Lack of Association between CARD15 Gene Polymorphisms and Hidradenitis Suppurativa: A Pilot Study

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Hidradenitis suppurativa (HS) is a chronic inflammatory disease of the apocrine gland-bearing skin of the axillae, groin, chest and perianal regions. It is characterized by follicular obstruction and secondary bacterial infection. The etiology and mechanisms are unknown, but genetic factors are suspected, considering that HS is a familial disorder in 30% of cases [1].

The association between HS and Crohn’s disease (CD) has been reported in short series [2]. In addition, the granulomatous inflammation in both diseases as well as their clinical response to anti-TNF therapy suggests similar pathophysiological mechanisms.

Association between polymorphisms within the CARD15/NOD2 gene and CD has been reported by many groups. CARD15 gene encodes for an intracellular sensor of bacterial cell wall muramyl dipeptide, and plays a major role in NFkB activation and inflammatory pathways. It also modulates the TLR2 pathway, suggesting that CARD15 mutations impair signaling in the innate immunity response to pathogens, leading to chronic inflammation. CARD15 mutations were also found in patients with Blau syndrome, a second granulomatous disease [3].

The relationship between HS and CD incited us to analyze CARD15/NOD2 in HS patients. Ten patients with HS and without CD who were recruited in our department of dermatology. Patients were included in the study independently of the severity, location of disease or treatment. Polymorphism analysis was performed on blood samples, by direct sequencing of the constant exons and intron-exon boundaries of CARD15 gene.

Only 1 of the 10 patients was found heterozygous for the R702W polymorphism, and none had the G908R or 1007fs polymorphisms. No additional polymorphism was identified.

Comparing the frequency of allelic polymorphism of CARD15 found in this population with that previously published in Caucasian healthy controls [4], we did not find any difference (1/20 vs. 15/206; p > 0.05; Fisher unilateral test). However, the frequency of allelic polymorphism was lower in HS than in CD (1/20 vs. 249/906; p = 0.0216; Fisher unilateral test).

In conclusion, this pilot study carried on a limited number of HS patients does not support the hypothesis that CARD15/NOD2 polymorphisms associated with CD have a comparable role in HS. Moreover, no additional polymorphism of CARD15/NOD2 coding sequence was observed in HS patients.

References

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