Interdigitating dendritic cell sarcoma presenting in the skin: diagnosis and the role of surgical resection, chemotherapy and radiotherapy in management

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Abstract

We report the case of an interdigitating dendritic cell sarcoma (IDCS) presenting in the skin. A 41-year old woman had a slowly enlarging mass on her right scapula that was excised multiple times under a presumptive diagnosis of a recurrent sebaceous cyst. However, the lesion was refractory to standard therapies. History and physical exam was unrevealing for any systemic signs or symptoms of disease. The patient's metastatic work-up was negative. The lesion was resected with wide margins and was found to be consistent with IDCS. Patients that present with IDCS on the skin may present concurrently with metastatic disease and may have increased risk of secondary malignancies. The use of adjuvant chemoradiation after primary resection is controversial. However, the use of chemoradiation likely has benefit for local regional control for primary tumors that are unamendable to complete primary resection.

Case Report

A 41-year old woman was referred to our care for a slowly enlarging mass on her right shoulder. The referring dermatologist documented a well-demarcated erythematous growth on the patient's right scapula, which was excised multiple times, under the presumption of a recurrent sebaceous cyst. However, when her lesion did not respond to standard therapies, a biopsy of the lesion was obtained and she was referred to our service. Upon further inquiry, the patient reported no constitutional symptoms including fevers, night sweats, or weight loss. Her history revealed a previous basal cell carcinoma of her lower back, which was previously resected. Her past medical history was only significant for anxiety and depression that was well controlled on antidepressants. She denied any drug, alcohol, or cigarette use and any exposure to chemotherapy or radiation therapy. Her family history revealed breast cancer in her biological mother and Parkinson's disease in her paternal grandmother.

The patient's physical exam revealed a 5 cm well-demarcated scar on her right scapula (Figure 1). The lesion showed a minimally ulcerated surface and associated granulation tissue with signs of progressive healing from the biopsy/excision. There appeared to be no other soft tumors in the area and no palpable lymphadenopathy. The rest of her physical exam was unremarkable. To assess if metastatic disease was present, the patient underwent PA and lateral X-rays, along with CT of the chest. The patient was found to have no signs of metastatic disease. The lesion was removed under anesthesia with wide margins.

A resection of the skin lesion, which was sent to Brigham and Women's Hospital for consultation, revealed a multinodular proliferation of spindle cells. A dense lymphoplasmacytic infiltrate was associated with tumor cells. The spindle cells had irregular vesicular nuclei containing 1-3 prominent nucleoli and pale cytoplasm with indistinct borders (Figure 2A). Mitotic figures numbered up to 6 per 10 high-power fields. The lesion was centered in the dermis, and no melanocytic junctional component was present in the overlying epidermis. Immunohistochemical studies showed the tumor cells to be positive for S100-protein (Figure 2B) and CD45RO. Immunohistochemical studies were negative for pan-keratin, Melan-A, MITF, smooth muscle actin, desmin, ALK, LCA, CD163, CD68, and PU-1. The morphologic features and immunohistochemical studies were characteristic for interdigitating dendritic cell sarcoma.

After two-weeks the patient recovered well from surgery and is currently undergoing close monitoring to assess for recurrence of her disease.

Discussion

Functional, morphological, and structural features are generally used to characterize cells of the immune system. Monocytes are generally divided into two groups based on these parameters: phagocytes and dendritic cells. Different types of dendritic cells are found throughout the body such as Langerhans (skin, vagina, stomach, esophagus), follicular dendritic cells (germinal center of lymph nodes), and the interdigitating dendritic cells. Interdigitating dendritic cells are non-lymphoid accessory cells responsible for antigen presentation and T lymphocyte stimulation. These cells are primarily localized to the peripheral lymphoid tissue, including the paracortex and deep cortex of lymph nodes, the splenic periarteriolar lymphoid sheaths, and the interfollicular areas of mucosa-associated lymphoid tissue. Interdigitating dendritic cells like Langerhans and melanoma cells are strongly S-100 positive. Although interdigitating dendritic cells have microscopic features similar to Langerhans, they lack the distinctive Birbeck granules and are negative for CD1a.[1,2]

Interdigitating dendritic cell sarcoma (IDCS) is an extremely rare tumor. There are approximately 100 reported cases of IDCS in the literature.[3] Furthermore, this is only the 8th case of IDCS ever reported on the skin (PUBMED search).[2-6] IDCS occurs across a large age range (8-77 years old, mean 52-56

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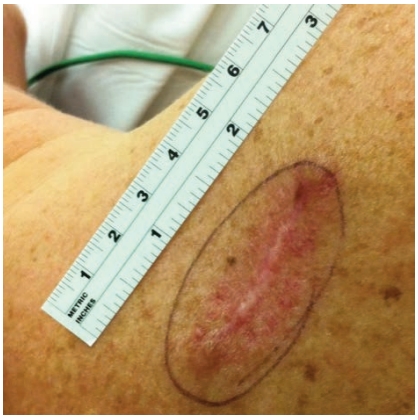

Figure 1. A 5 cm well demarcated scar/lesion after excision due to misdiagnosis as a sebaceous cyst.

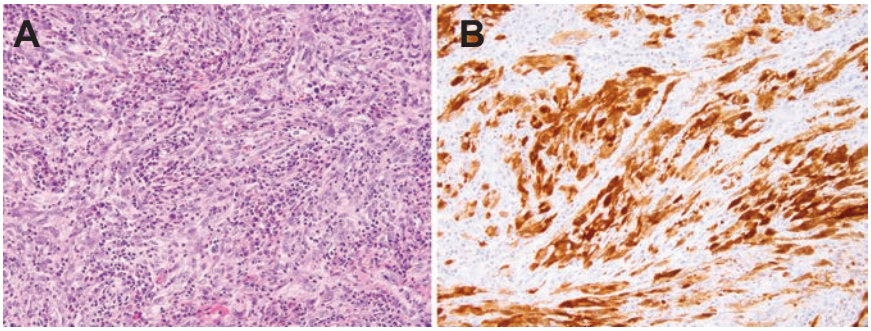

Figure 2. A) The tumor showed sheetlike growth of spindle cells associated with a lymphoplasmacytic infiltrate (Hematoxylin and Eosin stain); B) strong nuclear positivity for S100-protein in tumor cells (40× magnification).

years) and has a slight predilection for men.[7,8] Recent reports indicate that IDCS is being recognized with increasing frequency. However, it remains unclear whether this reflects a true increase in incidence or whether the neoplasm is now better recognized. No concrete risk factors have been identified for developing IDCS. It has been hypothesized that IDCS has a viral etiology, but no association to any virus has been shown.[9]

Although IDCS has been found on the eyelid,[4] pleura,[8] tonsil,[7] testes,[10] lung,[11] spleen,[12] and parotid gland,[9] it rarely involves these extra-nodal sites and is most often found in lymph nodes. According to the International Lymphoma Study Group, the majority of dendritic cell tumors can be classified with 6 markers in addition to morphological features: S100 protein, CD68, lysozyme, CD1a, CD21, and CD35.[13] IDCS most often presents with strong S100 protein expression, frequent CD45RO expression, and absent CD21, CD1a, and CD35 expression. Expression of CD68, CD163, and LCA are often variable.[13,14] A potential identifying feature of IDCS is its location within the paracortical portion of the lymph node. However, IDCS often effaces the entire lymph node, making this a less reliable way of recognizing this neoplasm. In extra-nodal cases, admixed lymphoplasmacytic infiltrate is diagnostically useful. On the other hand, other morphological features (*i.e.* fusiform spindle cells with oval nuclei) are often non-specific. IDCS should be considered in the differential in the context of a spindle cell neoplasm lacking melanocytic, neural, smooth muscle, or myofibroblastic differentiation.

IDCS classically presents with localized cervical or axillary lymphadenopathy. However, a review of the literature reveals that 5% and 35% of patients will present with locally advanced or metastatic disease, respectively.[8] A IDCS generally has a poor prognosis if the disease is metastatic at time of presentation with overall survival (OS) ranging from 9-15 months, despite a mixture of multi-modal treatments including surgical excision, chemotherapy, and/or radiotherapy. Per univariate analysis, patients at a young age or with intraabdominal involvement had an increased risk of local regional recurrence and death.[4,8,15] For localized disease, surgery has been the mainstay treatment. Approximately 50% of patients with early stage disease treated with surgical resection remain disease free with a median follow up of 12 months (range 2 months to 19 years). Outcomes of surgery have also been shown to be dependent on IDCS tumor size. With one pooled-analysis of IDCS and follicular dendritic cell sarcoma (FDCS) revealed that patients with tumors ≥5 cm had a 50% chance of recurrence compared to patients with a <5 cm tumor having only a 11.1% chance of recurrence with follow up of 2-18 months.[16]

Since IDCS is so rare, no optimal chemotherapy regimen is currently recommended. Multiple types of chemotherapy regimens have been tried including CHOP, ABVD, ICE, and EPOCH. Although results have been mixed, there has been one case report of IDCS with widespread metastatic disease, including extensive liver infiltration, which showed a complete response to six cycles of ABVD chemotherapy.[17]

Optimal adjuvant use of radiotherapy for this tumor has not been established. Small reviews indicate that adjuvant radiotherapy has no effect on OS. However, data to determine the role of adjuvant radiotherapy after primary surgical resection for improved local regional control is lacking. Yet, patients with IDCS have high rates of local regional failure despite negative margins.[16] Therefore, it may be of benefit to consider adjuvant radiotherapy in the presence of other unfavorable pathological features (*e.g.* large tumor primary). Radiotherapy is likely to be of significant benefit to patients with unresectable tumors. This is exemplified by a case report of IDCS presenting within the nasopharynx and found to be not amendable for surgery. The primary therapy given was definitive radiotherapy to 66 Gy and adjuvant chemotherapy with a good response. Typical doses of radiotherapy for IDCS are 50-60 Gy but without primary resection, patients may benefit from doses up to 66 Gy.[8,18]

Only approximately one quarter of the cases of IDCS that present on the skin have presented concurrently with confirmed metastatic disease.[2] However, of the few reports of IDCS on the skin, long-term prognosis for patients with cutaneous IDCS appears poor, regardless of the presence of metastatic disease with initial skin presentation. An example is from a case described by Boldin *et al.* in which IDCS presents on the eyelid of a patient who initially shows no signs of metastatic disease. After complete removal of the lesion, the patient declined chemotherapy or radiation to the area. The patient then recurred two years later with metastatic IDCS (confirmed on biopsy), rapidly deteriorated, and died.[4]

Patients with IDCS may also be at higher risk for additional malignancies. Recent research shows that patients with a history of IDCS often experience another solid organ (9%) or hematological (12%) malignancy throughout their lifetime.[8] The mechanism of this increased risk is not yet defined. These points illustrate the importance of continuous monitoring of patients with history of IDCS.

In summary, we report a case of a 41-year-old female with localized IDCS to the skin. The diagnosis was made based on morphology and immunohistochemistry staining. It is an extremely rare tumor, and in this instance is found in an unusual location. Although the patient appears disease-free since surgery (five months follow-up), careful monitoring for recurrence is necessary.

Conclusions

In this discussion we highlighted the epidemiology, diagnostics, treatments, and outcomes associated with IDCS. Primary surgical resection is the mainstay treatment for early stage disease. The use of adjuvant chemotherapy or radiation therapy for patients after primary resection of a local tumor is not firmly established. However, patients may benefit from improved local regional control with chemoradiation if primary complete resection is not possible.

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