LETTERS TO THE EDITOR

Methodological Considerations Regarding the Use of Galectin-3 Expression Analysis in Preoperative Evaluation of Thyroid Nodules

To the editor:

Preoperative characterization of thyroid nodules by using galectin-3 immunodetection on cytological smears from thyroid FNA is going to become a widely accepted diagnostic procedure in a large number of European institutions and university hospitals. As coauthors of the multicenter study in which this test-method has been proposed and validated (1), we are obliged to comment on the article entitled “Galectin-3 is not an universal marker of malignancy in thyroid nodular disease in children and adolescents” by M. Niedziela and colleagues, published in the September issue of JCEM (2).

To improve the conventional cytological evaluation of thyroid nodules, Niedziela and colleagues propose a RT-PCR-based technique instead of an immunocytochemical method. There are at least two important criticisms to this approach that need to be considered and discussed.

First, it should be stressed that analysis of galectin-3 expression in thyrocytes cannot be considered as a substitute for the conventional morphological evaluation of each specific lesion. For this reason, an immunocytochemical diagnostic approach to the preoperative characterization of thyroid nodules is mandatory, because this simple and cheap procedure combines a morphological and immunophenotypical evaluation of thyroid cells.

This strategy is crucial because expression of galectin-3 is normally observed in activated endothelial cells as well as in the so-called “foamy macrophages,” which are commonly observed in different benign (i.e. colloid goitres, Hashimoto’s thyroiditis, etc.) and malignant thyroid conditions. Moreover, it should be also considered that only the cytoplasm expression of galectin-3 is suggestive of malignancy, because nuclear immunoreactivity is physiologically observed in some benign thyroid conditions (3).

Consequently, the use of RT-PCR for evaluation of galectin-3 expression on morphologically undefined cytological material, as Niedziela and co-authors propose, doesn’t represent a reliable diagnostic method and is affected by a large number of false positive results.

With this in mind, we are not surprised about the reported results regarding galectin-3 expression in Hashimoto’s thyroiditis and other benign thyroid lesions (2). For the reason discussed above we strongly discourage the use of RT-PCR for this specific diagnostic purpose. A reliable use of RT-PCR for characterization of thyroid nodules requires the set-up of expensive and time consuming tissue micro-dissection procedures to be applied on cytological and histological preparations.

Regarding the second point of discussion, expression of galectin-3 in some Hashimoto’s thyroiditis has been previously described in a very limited number of cases (1). Although the number of galectin-3 positive Hashimoto’s thyroiditis decreased consistently when a purified monoclonal antibody to galectin-3 and a biotin-free detection system were used in immunocytochemistry (4), we confirm the possibility that some of these thyroid diseases may express galectin-3.

The significance of galectin-3 expression in focal areas of oncocytic changes observed in some Hashimoto thyroiditis is currently under investigation (paper in preparation), but the conclusion of Niedziela and colleagues that an “abundant number of oxyphilic cells in this disorder is a consequence of neoplastic transformation within Hashimoto’s goiters” appears quite imprudent, especially if this conclusion is not supported by an adequate morphological study of these intriguing lesions.

References

Authors’ Response: Methodological Considerations Regarding the Use of Galectin-3 Expression Analysis in Preoperative Evaluation of Thyroid Nodules

To the editor:

We are grateful to Professor Bartolazzi and his co-workers for their comments on our paper and will attempt to answer their pertinent queries. First, it was their previously published papers (1–3) that led us to investigate galectin-3 expression in our series of children with thyroid nodules. The aim of our study was to determine whether galectin-3 expression using the RT-PCR-based technique would improve the accuracy of preoperative diagnosis of thyroid carcinomas, because the results of fine-needle aspiration biopsies are not infallible.

We reported positive expression in proliferative forms of autoimmune thyroiditis and Hashimoto thyroiditis coexisting with a follicular adenoma (4). They say that these may be false-positive RT-PCR results. The two important criticisms contained in the letter were, in our opinion, covered in our paper. First, we stated that the aim of our galectin-3 expression analysis was “to improve the classical cytological evaluation of the material obtained with ultrasound-guided biopsy,” but importantly added that this technique was not the only diagnostic approach to be employed.

Secondly, they wonder whether some of the cells in the biopsy material are target cells for galectin-3 and, therefore, that false-positive results are possible in such cases. We disagree with their statement that our examination of galectin-3 expression was performed on “morphologically undefined cytological material” because we included a description of the representative cytological material obtained from biopsies, as shown in Table 1 of our paper (4).

Our data concerning galectin-3 expression in Hashimoto thyroiditis, based on the RT-PCR method, are in agreement with Herrmann et al. (5) who showed that “galectin-3 was also expressed focally and weakly in reactive follicular epithelium and entrapped follicles in chronic lymphocytic thyroiditis.” This paper was published precisely at the time our manuscript was being reviewed by JCEM experts. There are, however, a number of published papers supporting the possible false-positive expression of galectin-3, including those of Herrmann et al. (5) and of

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Beesley and McLaren (6), which are based on immunohistochemical analysis as well as those of Bernet et al. (7) and Martins et al. (8), based on the RT-PCR technique.

We therefore postulate that both RT-PCR and immunocytochemical diagnostic approaches performed preoperatively and RT-PCR and immunohistochemical analysis performed postoperatively on the same specimen would help in the phenotyping of target cells for galectin-3 and thereby answer the question as to whether a straight correlation exists between the two methods or not.

Finally, our paper does not disagree with their previously published findings (1–3) and even supports their usefulness in the preoperative detection of thyroid carcinoma. On the other hand, our paper may indicate some limitations in cases with pathogenetic and clinical diversity, such as Hashimoto thyroiditis and a solitary nodule. We want to stress that the preoperative expression of galectin-3 must be interpreted in such cases with great caution and only in parallel with routine conventional cytology, thereby improving it as a diagnostic or prognostic adjunct.

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