The elusive differential diagnosis of cutaneous apocrine adenocarcinoma vs. metastasis: the current role of clinical correlation

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Dear sir,

Cutaneous apocrine carcinoma (CAC) is a less frequent variant of skin tumor (1) and is quite elusive in differential diagnosis with metastasis to the skin, mainly from the breast. This is so much the case that, in the last World Health Organization classification of skin tumors, it was claimed that "apocrine carcinoma is otherwise indistinguishable from apocrine mammary carcinoma metastatic to the skin or apocrine carcinomas arising in ectopic breast tissue in the axilla" (1). The same point is defended by Perna et al., who claim that "this tumor is histologically and immunohistochemically identical to metastatic breast apocrine carcinoma of the breast and can be distinguished only by close clinical correlation" (2).

Even the immunohistochemical assistance that immunohistochemistry could provide seems to have failed in this area.

For instance, it has recently been claimed that p63 is a useful tool in differential diagnosis between primary adnexal tumors versus metastatic adenocarcinomas to the skin (3–5): a positive result favors an adnexal cutaneous origin. Nevertheless, such a marker does not work in cases of CAC: neither the primary tumor nor its metastases express any p63 (3).

Many other markers have previously failed in literature in the same field. Carcinoembryonic antigen (CEA) and GCDFP-15 are good examples (6–10).

Other markers more recently introduced in the literature that have proved to be useful in supporting a diagnosis of a primary adnexal neoplasm over a metastasis, such as cytokeratin 5/6, have not been studied in CAC (5, 11). Nevertheless, whenever investigated in cutaneous metastasis of breast carcinoma, CK5/6 has been expressed by nearly half of the cases in some studies (11), whereas it has been negative in others (5), up to the point that some have drawn attention to the limitations of the use of CK5/6 in the differential diagnosis between cutaneous metastasis from the breast and CAC (11). CK7 is another relatively new marker used in differential diagnosis between cutaneous adnexal tumors and metastasis; however, CK7 has been demonstrated to be expressed by metastasis of breast ductal carcinoma (5), as well as by apocrine variants of cutaneous carcinoma (12, 13).

More recently, the use of podoplanin has been proposed in distinguishing primary skin adnexal carcinomas from metastasis to the skin (14). Nevertheless, although the authors studied several types of adnexal tumors (among which sebaceous, trichilemmal, and porocarcinomas were included, as well as some not otherwise specified variants), they did not include any apocrine carcinomas. The reason given by the authors regarding this exclusion is that some malignant sweat gland tumors of apocrine or eccrine origin bear close resemblance to metastatic adenocarcinoma, and so unequivocal diagnosis is not possible in some instances. This is nonetheless the context in which immunohistochemistry plays its most useful role.

In conclusion, it seems that the differential diagnosis between CAC and a cutaneous metastasis from the breast a) will have to wait for more effective and useful immunohistochemical markers and b) should always count and rely more on clinical information, which offers mandatory assistance in searching for an internal apocrine neoplasia.

KEY WORDS

podoplanin, cutaneous adnexal carcinoma, apocrine adenocarcinoma, D2-40

REFERENCES

1. Requena L, Kutzner H, Hurt MA, et al. Malignant tumours with apocrine and eccrine differentiation. In: LeBoit PE, Burg G, Weedon D, et al., eds. World Health Organization Classification of Tumours. Pathology & Genetics. Skin Tumours. Lyon: IARC Press; 2006:125–38.

2. Perna AG, Prieto VG, Lazar AJF, Ivan D. Primary cutaneous adnexal neoplasms and their metastatic look-alikes. Pathol Case Rev. 2007;12:61–9.

3. Ivan D, Diwan AH, Prieto VG. Expression of p63 in primary cutaneous adnexal neoplasms and adenocarcinoma metastatic to the skin. Mod Pathol. 2005;18:137–42.

4. Ivan D, Nash JW, Prieto VG, et al. Use of p63 expression in distinguishing primary and metastatic cutaneous adnexal neoplasms from metastatic adenocarcinoma to the skin. J Cutan Pathol. 2007;34:474–80.

5. Qureshi HS, Ormsby AH, Lee MW, et al. The diagnostic utility of p63, CK5/6, CK7, and CK20 in distinguishing primary cutaneous adnexal neoplasms from metastatic carcinomas. J Cutan Pathol. 2004;31:145–52.

6. Cameseille-Teijeiro J, Cameseille-Teijeiro JF. Homologous carcinomas of the breast and skin. Am J Clin Pathol. 1999;111:709–12.

7. Miyamoto T, Hagari Y, Inoue S, et al. Axillary apocrine carcinoma with benign apocrine tumours: a case report involving a pathological and immunohistochemical study and review of the literature. J Clin Pathol. 2005;58:757–61.

8. Nishikawa Y, Tokushashi Y, Saito Y, et al. A case of apocrine adenocarcinoma associated with hamartomatous apocrine gland hyperplasia of both axillae. Am J Surg Pathol. 1994;18:832–6.

9. Wick MR, Ockner DM, Mills SE, et al. Homologous carcinomas of the breast, skin, and salivary glands. A histologic and immunohistochemical comparison of ductal mammary carcinoma, ductal sweat gland carcinoma, and salivary duct carcinoma. Am J Clin Pathol. 1998;109:75–84.

10. Yoshida A, Kodama Y, Hatanaka S, et al. Apocrine adenocarcinoma of the bilateral axillae. Acta Pathol Jpn. 1991;41:927–32.

11. Plumb SJ, Argenyi ZB, Stone MS, et al. Cytokeratin 5/6 immunostaining in cutaneous adnexal neoplasms and metastatic adenocarcinoma. Am J Dermatopathol. 2004;26:447–51.

12. Fernandez-Flores A, Pol A, Juanes F, Crespo LG. Immunohistochemical phenotype of cutaneous cribriform carcinoma with a panel of 15 antibodies. Med Mol Morphol. 2007;40:212–7.

13. Misado N, Narisawa Y. Sebaceous carcinoma with apocrine differentiation. Am J Dermatopathol. 2001;23:50–7.

14. Liang H, Wu H, Giorgadze TA, et al. Podoplanin is a highly sensitive and specific marker to distinguish primary skin adnexal carcinomas from adenocarcinomas metastatic to skin. Am J Surg Pathol. 2007;31:304–10.

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