LETTERS TO THE EDITOR

Behçet disease: advantageous against development of neoplasia?

Although a good deal is known about the late occurrence of malignancy in the connective tissue disorders and other vasculitides, including the autoimmune diseases, for example, rheumatoid arthritis, progressive systemic sclerosis, Sjögren syndrome, systemic lupus erythematosus, and so on,¹ there have been few reports on concurrent neoplasms in Behçet disease and all of these were devoid of any documented pathophysiology except for the possibility of a drug induced relationship.²⁻⁵

In our referral teaching hospital, over 400 Behçet disease patients have been followed in the last 15 years on single agent and/or combined treatment protocols consisting of non-steroidal anti-inflammatory drugs, corticosteroids, colchicine, and occasionally azathioprine (required in less than 1%). The median follow up duration for our patients is 9.8 years (range 1.2 to 15+ years) and no patients have been lost to follow up. In spite of the frequent controls and various treatment methods used in our several randomised trials for the management of Behçet disease and its related vasculitic complications, we noticed the absence of de novo or drug related malignancy in any of the cases during the long term follow up.

Behçet disease is a syndrome complex of chronic relapsing vasculitis where the precise underlying pathogenic mechanism is not clear. Though not universal, the strong association of Behçet disease with HLA-B5 in several ethnic groups is well described,

which suggests an HLA related immunopathogenic explanation.⁶ Also, the presence of HLA-B5 in Behçet disease contrasts with other autoimmune conditions and collagen vascular diseases in that it has the unique feature of being unrelated to HLA-A, C, D, or DR antigens. Thus this specific antigenic determinant of Behçet disease forms a unique clinical picture characterised by antibody formation restricted only to certain local conditions secondary to vasculitic endothelial injury, with absence of systemic derangements in the immune system. In addition, large patient series from various countries do not suggest there is a link between Behçet disease and particular collagen vascular diseases^{7,8} and this might further contribute to the lowered incidence of neoplasia in these individuals.

Behçet disease shows a wide spectrum of presentations which vary among different races, and this observation in our particular ethnic group needs to be confirmed in others. As no specific gene rearrangement or evidence of a tumour-suppressor gene have yet been described as a possible explanation, it remains to be determined through further study whether Behçet disease patients are lucky in possessing a protective HLA subtype against malignant transformation.

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Parvovirus B19 and acute joint swelling in rheumatoid arthritis patients

Human parvovirus B19 is the aetiological agent of erythema infectiosum and transient aplastic crisis in patients with shortened red cell survival.¹ Joint symptoms associated with B19 infection occur in up to 80% of infected adults, and usually occur symmetrically in the hands, wrists, knees, and cervical spine.¹ Arthralgia is usually acute and self limiting, but may be chronic and recurrent. Most patients with these symptoms are women^{2,3} and rheumatoid factor may be present or rise following B19 infection.³ In these patients, the 1987 American Rheumatism Association criteria for diagnosis of rheumatoid arthritis are often met. Although B19 DNA has been demonstrated in synovial fluid,⁴ synovial fluid cells,⁵ and synovial tissue,⁶ the evidence for the role of B19 in the causation of rheumatoid arthritis has been conflicting. We hypothesised that if persistent B19 infection triggers a chronic polyarthritis identical to rheumatoid arthritis, then patients with rheumatoid arthritis may, at the time of acute joint swelling, have B19 DNA in the serum, synovial fluid, and synovial fluid cells significantly more often than controls.

Twenty nine patients with acute joint swelling requiring knee joint aspiration were assessed: 18 test patients had rheumatoid arthritis, and 11 control patients had nonrheumatoid (non-RA) disease. Among the rheumatoid arthritis group (patients 1-18), the female to male ratio was 2:1 and the age range was 13-72 years, with a mean of 53.7 years. Duration of rheumatoid disease ranged from two to 30 years with a mean of 12.9 years. Among the non-RA group (patients 19-29), the female to male ratio was 7:4 and the age range was 15 to 83 years, with a mean of 52 years (table).

Ten millilitres of both synovial fluid and serum were taken from each patient. C reactive protein was measured in serum using laser nephelometry. Anti-B19 IgM and IgG were assayed in serum and synovial fluid by a fluorescent antibody technique as described previously.⁷ Hyaluronidase was added to synovial fluid (100 IU ml⁻¹), and synovial fluid cells were pelleted by centrifugation at 400 g and separated from the supernatant. DNA was obtained from serum and synovial

Patients details and results of serum and synovial fluid testing

Patient number	Age (years)	Sex	Diagnosis*	Duration of disease (years)	C reactive protein (mg l ⁻¹)	Serum B19 IgG	Synovial fluid B19 IgG
1	54	F	RA	16	1.6	+	+
2	62	F	RA	17	< 0.99	+	-
3	72	F	RA	5	98.5	-	-
4	56	M	RA	20	12.1	-	-
5	43	M	RA	9	43.5	+	+
6	58	M	RA	10	67.2	+	-
7	72	F	RA	20	17.0	+	+
8	45	F	RA	17	37.1	+	+
9	52	F	RA	12	99.5	+	-
10	62	F	RA	13	73.2	+	-
11	63	F	RA	8	17.0	+	+
12	48	M	RA	2	21.3	+	-
13	72	F	RA	5	97.0	+	+
14	68	F	RA	30	82.5	+	+
15	56	F	RA	18	2.79	-	-
16	56	M	RA	-	11.1	-	-
17	13	F	RA	-	1.41	+	+
18	14	M	RA	4	10.6	+	+
19	61	M	OA	-	57.7	+	+
20	83	F	OA	-	< 0.99	-	-
21	66	F	OA	-	< 0.99	-	-
22	72	F	OA	-	1.69	+	+
23	68	F	OA	-	3.28	+	-
24	80	F	OA	-	2.47	+	+
25	27	M	Psor	-	91.3	+	+
26	45	F	Psor	-	23.7	-	-
27	36	M	Psor	-	5.69	+	+
28	18	F	Reactive	-	101.	+	+
29	15	M	Reiter	-	73.3	+	+

*RA, rheumatoid arthritis; OA, osteoarthritis; Psor, psoriatic arthritis; Reiter, Reiter syndrome.