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CORRESPONDENCE

HER2-amplified endometrial carcinoma and AFP-producing endometrial carcinoma

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TO THE EDITOR:

Ross et al. recently reported the histopathologic and genetic characteristics of 77 cases of *HER2*-amplified endometrial carcinomas[1]. In their study, most tumors harbored *TP53* mutation (72 cases, 94%). While serous carcinoma was the most frequent histological subtype (29 cases, 38%), a significant proportion of cases (20 cases, 26%) were difficult to classify and reported as "high-grade endometrial carcinomas with ambiguous features (HGEC)". Added to these, some (numbers not reported) of carcinosarcomas (18 cases, 23%) also contained HGEC as an epithelial component. It would be interesting to know whether some of these HGECs can be accounted for as α-fetoprotein (AFP)–producing endometrial carcinomas, which we recently described in a case series[2].

AFP-producing endometrial carcinoma is morphologically analogous to AFP-producing gastric carcinoma and exhibits high-grade nuclear features and fetal gut-like and/or hepatoid architecture. They are associated with *TP53* abnormalities and sometimes arise as an epithelial component of carcinosarcoma. Further reinforcing the similarity to AFP-producing gastric carcinomas, many of which are known to overexpress HER2[3], some AFP-producing endometrial carcinomas also overexpress HER2[2], although only a small number of cases has been tested to date and the exact frequency of HER2 amplification and/or overexpression in AFP-producing endometrial carcinoma is still to be elucidated.

Our conjecture is that *HER2*-amplified AFP-producing endometrial carcinomas account for a subset of the tumors that the authors reported as *HER2*-amplified HGEC. AFP-producing endometrial carcinoma is characterized by clear cytoplasm, SALL4 and AFP expression on immunohistochemistry, and elevated serum AFP level. While the microphotographs of HGEC published in the article are not particularly reminiscent of AFP-producing endometrial carcinomas, we would be grateful if the authors could provide the frequency of the above features in their cases of HGEC and carcinosarcoma with HGEC. The authors report in their article that one of their cases of *HER2*-amplified carcinosarcoma contained yolk sac tumor component. AFP-producing endometrial carcinoma has characteristics that overlap with those of yolk sac tumor, especially somatically derived yolk sac tumor of endometrium[4,5], but the nosological relationship between them is not fully understood. Morphologically, AFP-producing endometrial carcinoma does not exhibit reticular/microcystic pattern or Schiller–Duval bodies that would be seen in a classic case of yolk sac tumor and look more akin to conventional adenocarcinomas. If identified, the genomic characteristics of AFP-producing endometrial carcinomas in Ross' cohort would also be of great interest, as the genomic alterations in AFP-producing endometrial carcinomas are still not well characterized and we could only examine a handful of genes in our study.

Although the histological subtypes might be of less importance if we are to follow the authors' recommendation that all high-grade or p53-aberrant endometrial carcinomas be screened for *HER2* amplification[1], it is always pleasing to see the morphology and genetic alterations correlated. Moreover, as the diagnosis of AFP-producing endometrial carcinoma has clinical implications, including the use of serum AFP levels to monitor disease activity, it would be good to know whether we could use *HER2* amplification as a clue to the diagnosis of AFP-producing endometrial carcinoma.

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AUTHOR CONTRIBUTIONS

T.O. wrote the first draft of the paper. N.M. and A.I. revised it. All authors approved the final paper.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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