Intravascular ALK-Positive Anaplastic Large-Cell Lymphoma Mimicking Inflammatory Breast Carcinoma

A 33-year-old woman presented for urgent evaluation secondary to persistent right breast heaviness, pain, and erythema. The patient was seen initially by her primary care physician, who prescribed a course of dicloxacillin for presumed staphylococcal cellulitis. No history of trauma or prior infection to this breast was elucidated. The physical exam findings were notable for general obesity, which precluded an accurate deep soft tissue exam. The breasts displayed mammary hypertrophy with near-complete replacement of the right breast skin (Fig 1A) with erythematous changes that extended into the posterior axillary line in the lateral direction (Fig 1B). The right breast skin exhibited diffuse thickening, induration, and variable edema, in a manner reminiscent of peau-de-orange-type changes. The nipple was spared of involvement, and no discharge was elicited. Despite the difficulty in evaluating the soft tissues, a 2-cm mobile nodule was identified in the right supraclavicular space. No other discrete masses or lesions were noted on either breast, or elsewhere on exam. Based on a presumptive diagnosis of progressing bacterial cellulitis, the patient was prepared for inpatient admission for intravenous antibiotic therapy. Given the general appearance of the right breast changes, two punch biopsies of the breast skin were performed to exclude the possibility of inflammatory breast carcinoma. Low-power examination of the hematoxylin and eosin stain (H&E) sections were unimpressive and showed scattered pockets of chronic inflammatory cells within the deeper areas of the dermis (Fig 2A; H&E, ×20); however, higher-power examination demonstrated the presence of highly atypical cells associated with the areas of chronic inflammation. These cells were characterized by high nuclear to cytoplasmic ratios, irregular nuclear contours, and occasionally prominent nucleoli. The cells appeared to localize within angiolymphatic spaces (Fig 2B; H&E, ×400). An initial panel of immunohistochemistry markers failed to show reactivity with several epithelial antibodies (pan-keratin, MOC31, cytokeratin 7) and several hematolymphoid antibodies (CD45, CD2, CD3, CD5, CD20, CD79a, CD43, CD56). Together, these markers provided no support for intralymphatic carcinoma, diffuse large B-cell lymphoma, or a peripheral T-cell lymphoma. Subsequent immunohistochemical studies demonstrated strong reactivity for CD30 and anaplastic lymphoma kinase (ALK). Of particular significance was the pattern of Alk immunoreactivity demonstrating both cytoplasmic and nuclear staining—a feature that is associated with a translocation involving the ALK gene on chromosome 2 and the NPM1 gene on chromosome 5. Figure 2C (×400) demonstrates this pattern of Alk reactivity in the large cells, which also shows coexpression of CD30 (see inset). These same cells (Fig 2D; ×400, designated by an asterisk) are clearly present within angiolymphatic spaces, as highlighted by CD31. Based on these findings, a diagnosis of ALK-positive anaplastic large-cell lymphoma (ALCL) within angiolymphatic spaces was rendered. The patient was subsequently staged with imaging studies that demonstrated the presence of multiple enlarged lymph nodes within the mediastinum and abdomen, as well as subtle soft tissue lesions in the region of the breast. A biopsy of one of the mediastinal lymph nodes confirmed the presence of ALK-positive ALCL with histologic features similar to the original skin tumor. The intravascular component, while present focally, was not a significant feature of the nodal lesion. The patient was treated with chemotherapy, and showed good initial response with resultant reduction in breast size to her normal state. Subsequently, the patient suffered multiple systemic relapses of her lymphoma, which were often heralded by fevers, and continues to undergo chemotherapeutic treatment.
Intravascular lymphomas (IVLs) are predominantly of B-cell lineage, and account for the vast majority of reported cases. In addition, IVLs of T-cell lineage (IVLTCL) constitute an even smaller number of cases. Several recent reviews of IVL have described approximately 40 cases with apparent T-cell lineage in the literature by various immunohistochemical measures. As noted by other authors, the accurate definition of these cases is limited by the variable immunohistochemical profile of the individual publications. The majority of these IVLs probably represent peripheral T-cell lymphomas, not otherwise specified. Review of the literature demonstrates only five documented cases of T-cell IVL with CD30 immunoreactivity, suggesting ALCL as the tumor type. In only one of these cases was Alk expression evaluated by immunohistochemical methods, and shown to have an absence of reactivity. Identification of Alk immunoreactivity plays a vital role in separating two morphologically similar diseases, with different outcome characteristics. Namely, ALCLs with Alk immunoreactivity tend to occur in younger patients, involve fewer extranodal sites, and have better overall survival (93% vs 37% 5-year overall survival) with chemotherapy when compared with the ALK-negative counterparts. In general, skin involvement by ALK-positive ALCL is a secondary manifestation of systemic disease. In the reported English literature, presentation in the skin with IVLTCL was seen in 16 cases (13 skin only, three skin and other extracutaneous site). This is a remarkable case of ALK-positive ALCL presenting intravascularly. This case also adds to the differential diagnosis of breast lesions that clinically suggest inflammatory breast carcinoma. Certainly, we cannot exclude that a subset of the previously published cases of IVLTCL contain cases of ALK-positive ALCL that were simply not evaluated for CD30 and ALK. Accurate evaluation of long-term outcome in patients with IVLTCL is difficult to address, due to the incomplete nature of the immunophenotypic characterization of the published cases. IVLTCL, however, appears to have an aggressive course. It is unclear whether patients with an intravascular component of systemic ALK-positive ALCL behave with the same good overall outcome of ALK-positive ALCL. To the best of our knowledge, this is the first reported case of an ALK-positive ALCL to present intravascularly. In addition, this may be the first reported case in which ALCL has been shown to clinically mimic inflammatory breast carcinoma.

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Fig 2.
AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST
The author(s) indicated no potential conflicts of interest.

REFERENCES

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