ENDOGLIN: A MARKER OF NEOPLASIAS OR RATHER OF NEO-ANGIOGENESIS?

To the Editor:

We read the recent article by Eleno et al. entitled “Endoglin as a marker of cervical paragangliomas.” The authors analyzed and compared the expression of endoglin, vascular endothelial growth factor (VEGF), hypoxia inducible factor (HIF), and of vascular cell adhesion molecule 1 (VCAM-1) in 5 surgically resected paragangliomas and in specimens of non-neoplastic lung, obtained from 5 patients submitted to pulmonary resection of lung tumors. They found a higher amount of endoglin, HIF-1, and VCAM1, but not of VEGF, in paragangliomas in comparison to lung parenchyma. Finally, they stated that endoglin may have a remarkable diagnostic, prognostic, and therapeutic relevance in tumor development and malignancy of cervical paragangliomas.

In our opinion, it would have been useful to analyze the expression of the above-mentioned factors in lung parenchyma also through immunohistochemistry. Indeed, Western Blot does not allow one to assess the precise location of proteins in the different cell types within a tissue. Moreover, histologic examination of lung parenchyma used for the experiments should have been performed, since non-neoplastic alterations may also modify endoglin expression, as this protein may also be expressed by the vessels of regenerating or inflamed tissues. Besides, the authors themselves think that quantification of protein bands exhibited in immunoblots is limited and can hide some interesting considerations.

In addition, we do have some reservation about the potential diagnostic and prognostic usefulness of endoglin in paragangliomas as emerging from this study. Endoglin is a 180-KDa protein, which is predominantly expressed on cycling endothelial cells in tissues which undergo active angiogenesis. Its expression has been shown in the vessels of several tumors, such as meningiomas or colorectal carcinomas, and endoglin has been demonstrated as a specific marker for neo-angiogenesis in neoplasias. As such, its immunohistochemical evaluation has been largely used in order to assess the microvessels density (MVD) of tumors, which has been demonstrated to be a prognostic marker related to adverse clinical course in terms of overall and disease-free survival.

The existence of neo-angiogenic switch in paragangliomas had been previously hypothesized by other authors; nonetheless, in the assessment of MVD they used CD31, a pan-endothelial marker less specific than endoglin for the evaluation of neo-angiogenesis. Thus, we suggest that endoglin immunoexpression may be used to evaluate MVD in cervical paragangliomas so as to analyze whether tumors characterized by higher counts of vessels stained by anti-endoglin antibody display different biological behavior in terms of recurrences and to investigate its correlations with the expression of proangiogenic factors.
Finally, we think that the demonstration of endoglin expression in the vessels of paragangliomas may be considered as a hallmark of neoangiogenesis in these tumors, rather than a diagnostic tool.

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Reply
We thank Drs. V. Barresi and G. Barresi for their letter to the editor and for their interest in our recently published article.1 We agree with most of their points, although we would like to comment on some of them.

First, Drs. V. Barresi and G. Barresi suggest that it would be useful to analyze the expression of endoglin, vascular endothelial growth factor (VEGF) and vascular cell adhesion molecule (VCAM-1) in lung tissue by immunohistochemistry. It should be noted that our study was focused on paragangliomas; lung tissue was only used as a control of the quantitative amounts of these molecules in a normal, highly vascularized tissue, and we were not interested in the distribution of these molecules in lung tissue.

With respect to their reservations about the potential diagnostic and prognostic usefulness of endoglin in paragangliomas, there is no doubt that endoglin is considered a very specific marker of tumor angiogenesis and a prognostic marker of overall and disease-free survival for a variety of tumors.2 In addition, the amount of endoglin seems to regulate tumoral and non-tumoral angiogenesis.3,4 We agree with Drs. V. Barresi and G. Barresi that endoglin is a hallmark of neo-angiogenesis in paragangliomas as our study only deals with benign cervical paragangliomas, not metastatic, whose major problems are based on their mass effect.5 Nevertheless, paragangliomas are highly vascularized and tumor growth is dependent on angiogenesis, and thus, we can suggest that endoglin can be an accurate marker of morbidity in these tumors.

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