Correspondence

Chondroma of Epithelial Cell Origin

To the Editor-in-Chief:

In the interesting study of chordomas, Gottschalk et al¹ suggest that some cartilaginous tumors could be, in fact, chondroid chordomas in which complete cartilaginous differentiation occurred. Nevertheless, the authors mention that such a phenomenon seems to them as an unlikely extreme, analogous to pleomorphic adenoma of the salivary gland with unidirectional cartilaginous differentiation (chondroma-like pleomorphic adenoma) that was not described, and that such an event still only represents a theoretical possibility. However, I remember that a case of a salivary gland pleomorphic adenoma composed exclusively of cartilage had been described in a study of salivary gland neoplasms by Gusterson et al.² This tumor showed morphology of typical chondroma and its epithelial nature was manifested only in a form of epithelial membrane antigen positivity. This observation can support the above-mentioned suggestion by Gottschalk et al¹

I believe that modern ancillary techniques will discover, in the future, further lesions with unidirectional cartilaginous differentiation derived from a non-cartilaginous or non-mesenchymal cell. An interesting example for this is a case of a morphologically typical low-grade chondrosarcoma in which only a cytogenetic analysis was able to prove a germ cell origin.³

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References

1. Gottschalk D, Fehn M, Patt S, Saeger W, Kirchner T, Aigner T: Matrix gene expression analysis and cellular phenotyping in chordoma reveals focal differentiation pattern of neoplastic cells mimicking nucleus pulposus development. *Am J Pathol* 2001, 158:1571–1578
2. Gusterson BA, Lucas RB, Ormerod MG: Distribution of epithelial membrane antigen in benign and malignant lesions of the salivary glands. *Virchows Arch A Pathol Anat Histol* 1982, 397:227–233
3. Fuzesi L, Rixon H, Kirschner-Hermanns R: Cytogenetic findings in a metastasizing primary testicular chondrosarcoma. *Am J Surg Pathol* 1993, 17:738–742

Author's Reply:

We are grateful for the comments of M. Zamecnik on our article entitled, "Matrix Gene Expression Analysis and

Cellular Phenotyping in Chordoma Reveals Focal Differentiation Pattern of Neoplastic Cells Mimicking Nucleus Pulposus Development."¹ He mentions a potentially very interesting tumor case of a salivary gland reported by Gusterson et al² showing only chondroid and myxoid areas and being positive for EMA. Certainly, this case would be interesting to review, but the question arises whether or not the polyclonal antibodies used were really monospecific. We and others never found (significant) positivity of the chondroid areas of pleomorphic adenomas for epithelial cytokeratins³ or EMA (clone E29 von Dakopatts, Denmark (Figure 1)).⁴

Figure 1. Immunostaining with a monoclonal antibody to epithelial membrane antigen (EMA: clone E29 Dakopatts, Denmark) does not show positivity in chondroid areas of two pleomorphic adenomas (**a** and **b**), whereas surrounding ductular structures were strongly labeled (**Bars**, 100 μ m).

Also, the testicular teratoma⁵ showing complete chondrosarcomatous differentiation is an interesting case although the histology shown in the manuscript does not clearly correspond to conventional chondrosarcoma but rather shows additionally undifferentiated mesenchyme. Again, a reinvestigation of the case with currently available tools would be worthwhile, which would allow identification and classification of chondrocyte differentiation.^{6,7}

Overall, clearly single (ie, very exceptional) cases may exist that represents extreme variants of neoplastic differentiation spectra. Whether this includes chondroma-identical pleomorphic adenoma and chondrosarcoma-identical chondroid chordoma requires further investigations. However, one should not forget, in practice, that these "extreme" cases are very rare—if they exist at all. Thus, particularly in cases in which the neoplastic counterparts (ie, chondrosarcoma for chondroid chordomas) are rather common, one should be very reluctant not to take these as a first diagnostic choice, even though this might, in a very exceptional case, be wrong.

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References

1. Gottschalk D, Fehn M, Patt S, Saeger W, Kirchner T, Aigner T: Matrix gene expression analysis and cellular phenotyping in chordoma reveals focal differentiation pattern of neoplastic cells mimicking nucleus pulposus development. *Am J Pathol* 2001, 158:1571–1578
2. Gusterson BA, Lucas RB, Ormerod MG: Distribution of epithelial membrane antigen in benign and malignant lesions of the salivary gland. *Virchows Arch* 1982, 397:227–233
3. Aigner T, Neureiter D, Völker U, Belke J, Kirchner T: Epithelial-mesenchymal differentiation and extracellular matrix gene expression in pleomorphic adenomas of the salivary glands. *J Pathol* 1998, 186:178–185
4. Stead RH, Qizilbash AH, Kontozoglou T, Daya AD, Riddell RH: An immunohistochemical study of pleomorphic adenomas of the salivary glands. *Hum Pathol* 1988, 19:32–40
5. Füzesi L, Rixen H, Kirschner-Hermanns R: Cytogenetic findings in a metastasizing primary testicular chondrosarcoma. *Am J Surg Pathol* 1993, 17:738–742
6. Aigner T, Dertinger S, Vornehm SI, Dudhia J, von der Mark K, Kirchner T: Phenotypic diversity of neoplastic chondrocytes and extracellular matrix gene expression in cartilaginous neoplasms. *Am J Pathol* 1997, 150:2133–2141
7. Aigner T, Loos S, Müller S, Sandell LJ, Perris R, Unni KK, Kirchner T: Cell differentiation and matrix gene expression in mesenchymal chondrosarcomas. *Am J Pathol* 2000, 156:1327–1335

The Function of COX-2 in Human Ovarian Carcinoma

To the Editor-in-Chief:

Denkert et al¹ conducted an elegant study demonstrating the pattern of COX-1 and COX-2 expression in ovarian cancer with important implications for ovarian cancer

prevention and therapy. However, their contention that COX-2 is an independent prognostic factor is invalid, as several studies have shown that optimal surgical debulking and platinum-based chemotherapy are important independent prognostic variables in patients with ovarian cancer,^{2,3} and, unfortunately, data on patient treatment is lacking in Denkert et al's paper.¹

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References

1. Denkert C, Köbel M, Pest S, Koch I, Berger S, Schwabe M, Siegert S, Reles A, Klosterhalfen B, Hauptmann S: Expression of cyclooxygenase 2 is an independent prognostic factor in human ovarian carcinoma. *Am J Pathol* 2002, 160:893–903
2. Voest EE, van Houwelingen JC, Neijt JP: A meta-analysis of prognostic factors in advanced ovarian cancer with median survival and overall survival measured with the log (relative risk) as main objectives. *Eur J Cancer Clin Oncol* 1989, 28A:1328–1330
3. Hunter RW, Alexander NDE, Soutter WP: Meta-analysis of surgery in advanced ovarian carcinoma: is maximum cytoreductive surgery an independent determinant of prognosis? *Am J Obstet Gynecol* 1992, 166:504–511

Author's Reply:

The function of COX-2 in ovarian carcinoma is still the topic of an ongoing discussion in the scientific community. We thank Dr. Agarwal for his interest in our study¹ and for his comments, which provide us with the opportunity to present some additional data that, we believe, will be helpful to answer the questions raised.

We completely agree that chemotherapy and the extent of surgical therapy are important prognostic factors in ovarian carcinoma that have been identified by several meta-analyses.^{2–5} Based on these results, platinum-based chemotherapy as well as optimal surgical debulking are now established therapeutic strategies for treatment of ovarian carcinoma.

To investigate whether the expression of COX-2 is a prognostic parameter in the subgroup of patients receiving a platinum-based chemotherapy, we have updated our exploratory statistical analysis. Data on chemotherapy was available for 58 (67%) of the 86 patients with invasive ovarian carcinoma. Of these patients, 81.4% received a platinum-based chemotherapy, 8.4% were treated with non-platinum chemotherapy and 10.2% did not receive any chemotherapy. In our study, the type of chemotherapy (platinum-based *versus* other *versus* none) was not a prognostic factor in univariate survival analysis. This is in line with the remark by Bristow³ that "survival comparisons of platinum- and non-platinum-treated patients are largely of historical interest," due to the fact that the majority of patients now receive platinum-based primary chemotherapy. Furthermore, the distribution of COX-2-positive and -negative cases was not significantly different in the different therapeutic groups. We performed an exploratory survival analysis for the subgroup