A quick review of the pathology literature will reveal numerous examples of "benign" lesions that can rarely spread to distant sites: uterine leiomyoma (universally described as "benign metastasizing leiomyoma"),[3] dermatofibroma/benign fibrous histiocytoma[4] (familiar to all dermatopathologists), pleomorphic adenoma,[5] meningioma,[6] and giant cell tumor of bone[7] are the most easily recalled examples. Indeed, a clonal relationship, inferred from identical somatic mutations and a similar pattern of copy number variations, has been established between paired synchronous primary uterine and metastatic pulmonary leiomyomas.[3] We do not think there is any serious suggestion that such behaviour warrants relabelling these tumors as malignancies.

The World Health Organization, in its classification of Soft Tissue Tumours, notes in its definition of "benign" that benign tumors may "exceedingly rarely" give rise to "distant metastases",[8] codifying the important concept that the biological behaviour of neoplasms (particularly non-epithelial neoplasms) falls on a continuum rather than representing a benign–malignant dichotomy. The latter concept has been also supported by experts in the field of surgical pathology.[9]

The presence of cells of Spitz nevi, pigmented epithelioid melanocytoma and blue nevi among others, in regional nodes is familiar in the era of sentinel node biopsy and is known to be devoid of prognostic significance.[10–12] We tend not to call this "metastasis," although it seems plausible (in our view likely) that this presence in nodes is in fact indistinguishable mechanistically from metastasis, that is, that some cells from the primary site, proliferating due to specific genetic events such as tyrosine kinase fusions,[13] make their way via lymphatic channels (or otherwise) to a remote site, where they persist and possibly proliferate, until oncogene-induced senescence or other mechanisms lead to stabilization/regression.

From an empirical point of view, the idea that Spitz nevus does not metastasize (or if one prefers, does not do something that looks exactly like metastasis histologically) was regularly, clearly, and emphatically refuted in routine practice during the time when sentinel nodes were performed on these lesions—indeed, we now deliberately and explicitly avoid sentinel node biopsy in Spitz nevi because we know we may find "metastasis" in the node, but we also know that this finding will not be diagnostically or prognostically important and that no further management will be required.[10]

Spread of a morphologically and cytogenetically benign melanocytic lesion beyond the regional nodal basin, which we illustrated, is much less common and, in our view, is certainly difficult to explain by invocation of migration arrest, mechanical displacement, or any mechanism other than active spread of the tumor from its initial site (the logical Greek construction for this would seem to be metastasis).

Of course, it is possible to argue in a post hoc fashion in any of these scenarios that either the lesion looks benign but is not or to argue definitionally that the spread looks like metastasis but is not. However, it seems cumbersome to differentially label such similar findings depending on classification (accurate or otherwise) of the primary lesion. This melanoma has sentinel node metastasis and that Spitz nevus has sentinel node deposits; but if I was wrong and the melanoma was actually a Spitz nevus, then the metastasis was in fact just a "deposit" and vice versa!

In our view, a much more elegant and biologically accurate approach is to acknowledge that lesions which look entirely benign (and should be called benign for practical purposes) can occasionally do something which looks just like metastasis (which should be called metastasis). For these reasons, in our opinion, there is indeed such a thing as "metastatic cellular blue nevus," and we feel that we illustrated such a case!

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Coexistence of a Basal Cell Carcinoma and Leiomyosarcoma: An Unusual Collision Tumor

To the Editor:

Basal cell carcinoma (BCC) is one of the most common non-melanoma skin cancers. Its association with

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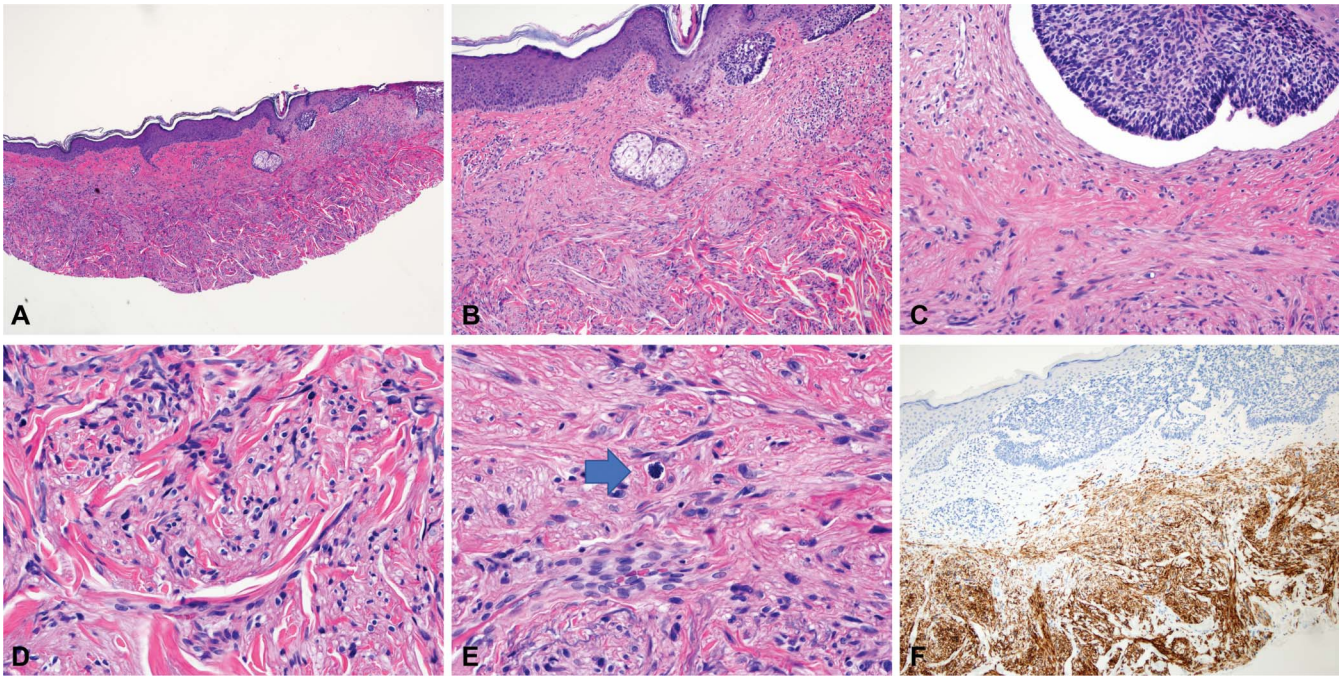

FIGURE 1. A, Low magnification of superficial BCC (×40). B and C, The stroma present underneath the neoplasm is more cellular and lacks the fibrosis and myxoid changes present in typical BCC (×100 and ×200, respectively). D and E, Closer inspection of the spindle cell lesion show cigar-shaped cells with vacuolated cytoplasm. A rare atypical mitotic figure is noted and highlighted by an arrowhead. F, The spindle cell neoplasm is diffusely positive for desmin.

different neoplasms in the same biopsy specimen is relatively common. It can be found as a collision neoplasm in association with melanocytic proliferations, seborrheic keratoses, dermatofibromas, neurofibromas, and adnexal tumors.[1] Herein, we present a case of a BCC in association with a cutaneous LMS. To the best of our knowledge, this is the first report of such peculiar combination.

A 63-year-old woman presented with a solitary nodule of unknown duration on her back. The lesion was clinically concerning for a BCC. A shave biopsy was performed that revealed 2 distinct histopathological processes (Fig. 1): The epithelial component showed a basaloid proliferation with characteristic peripheral palisading and retraction from the stroma, diagnostic of BCC. The underlying dermis contained an ill-defined tumor composed of interlacing fascicles of elongated spindle-shaped cells with eosinophilic cytoplasm and eccentric, cigar-shaped nuclei embedded in a collagenous stroma. There was variable cytological pleomorphism and scattered mitotic figures. By immunohistochemistry, the spindle cells were diffusely positive for desmin and muscle-specific actin. These features were indicative of a cutaneous LMS. Based on the histopathological findings, a diagnosis of a collision tumor comprised of BCC and cutaneous leiomyosarcoma (LMS) was made.

Collision neoplasms are defined by the existence of 2 different tumors of distinct cell lineages in the same anatomic location.[2] They usually contain epithelial elements, but occasionally, mesenchymal elements can be a part of them. BCC has been reported as being the most common component of a collision tumor, in addition to seborrheic keratosis.[1] BCC is the most frequent skin cancer worldwide. It is a slow growing lesion that very rarely can have metastatic potential.[3] Cutaneous LMS usually has a relative indolent behavior compared to subcutaneous LMS. Unlike BCC, cutaneous LMS can metastasize and warrants surgical intervention and long-term follow-up.[3] It has been estimated that approximately 5% of cutaneous LMS and 30%–60% of subcutaneous LMS can develop metastasis. The rate of recurrence for cutaneous LMS is approximately 50%–60% after local excision.

In BCC, it is well known that the interplay of the tumor stroma with the malignant epithelial elements is necessary for its growth.[4] Some molecular markers were identified for the stromal–epithelial interplay and tumorigenesis in BCC.[4,5] Platelet-derived growth factor (PDGF) is one of the most extensively investigated markers for control of multiplication and differentiation of mesenchymal elements.[6] PDGF A and B chain were mainly found in BCC cells, in hair matrix, and in sweat gland epithelium; however, PDGF α and β receptors were found in the stroma components of BCC, dermal hair papilla, and sweat glands but not in the epithelial structures.[4] Pontén et al[4] implied that the PDGF/PDGF receptor interplay might be responsible for the growth of BCC. In addition to PDGF, fibroblasts in the surrounding tumor stroma seem to be essential for promotion of growth, secreting specific cytokines and chemokines (CXCL12, CCL17).[5] Such particular microenvironment of the BCC can produce mesenchymal overgrowth, proliferation, and potentially lead to the development of the second spindle cell malignancy.

Apart from the stromal induction theory, epidermal induction changes may be another explanation for collisions with BCC. Schoenfeld[7] first pointed out the "mesenchyme factor theory" for explanation of the epidermal changes overlying dermatofibromas. In the literature, it has been suggested that growth factors or other chemokines released by the fibroblasts might be responsible for inducing hair follicle and sebaceous lobules overlying a dermatofibroma.[7,8] Morgan et al[9] demonstrated the expression of epidermal growth factor receptor in the dermal dendritic spindle cells and the epidermis in 20 cases of dermatofibroma and proposed that epidermal growth factor receptor might have a significant role in the epidermal induction changes. One could speculate that the epidermal pattern diagnostic of BCC overlying the leiomyosarcoma might be the result of epidermal induction changes. Another clue to a possible relationship between BCC and LMS can be pointed in the diagnosis of BCC nevus syndrome (Gorlin–Goltz syndrome), an autosomal dominant disorder linked to *PTCH* gene mutations. Those patients, who generally developed multiple BCC early in life, have been reported to have an increased incidence of other tumors, including LMS.[10]

In conclusion, pathologists should be aware of the potential relationship and finding of the coexistence of BCC and LMS as a collision neoplasm.

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