To the editor:

Bugs and marginal zone lymphoma of the ocular adnexae: is the future already here?

We read with great interest the review article by Drs Stefanovic and Lossos on extranodal marginal zone lymphoma of the ocular adnexa (OAML).\(^1\) Although we agree on most of the issues covered and authors’ viewpoints, we would like to add constructive comments on the topic of OAML to allow Blood readers to consider equally important critical issues complementary to those raised by the authors.

The most relevant issues of this letter involve the relationship between Chlamydia psittaci (Cp) infection and OAML.\(^2\) In this context, it is important to highlight that some recent studies have increased the level of evidence supporting this association. In a large cumulative series, the presence of Cp in OAML has been demonstrated by 3 different polymerase chain reaction techniques, immunohistochemistry, immunofluorescence technique, and electron microscopy.\(^3\) In addition, a prospective case-control study has confirmed both viability and infectivity of Cp by means of in vitro isolation and growth in OAML patients,\(^4\) fulfilling the second Koch postulate for this bacterium-lymphoma association. Together with Helicobacter pylori, Cp is presently the only bacterium with lymphomagenic potential isolated so far in in vitro cultures from lymphoma patients.

A worldwide variability in the prevalence of Cp infection in OAML patients was also discussed by Drs Stefanovic and Lossos, but in a way suggesting that, after initial reports describing a strong Cp-OAML association,\(^5\) subsequent studies did not show these figures. This issue is probably much more complex, and the recent demonstration of the presence of Cp in a significant population of OAML Austrian\(^6\) and Korean\(^7\) patients does not support the authors’ view. A multicenter study with centralized molecular analyses has confirmed a certain geographical heterogeneity by detecting discrepancies in Cp prevalence among countries and among different regions within the same country.\(^7\) Discrepancies in the prevalence of OAML-Cp association could be also explained by methodologic biases. Moreover, the use of antibiotics may reduce the tissutal load of chlamydiae below the threshold of polymerase chain reaction detection, thus yielding false negative results. As pointed out in the above-mentioned review,\(^1\) these data strongly emphasize the need for performing methodologically rigorous studies on worldwide geographical distribution of Cp infection in OAML within international prospective trials. Since 2007 an international prospective study (perhaps the only available for OAML so far), named IELSG27, was launched under the sponsorship of the International Extranodal Lymphoma Study Group (www.ielsg.org/trialsonfr.html). This trial includes both clinical and biologic endpoints focused on the efficacy of antibiotic therapy and the worldwide distribution of OAML-related infectious agents, including viruses. This international, open trial could be presently one of the best unbiased tools to find answers to most of the open questions highlighted in the discussed review.\(^1\)

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References


Response

Variability in the prevalence of Chlamyophila psittaci infection in patients with OAML

We thank Drs Ponzoni et al for their interest in our review on extranodal marginal zone lymphoma of the ocular adnexa (OAML) and would like to express our point of view regarding the comments the authors are raising on the association between Chlamyophila psittaci (Cp) and OAML. As illustrated in our review, we indeed acknowledge the existing evidence supporting this association in certain but not all geographical areas as well as the epidemiologic and scientific approaches the authors have undertaken.\(^1,2\) However, there is convincing evidence in the literature that this association is not as prevalent as indicated by the 2 series from Italy and Korea, which reported a prevalence of Cp infection in approximately 80% of OAML.\(^1,3\) In fact, there appears to be considerable geographic variability in the prevalence of Cp infection in patients with OAML worldwide, with a wide range from 0% to 80%. The most heterogeneous data regarding the association...
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