

Reflections on the prevalence of human leukocyte antigen-B27 and human leukocyte antigen-B51 co-occurrence in patients with spondylarthritis

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Abstract

We performed a literature mini-review of the clinical profile of patients with spondylarthritis who are also human leukocyte antigen (HLA)-B51-positive. It seems to us that patients with HLA-B27 and HLA-B51 are more common in men, Asians and between the third and ninth decades of life. They are more likely to develop peripheral joint conditions, with cutaneous manifestations (e.g., oral ulcers) and uveitis. Therefore, more robust epidemiological studies with more accurate methodology and multicenter locations are needed to better map the role of the interaction between HLA-B51 in patients with spondylarthritis.

Key Words: HLA-B27; HLA-B51; Ankylosing spondylitis; Spondylarthritis; Human leukocyte antigen

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Core Tip: Patients with human leukocyte antigen-B51 and human leukocyte antigen-B17 tend to be male, Asians and between the third and ninth decades of life with more peripheral arthritis, uveitis and oral ulcers.

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Table 1 Patients with spondylarthritis and human leukocyte antigen-B51-positivity

Ref.	Sample	Sample	Age in yr/male, n	Oral ulcer, n	Genital ulcer, n	Uveitis, n	Peripheral arthritis, n	Axial arthritis, n	Skin lesion, n	Gastrointestinal involvement, n	Cardiac involvement, n	Urethritis, n	HLA B27+
Jung <i>et al</i> [5]	16	16	39.5 ± 11.6/11	6	0	2	10	0	4	0	0	0	Y
Chang <i>et al</i> [2]	3	3	25-55/3	3	3	2	2	2	2	0	0	0	Y
Taniguchi <i>et al</i> [3]	1	1	32/1	0	0	1	1	0	0	0	0	1	N
Shimamoto <i>et al</i> [4]	1	1	28/1	0	0	1	1	0	0	0	0	1	N
Total (%)	21 (100)	21 (100)	25-82	9 (42.8)	1 (4.7)	7 (33.3)	14 (66.6)	4 (19.0)	6 (28.5)	0	0	2 (9.5)	19 (90.4)

HLA: Human leukocyte antigen; Y: The patient has the characteristic; N: The patient does not have the characteristic.

TO THE EDITOR

I have read the work of Lim *et al*[1] about human leukocyte antigen (HLA)-B51 positivity in patients with ankylosing spondylitis (AS)/spondylarthritis (Sp) who test negative for HLA-B27. The author aimed to report the first case series of HLA-B51-related occurrences of AS in a family. We performed a literature mini-review of the clinical profile of patients with Sp who are also HLA-B51-positive.

The incidence of HLA-B51 in patients on the Sp spectrum with HLA-B27-positivity is rare. According to literature data (Table 1), there are 21 cases described between case reports[2-4] and a cohort study[5]. As shown in Table 1, 90.4% of the patients were HLA-B51 and HLA-B27-positive. In the sample, 76% of the patients were male, all Asian and aged between the third and ninth decades of life. This epidemiological profile is similar to that of our patient, which corroborates this trend in the literature. Two possibilities are imposed here: (1) The existence of HLA-B51 by chance, due to its high prevalence in Asian populations; or (2) A correlation with the more peripheral AS frames. Thus, epidemiological studies of high prevalence of HLA-B51 in healthy groups of studies were carried out in countries that form the Silk Road, such as China, Turkey, South Korea, Japan and Iraq[1], reaching rates in control groups of 12.0% to 13.6%[6,7].

The relationship between HLA-B51 and HLA-B27-positive AS is still unclear. It is known that both genes are involved in the activation of tumor necrosis factor alpha, which would explain: (1) The favorable response of AS and Behçet's disease (BD, characteristically associated with HLA-B51) to tumor necrosis factor alpha inhibitors; and (2) The peripheral manifestations, common to both diseases of the articular system (*e.g.*, oligoarthritis, enthesitis and sacroiliitis) and ocular system (*e.g.*, anterior and posterior uveitis)[5]. There is a strong correlation between AS and the transport of certain intracellular amino acids at position 97 of HLA-B. Position 97 is also correlated with HLA-B51[3,4,8,9]. Furthermore, a recent review study points out the possible participation of HLA-B51 in the activation of helper T (Th)17 and Th1 lymphocytes[10]. The Th17 pathway is a pharmacological target of treatment for peripheral Sp, specifically of drugs that inhibit IL-17A. It is important to remember that the activation of Th17 lymphocytes is correlated with the activation of neutrophils, one of the cells known to be involved in BD[11].

In our review, there is a predominance of peripheral arthritis (66.6%), oral ulcers (42.8%), uveitis (33.3%) and skin lesions (28.5%) (Table 1). Interestingly, two reports[3,4] demonstrate cases of AS with HLA-B27-negativity but the presence of HLA-B51-positivity. Most cases demonstrate a predominance of significant peripheral joint involvement, including Reiter's syndrome commonly described[3,4]. A retrospective study carried out in Italy among patients with uveitis showed that among the systemic diseases AS and BD were the most correlated, with HLA-B27 and HLA-B51 presenting an odds ratio of 6.6 and 3.7, respectively[12].

Finally, it seems to us that patients with positive AS HLA-B27 and HLA-B51 are more common in men, Asians and aged between the third to ninth decades of life. They are more likely to develop peripheral joint conditions with cutaneous manifestations (*e.g.*, oral ulcers) and uveitis. Besides that, it is important to highlight the lack of studies with a more robust methodology in the literature and larger samples due to the low incidence and prevalence of AS as well as the lack of resources in several places to perform genetic tests. Thus, more robust epidemiological studies with more accurate methodology and multicenter locations are needed to better map the role of the interaction between HLA-B51 in patients with AS and its correlation with possible overlapping with BD.

FOOTNOTES

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