easily diagnosed and treated. Most patients present with pain in the muscles of the shoulder and pelvic girdles accompanied by severe morning stiffness, and most patients respond dramatically to a small dose of steroids. The only laboratory abnormality is a raised erythrocyte sedimentation rate, and the steroids can usually be slowly withdrawn over two to four years. The association of this disease with temporal arteritis is well known,¹ but polymyalgia may occasionally be the presenting feature of some other serious disease, as we report.

Case reports

The important features of six cases of polymyalgia rheumatica complicated by some other disease are shown in the table. Cases one to four had an underlying malignancy, which in all but one was discovered when polymyalgia rheumatica was diagnosed. There was in every case a clue that led to the diagnosis of the underlying condition. In case one this clue, an abnormal shadow in a chest radiograph, did not appear until two years after the onset of muscular symptoms. At this time, however, the patient still had active polymyalgia and still needed prednisolone, 11 mg daily, to control it. These four cases were treated with corticosteroids (initially prednisolone 40 to 15 mg daily), with adequate symptomatic relief. In case five symptoms of polymyalgia rheumatica were the presenting feature of infective endocarditis and responded to antibiotics. Case six had typical polymyalgia rheumatica, which responded to steroids. After 18 months when the disease was well controlled on prednisolone, 5 mg daily, the patient developed pain and swelling of peripheral joints with a positive latex test result and has since then followed the typical course of rheumatoid arthritis.

Details of six cases of polymyalgia rheumatica that were complicated by some other disease

Case No	Age	Sex	Underlying condition	Clue
1	45	M	Hodgkin's disease	Abnormal chest radiograph
2	58	F	Carcinoma bronchus	Lumps on back
3	54	M	Carcinoma	Localised back pain
4	60	M	Myeloma	Wasted hand and proteinuria
5	54	M	Infective endocarditis	Mitral valve disease
6	65	F	Rheumatoid arthritis	None

Comment

Polymyalgia rheumatica is a distinct clinical entity. All the patients described had typical symptoms—a raised erythrocyte sedimentation rate and no evidence of polymyositis as judged by muscle enzymes, electromyography, and muscle biopsy.

The association of polymyalgia rheumatica with malignancy and other serious systemic diseases is neither well known nor well documented. McKenzie² reported a case in which symptoms of polymyalgia preceded those of carcinoma of the stomach and also noted associations with temporal arteritis, rheumatoid arthritis, polymyositis, and hypothyroidism. Macleod³ reported three cases with carcinoma of the cervix, stomach, and rectum, though in one the carcinoma appeared five years after the onset of polymyalgia. This could be coincidental since polymyalgia is a disease of an older age group. In our cases the time course of the two conditions suggested a causal relationship. Looking back, our cases had clinical clues that suggested that there was some underlying disease and which serve as a reminder of the need for a careful history and full physical examination of a patient with polymyalgia rheumatica. The only exception was the patient who developed rheumatoid arthritis, which seems to be an entirely unpredictable sequel of the disease in occasional patients. The association of polymyalgia and infective endocarditis has been noted by Deshayes *et al*.⁴

Laboratory tests were not particularly helpful in distinguishing this group of patients. The only additional clues were the unexpected youth of one patient, a rather larger than normal dose of steroids, or difficulty in reducing the dose over the normal period of about two years.

When diagnosing polymyalgia rheumatica, a careful physical examination for evidence of any underlying serious disorder should always be made.

¹ Dixon, A St J, *et al*, *Annals of Rheumatic Diseases*, 1966, **25**, 203.
² MacKenzie, A H, *Geriatrics*, 1969, **24**, 158.
³ Macleod, M, *The Practitioner*, 1973, **211**, 351.
⁴ Deshayes, P, *et al*, *Revue du Rhumatisme*, 1974, **41**, 135.

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