

Interdigitating dendritic cell sarcoma located in the groin: a case report and literature review Journal of International Medical Research 2018, Vol. 46(11) 4791–4799 © The Author(s) 2018 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/0300060518792444 journals.sagepub.com/home/imr



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#### Abstract

Interdigitating dendritic cell sarcoma (IDCS) is an extremely rare subtype of dendritic cell neoplasms, and current knowledge on this tumor is limited. We herein report a case of an IDCS in a 64-year-old man who presented with a right inguinal mass combined with extensive retroperitoneal, pulmonary, hepatic, renal, and bone marrow infiltration. Because of the advanced stage of the disease, we performed five cycles of chemotherapy, including cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP); doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD); and ABVD combined with cisplatin, and one cycle of radiotherapy. The patient's inguinal mass became smaller during the treatment, but there was no change in the extent of infiltration at the other sites. The patient died 8 months after the initial diagnosis. We also herein review the etiology, diagnosis, differential diagnosis, treatment, and prognosis of IDCS, and analyze the characteristics of IDCS in Chinese patients.

#### **Keywords**

Interdigitating dendritic cell sarcoma, dendritic cell neoplasm, inguinal mass, chemotherapy, radiotherapy, prognosis

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### Introduction

Interdigitating dendritic cells (IDCs) originate from hematopoietic precursors, and IDC sarcoma (IDCS) is a rare malignant <sup>1</sup>First Department of Hematology, Shengjing Hospital, China Medical University, Shenyang, Liaoning, P.R. China <sup>2</sup>Intensive Care Unit, Taizhou Central Hospital, Taizhou, Zhejiang, P.R. China

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We herein report a case of an IDCS with extensive infiltration in a 64-year-old patient. He received five cycles of systemic chemotherapy and one cycle of radiotherapy. His prognosis was poor, and he died 8 months after the initial diagnosis. The purpose of this case report and literature review is to increase the current knowledge of IDCS and thus assist physicians in clinical practice.

# **Case report**

## Medical history and examinations

This case study was approved by the ethics committee of Shengjing Hospital. The patient's wife provided written informed consent.

A 64-year-old man was admitted to our hospital with a 3-month history of a painless mass in his right groin. He underwent a right inguinal lymph node biopsy in the general surgery department in February 2016. Examination of the biopsy specimen revealed IDCS, and he was admitted to our department for further evaluation and treatment.

The patient had a productive cough with blood-streaked sputum and occasional upper abdominal discomfort. He had no systemic symptoms such as fever, night sweats, weight loss, or fatigue. Physical examination revealed no palpable superficial lymph nodes anywhere except in the right groin. The right inguinal mass was smooth, hard, and painless with poor mobility and a size of approximately  $5 \times 4$  cm. Positron emission tomography– computed tomography showed multiple enlarged lymph nodes and elevated fluorodeoxyglucose metabolism in the right inguinal area, retroperitoneum along the right iliac artery, and lungs. There were also foci of elevated fluorodeoxyglucose metabolism in the right liver lobe and at the upper pole of the left kidney. Laboratory studies revealed an elevated serum  $\beta^2$  microglobulin level (2.12 mg/L), while the complete blood count, renal and liver function test results, cancer antigen 125 level, lactate dehydrogenase level, and C-reactive protein level were normal. Additionally, hepatitis B virus DNA, Epstein–Barr virus DNA, and human immunodeficiency virus tests were negative. Other laboratory indicators were also within normal limits.

## Treatment process and prognostics

On 4 March 2016, the patient received one cycle of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) chemotherapy. However, no response was shown. We administered one cycle of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) chemotherapy following the month (5 April 2016). At this point, ultrasonography showed that the right inguinal and iliac fossa lymph nodes were shrinking, but contrast-enhanced chest computed tomography showed that the number and size of the tumor masses in the lungs were increasing. We administered the ABVD regimen combined with a 4-day course of cisplatin for two cycles beginning on 19 May and 20 June, respectively. Additionally, one cycle of CHOP+etoposide chemotherapy was administered on 8 August 2016. However, the tumor was not sensitive to these agents, and the patient showed no improvement. Finally, one cycle of radiotherapy was performed in October 2016, but again no response was seen. By this time, the patient had hemoptysis, and contrast-enhanced chest computed tomography showed an extensive tumor mass involving the whole lung. Considering the poor condition of the patient after chemotherapy, we proposed palliative care.

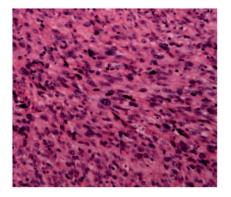
The patient died of respiratory failure on 13 October 2016, 8 months from the date of diagnosis.

## Detailed pathology findings

The biopsy specimen consisted of two inguinal lymph nodes of 0.6 and 1.5 cm in diameter. Microscopic examination revealed destruction of the lymph node architecture with residual follicles and short spindleshaped tumor cells forming a woven growth pattern interspersed with occasional giant tumor cells.

Immunophenotypic analysis showed the following results: S100 (+), vimentin (+), CK (-), CD1a (-), CD21 (-), CD23 (-), CD34 (-), CD35 (-), CD117 (-), Melan-A (-), HMB-45 (-), smooth muscle actin (SMA) (-), desmin (-), langerin (-), DOG1 (-), Ki-67 (+) (approximately 40%), and p53 (+) (approximately 70%). Thus, S100 and vimentin staining were positive and all markers for follicular dendritic cell sarcoma (FDCS), Langerhans cell sarcoma, and melanoma were negative. A histopathologic image of a lymph node specimen is shown in Figure 1.

The bone marrow smears showed 1.60% tumor cells. In summary, the morphological



**Figure 1.** Histopathologic image of the right inguinal lymph node biopsy of the 64-year-old man described in the present report (magnification:  $\times 100$ ).

and immunophenotypic features were consistent with IDCS.

# Discussion

Various types of dendritic cells are found throughout the body, including Langerhans cells (skin, vagina, stomach, and esophagus), follicular dendritic cells (germinal center of lymph nodes), and IDCs.<sup>1</sup> IDCs are mainly found in T-cell zones of lymphoid organs, including the paracortex of the lymph nodes, the lymphatic sheath around the splenic artery, and the follicular portion of mucosa-associated lymphoid tissues. IDCs present antigens to T cells and stimulate T cells. They originate from hematopoietic precursors via conversion of Langerhans cells during migration to the lymph node to capture antigens or through differentiation of myeloid or lymphoid precursor cells.<sup>1–3</sup> IDCS is a rare tumor arising from IDCs. Diagnosis of IDCS is challenging, and we still do not have a standard treatment protocol for this tumor.

Saygin et al.<sup>3</sup> reported that only 100 cases of IDCS were reported in the Englishlanguage literature from 1978 to 2012, of which 40% occurred in Asia, 32% in the United States, 20% in Caucasians, and 5% in Hispanics. IDCS affects a large age range of 1.8 to 88 years (mean, 56.5 years) with a male:female ratio of 1.38:1.00. We reviewed the literature and identified an additional 17 cases of IDCS<sup>4-20</sup> that were reported in the English-language literature from 2012 to 2016. The mean age of onset among these cases was 53.5 years (range, 19-87 years), and the male:female ratio was 1.13:1.00. We further identified cases of IDCS reported in the 2005-2016 database of Chinese patients. We searched the Chinese National Knowledge Infrastructure, Chinese Biomedical Literature Database, Chinese Wanfang Database, and Chinese Scientific Journal Database. The following key words were used: "interdigitating dendritic cell sarcoma" and "dendritic cell neoplasm." Additionally, all articles were included by manual operation, and studies matching the eligible criteria were retrieved for further data extraction and quality assessment. Finally. 45 cases were included. $^{21-52}$ Among these patients, the mean age at onset was 38.8 years (range, 8 months to 73 years), which is lower than that reported in the above data. Additionally, a slightly higher proportion of men was affected (male:female ratio, 1.25:1.00). Among the Chinese patients, 66.7% (30/45) had lymph node involvement, mainly the cervical (18 patients) and inguinal (8 patients) lymph nodes, and 33.3% (15/45) had extranodal infiltration, mainly affecting the liver (5 patients) and spleen (5 patients).

The etiology of IDCS is not clear. Epstein-Barr virus has been implicated as a causative factor in the pathogenesis of FDCS,<sup>53</sup> but there is no evidence of an association between viral infection and IDCS.<sup>54,55</sup> Nayer et al.<sup>56</sup> found that clonal cytogenetic abnormalities and rearrangement might be associated with the development of IDCS. Moreover, three patients developed IDCS following the use of calcineurin inhibitors, tacrolimus, and pimecrolimus.57,58 These drugs show their effect by dampening the responses of T cells to which IDCs present antigens. Dysregulation of the immune system may facilitate malignant transformation of IDCs, but further data are required to determine whether this occurs.<sup>3</sup> IDCS may occur in some patients as a result of malignant transformation after radiotherapy and chemotherapy. One systematic review showed that 17% of patients with IDCS had a prior malignancy and had undergone radiotherapy or chemotherapy before being diagnosed with IDCS.<sup>4</sup>

At present, the diagnosis of IDCS is based mainly on clinical manifestations, cell morphology, and immunohistochemical characteristics. Most patients present with painless lymphadenectasis, while constitutional

symptoms such as fever, weight loss, night sweats, and fatigue affect only 25% of patients.<sup>3</sup> Microscopically, the neoplastic cells of IDCS are large, fusiform spindle cells with indistinct cell borders, oval central nuclei, micro-eosinophilic cytoplasm, finely dispersed chromatin, and small but prominent nucleoli, and they often form a storiform or whorled fascicular growth pattern. There are always small lymphocytes, plasma cells, or other inflammatory cells surrounding the tumor cells, but they lack melanin, nerve, smooth muscle, or myofibroblast differentiation. A key diagnostic feature is the presence of tumor cells in the subcortical region of the lymph nodes.<sup>5,59,60</sup> The main immunohistochemical characteristics are 100% expression of S100 protein and vimentin, frequent CD45RO and CD68 expression, and negative CD1a, CD21, CD23, CD35, Melan-A and HMB-45 expression. Expression of CD4. CD43. CD163. and SMA is variable. Cytokeratins, epithelial membrane antigen (EMA), B-cell markers, T-cell markers, CD30, CD34, ALK, langerin, and myeloperoxidase are negative.4-20

The differential diagnosis of IDCS includes malignant melanoma, malignant peripheral nerve sheath tumor, malignant lymphoma, malignant fibrous histiocytoma, atypical fibrosarcoma, and other types of dendritic cell neoplasms. Melanoma may show nested growth patterns and epithelioid morphology associated with HMB45 and Melan-A positivity, and melanosomes may be present under electron microscopy.<sup>61</sup> Malignant peripheral nerve sheath tumor is CD68- and CD45-negative, while EMA/ CD30, CD21/CD35/clusterin, factor XIIIa/ desmin/vimentin/SMA/cytokeratins, and CD1a can be used to establish the diagnoses of anaplastic large cell lymphoma, FDCS, fibroblastic cell tumor, and malignant Langerhans histiocytosis, respectively.4-20,59

No precise treatment guidelines have yet been developed for IDCS because this tumor is uncommon and prospective clinical data are limited. The current treatment of IDCS includes surgery, radiotherapy, chemotherapy, and targeted therapy. Radical surgery has been the main treatment for patients with local disease. Chemotherapy is usually recommended as the main treatment for advanced IDCS. Several chemotherapeutic regimens have been reported, including CHOP; ABVD; ifosfamide, carboplatin, and etoposide (ICE); dexamethasone, and high-dose cisplatin, cytarabine (DHAP); and etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin (EPOCH).<sup>61-64</sup> However, none has shown a consistent effect, although some studies have associated ABVD with an improved prognosis.6,65,66

In one study, the median survival time for patients with metastatic disease was 9 months (range, 0.25–72 months).<sup>3</sup> The median survival rates were not reported for patients with local disease because 82% were still alive at the last follow-up. The overall survival rates at 1 and 2 years for patients with local disease were 84.8% and 38.5%, and those for patients with metastatic disease were 68.1% and 15.8%, respectively.<sup>3</sup> The authors of a small retrospective study found that mitotic counts, percent necrosis, and nuclear pleomorphism may serve as prognostic factors, but no further study has been performed to confirm these findings.<sup>62</sup> Other factors that have been associated with a poor prognosis include younger age, larger tumor diameter, higher expression of Ki-67, p53 positivity, extranodal disease, and abdominal tumor infiltration.<sup>3,60</sup> In the present study, we performed a thorough search of published articles regarding IDCS in Chinese from 2005 to 2016. We found 45 reported cases of IDCS in China.<sup>21-52</sup> We used the chisquare test to analyze the association between clinicopathological features (age, sex, histological features, intra-abdominal involvement, and cytokeratin positivity)

and adverse outcomes (local recurrence, distant metastasis, and death). We found no significant association with sex, mitotic counts, age, or tumor size. The latter two findings differ from those reported by Saygin et al.,<sup>3</sup> but our finding that abdominal involvement, high Ki-67, extranodal disease, and advanced clinical stage were associated with a poor prognosis are in agreement with the study by Saygin et al.<sup>3</sup> (Table 1).

In summary, we have presented a rare case of IDCS in a 64-year-old man. We have gained a better understanding of IDCS after reviewing its etiology, diagnosis, treatment, and prognosis. We also analyzed

 Table 1. Univariate analysis of factors associated

 with adverse outcomes in 45 Chinese patients with

 interdigitating dendritic cell sarcoma.

| Prognostic<br>factors | Positive events/<br>Total number | P<br>value |
|-----------------------|----------------------------------|------------|
| Age                   |                                  | 0.085      |
| ≥ <b>4</b> 0          | 11/28                            |            |
| <40                   | 17/28                            |            |
| Sex                   |                                  | 0.772      |
| Male                  | 17/28                            |            |
| Female                | 11/28                            |            |
| Tumor size            |                                  | 0.114      |
| $\geq$ 3 cm           | 9/23                             |            |
| <3 cm                 | 14/13                            |            |
| Mitosis               |                                  | 0.262      |
| $\geq$ 5/10 HPF       | 7/21                             |            |
| <5/10 HPF             | 14/21                            |            |
| Intra-abdominal       |                                  | 0.008      |
| involvement           |                                  |            |
| Present               | 7/25                             |            |
| Absent                | 18/25                            |            |
| Presentation          |                                  | 0.019      |
| Nodal                 | 22/28                            |            |
| Extranodal            | 6/28                             |            |
| Clinical stage        |                                  | 0.012      |
| Early                 | 20/28                            |            |
| Advanced              | 8/28                             |            |
| Ki-67                 |                                  | 0.043      |
| $\geq$ 20%            | 6/17                             |            |
| <20%                  | 11/17                            |            |

the characteristics of IDCS in Chinese patients with a literature review. However, the extreme rarity of this tumor still hinders clinical research; thus, well-designed prospective clinical trials are needed to guide physicians who encounter patients with this disease.

#### **Declaration of conflict of interest**

The authors declare that there is no conflict of interest.

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