Letters in Response to Previous Publication

A cluster of differentiation 19 + B-lymphocyte cell as a predictor of relapse in pemphigus vulgaris

Received: April, 2020
Accepted: July, 2020
Published: March, 2021

DOI:
10.25259/IJDVL_506_20

PMID:
*****

Sir,

We read with keen interest the article "Identification of clinical and immunological factors associated with clinical relapse of pemphigus vulgaris in remission" published in the Indian Journal of Dermatology, Venereology and Leprology, issue 3, Volume 86.[1] The study methodology of using one-time assessment of cluster of differentiation 19+ B-lymphocyte cells and cluster of differentiation 19+ cluster of differentiation 27+ memory B cells' count in an equal number of controls to have data regarding their counts in normal north Indian population does not seem to have enough external validity. Though a sample size of 40 for a rare disease like pemphigus seems acceptable, to derive the normal value of the cluster of differentiation 19+ B-lymphocyte cells in a population from 40 controls seems questionable given that the sample size is too small. Besides, the authors have not mentioned characteristics of controls in terms of age, sex, inclusion and exclusion criteria. A cluster of differentiation 19+ B-lymphocyte cell count can be confounded by many factors including immunogenetics of controls, recent infections and so on. Interestingly, data for normal values of various lymphocyte subpopulations in healthy Indians is available from a study conducted by a national task force constituted by the Indian Council of Medical Research.[2] Is there any specific reason for not using this data which was based on a much larger sample size and had the authors' institute as one of the centers in the study?

A peripheral cluster of differentiation 19+ B-lymphocyte cell count is significantly influenced by steroid use and steroid withdrawal as reported in other conditions.[3] Rituximab is the most potent cluster of differentiation 19+ B-lymphocyte depleter among all the previous treatments received by the patients in the study. Taking baseline cluster of differentiation 19+ B-lymphocyte cell count across the study population, which was treated with different treatment modalities in past with a few of them being on steroid and a few off steroid, add to the confounders in the final calculation of odds ratio. During a discussion of results, authors have compared their findings with that published by Albers *et al*., a study that was strictly limited to B cell repopulation after rituximab therapy.[4] Correlation of disease relapse and repopulation of cluster of differentiation 19+ B-lymphocyte after B cell depletion therapies are well-studied now for pemphigus and other autoimmune disorders. Authors' assumption that "B cell repopulation must occur irrespective of treatment modality used, preceding clinical relapse in a prototype immunoglobulin G-mediated disease," seems too generalized considering that no other treatment like steroid, azathioprine or dexamethasone-cyclophosphamide pulse is known to deplete B-cell from circulation as thoroughly as rituximab.

Analysis of patients previously treated with rituximab *vis-a-vis* other treatment modalities and performing baseline cluster of differentiation 19+ B-lymphocyte cell count among them and exploring subsequent trends in both the groups would have thrown more light on this very interesting aspect of relapse in pemphigus vulgaris. Pilot study on a cluster of differentiation 19+ B-lymphocyte cell behavior with various treatment modalities may also help understand more about this immunological marker in pemphigus.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

Nayankumar Harshadkumar Patel, Jignaben Krunal Padhiyar, Ranjan C Raval

GCS Medical College Hospital and Research Centre, Ahmedabad, Gujarat, India

How to cite this article: Patel NH, Padhiyar JK, Raval RC. A cluster of differentiation 19+ B-lymphocyte cell as a predictor of relapse in pemphigus vulgaris. Indian J Dermatol Venereol Leprol 2021;87:237-8.

Corresponding author:
Dr. Jignaben Krunal Padhiyar,
Department of Dermatology, Venereology and Leprology, GCS Medical College Hospital and Research Centre, Ahmedabad, Gujarat, India.
dr.jignapadhiyar@gmail.com

References

1. Guliani A, De D, Handa S, Mahajan R, Sachdeva N, Radotra BD, Kishore K. Identification of clinical and immunological factors associated with clinical relapse of pemphigus vulgaris in remission. Indian Journal of Dermatology, Venereology, and Leprology. 2020 May 1;86 (3):233.
2. Saxena RK, Choudhry V, Nath I, Das SN, Paranjape RS, Babu G, *et al*. Normal ranges of some select lymphocyte sub-populations in peripheral blood of normal healthy Indians. Curr Sci 2004;86:969-75.
3. Llinàs-Mallol L, Redondo-Pachón D, Pérez-Sáez MJ, Raïch-Regué D, Mir M, Yélamos J, López-Botet M, Pascual J, Crespo M. Peripheral blood lymphocyte subsets change after steroid withdrawal in renal allograft recipients: a prospective study. Scientific reports. 2019 May 15;9 (1):1-1.
4. Albers LN, Liu Y, Bo N, Swerlick RA, Feldman RJ. Developing biomarkers for predicting clinical relapse in pemphigus patients treated with rituximab. J Am Acad Dermatol 2017;77:1074-82.

Response to a reader's query on CD19+ B cell as predictor of relapse in pemphigus vulgaris

Received: May, 2020
Accepted: July, 2020
Published: March, 2021

DOI:
10.25259/IJDVL_758_20

PMID:
*****

Sir,

We thank the authors[1] for their interest in our article 'Identification of clinical and immunological factors associated with clinical relapse of pemphigus vulgaris in remission.'[2]

We understand that 40 may be a small control sample size to derive the normal value, and that sampling a larger number of normal individuals would have been better. We agree that use of a normative data from Indian population of over 1000 subjects would be useful. However, the journal that published the data of 1000 healthy Indians is indexed by Web of Science, Current Contents, Geobase, Chemical Abstracts, IndMed, and Scopus and not indexed in PubMed. Hence, we missed the reference to this article.[3] We appreciate the authors' efforts in finding it out.

However, since we were interested in not just the frequency of CD19+B cells but also the CD19+CD27+ memory B cells (which is lacking in the study referred to), we would still have to study the same age and sex-matched normal control subjects for comparison of CD19+CD27+B cells. The purpose of this analysis was not to project these data as a reference for normal healthy control subjects of North India, but only for comparative analysis of the study subjects in question. Moreover, since the blood samples of controls and subjects with pemphigus vulgaris were stained with the same lot and clone of the antibodies and were analyzed on the same flow cytometry platform, we were able to ensure assay uniformity. Additionally, practical difficulties such as willingness to participate despite not having the disease in question and financial constrains in respect to study funding are some important considerations in this type of study.

The controls were age and gender matched individuals with other dermatological diseases attending our outpatient department. One qualified as a control if s(he) did not have any recent infectious disease or autoimmune disease including pemphigus.

We agree with the authors that: 'Peripheral CD19+ B cell count being significantly influenced by steroid use and steroid withdrawal and rituximab being the most potent and total CD19+ B lymphocyte depleter among all the previous treatment', and that is why rituximab induces remission for a longer time. Other treatments also have effects on CD19+ B cells. The objective of the study was to see repopulation of CD19+ B cells and subsequent effects, not to study depletion of B cells with a particular treatment that is assumed to have had happened since the patients were in remission when they were included in the study.

To have clinical relapse, first step is immunological reactivation in the form of B-cell repopulation. There is no other known source of immunoglobulins. In other words, it can be assumed that B-cell repopulation must occur irrespective

How to cite this article: Guliani A, De D, Handa S, Mahajan R, Sachdeva N, Radotra BD, *et al*. Response to a reader's query on CD19+ B cell as predictor of relapse in pemphigus vulgaris. Indian J Dermatol Venereol Leprol 2021;87:238-9.