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Foundation

LETTER

Dear Editors,

While reading the case report by Vadász and colleagues[1] I was rather surprised that no real attempt was made to discuss the probable source of origin of the anaplastic carcinoma. I also asked myself whether it was more justified to call a carcinoma that involves small areas of abortive gland formation a poorly differentiated adenocarcinoma or an anaplastic carcinoma. In both cases the prognosis would be poor as predicted from the histological slides alone, and this is why this latter question remains a purely theoretical one.

Coming back to the first question, it seems very probable that the primary tumor coupled with the reported metastases was an occult breast cancer. This likely but unprovable hypothesis comes from the following observations and facts.

1. Occult breast cancers are by definition not visualized by mammography and the patient reported[1] had a negative mammogram. Occult breast cancers often manifest themselves as axillary lymphadenopathy, and biopsy of the lymph node(s) or fine needle aspirate proves that the process is a malignant one. The diagnosis is typically that of a metastatic cancer. It is also not uncommon to miss the occult primary tumor in mastectomy specimens.[2-5]

2. Of 60 patients with axillary metastases from unknown primary site seen during 20 years at the MD Anderson Cancer Center, 19 subsequently were found to originate from the breast, 24 died with undetermined site of origin, and 8 died with the primary site determined, but only 4 of these were epithelial tumors.[6] Ultimately, 9 patients survived 2 to 10 years with no evidence of disease or died of unrelated causes.[6] Survivals with no evidence of disease up to 8 years after axillary surgery (dissection or biopsy) and adjuvant therapy are reported in another series.[3]

3. Many authors agree that the most likely source of an undifferentiated axillary malignant lesion in women is the breast,[3,6,7] particularly in case of multiple involved nodes.[2] This is further strengthened by the exclusion of malignant melanoma as done in the cited report (HMB-45 and S-100 negative, EMA and cytokeratin positive cells).[1] Other occult primaries giving axillary metastases (reported as rare ones) are followings: lung, stomach, thyroid, colon and rectum, pancreas[3,6] and contralateral breast.[8,9] The origin from epithelial inclusions in the lymph node seems much more theoretical,[8] although exclusion of this possibility cannot be objective unless the primary site is found. Some authors also suggest that extramammary tumors probably produce more symptoms or may be larger, thus being easier to detect by the time axillary metastases are given.[4]

4. In most cases, axillary metastases of occult breast carcinomas are poorly differentiated.[6,8,10] In an analysis of breast cancers presentied as axillary metastases, the most common pattern was found to be that of sheets of large anaplastic cells with clear to pink granulated cytoplasm,[8] a pattern described and illustrated in the cited report.[1]

5. Adenoid differentiation (abortive gland formation) and EMA positivity are also compatible with breast cancer as primary.

6. Although estrogen receptor positivity is an argument in favor of mammary primary site, the negativity does not rule out this possibility. It seems that many tumors of this type are negative for steroid receptors,[3,7,11] and this is consistent with their poorly differentiated nature. Other possible reactions favoring the diagnosis of occult breast cancer include immunohistochemical demonstration of progesterone receptors and breast cancer antigen (BRCA)[2] or lactoferrin (L. Tiszlavicz personal communication).

7. Althoungh not all, but some authors agree that occult breast cancers have a somewhat better prognosis than detected stage II breast carcinomas.[10,11] This would also be substantiated by the 16 years of uneventful follow up in the reported case.[1] Minimal (unidentifiable) primary tumors, extensive axillary involvement and predominance of undifferentiated histological type are in contrast with the unexpectedly good prognosis, and this was claimed by Veronesi's team to represent a dissociated host resistance.[10] The fact that most reported cases were treated with further options after the axillary surgery does not change much on this latter statement.

We have recently met an occult breast cancer presenting bone metastases, and fully agree with Vadász et al. that this entity is a challenging one from both diagnostic and therapeutic ends. This review of the pertinent literature – even if not complete – could give some new aspects to the case, and it seems that the patient reported is unique in the sense that no treatment other than excision (biopsy) of the nodes was given to her.[1]

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