Clinical Case Report

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Interdigitating dendritic cell sarcoma of the spleen with hepatic failure after chemotherapy

A case report

Chengchen Zhao, MD[a], Xiaohui Xie, MD[c], Dong Zheng Gai, MD[b], Dengshu Wu, MD[b], Hongya Xin, MD[b,*], Tianlun Yang, MD, PhD[a,*]

Abstract

Rationale: Interdigitating dendritic cell sarcoma (IDCS) is an extremely rare disease originating from dendritic cells (DCs). There are few cases report interdigitating dendritic cell sarcoma of spleen along with their pathological characteristics and treatment.

Patient concerns: Here we report a case of IDCS in 53-year-old female who presented spleen enlargement and thrombocytopenia.

Diagnoses: The patient underwent surgical resection of spleen, and the pathology confirmed IDCS.

Interventions: She received surgical resection of spleen and one cycle of chemotherapy (ABVD with ifosfamide and oxaliplatin) after surgery.

Outcomes: She died of severe hepatic failure caused by chemotherapy.

Discussion: IDCS is a rare disease with insufficient treatment guidelines. We adopted chemotherapy of ABVD with ifosfamide and oxaliplatin which showed no improvement but led to life-threatening liver damage.

Abbreviations: ABVD = doxorubicin, bleomycin, vinblastine, dacarbazine, ALT = alanine aminotransferase, AST = aspartate transaminase, CD = cluster of differentiation, CHOP = cyclophosphamide, vincristine, doxorubicine, prednisolone, CT = computed tomography, DCs = dendritic cells, DHAP = dexamethasone, high-dose cytarabine, platinol, DNA = deoxyribonucleic acid, EBV = Epstein–Barr virus, EMA = epithelial membrane antigen, EPOCH = etoposide, prednisolone, oncovin, cyclophosphamide, hydroxydaunorubicin, FDCS = follicular dendritic cell sarcoma, FDG = fluorodeoxyglucose, HBV = hepatitis B virus, HCV = hepatitis C virus, HIV = human immunodeficiency virus, ICE = ifosfamide, carboplatin, etoposide, mesna, ICU = intensive care unit, IDCS = interdigitating dendritic cell sarcoma, MPO = myeloperoxidase, PET-CT = positron emission tomography and computed tomography, PTA = prothrombin time activity, SMA = smooth muscle actin, TB = total bilirubin.

Keywords: chemotherapy, interdigitating dendritic cell sarcoma (IDCS), spleen

1. Introduction

Tumors arising from dendritic cells (DCs) are rarely reported, among them, interdigitating dendritic cell sarcoma (IDCS) is an extremely rare malignant hematopoietic tumor derived from interdigitating dendritic cells (IDC), with about 134 case reports in English literature from 1978 to 2018. It has been reported that IDCS mostly occurred in lymph nodes, however, the presence of IDSC was also documented in lung, skin, breast, bone, liver, spleen, and intestine.[1–5] Diagnosis of IDCS relies on histological and immunohistochemical analysis rather than clinical presentations, which is positive for S-100 and Vimentin, negative for clusters of differentiation (CD)-1a, CD20, CD21, and CD35.[6,7] The treatment of IDCS has not come to a conclusion, while surgical intervention and chemotherapy were widely accepted.[8] Here we report a case of a woman who suffered from spleen enlargement, recurrent fever, thrombocytopenia and was subsequently diagnosed as IDCS by post-operative histopathology. Unfortunately, she died of liver failure after chemotherapy. The patient has provided written informed consent for publication of the case.

2. Case report

A 53-year-old woman was admitted to the hematology department with chief complaint of abdominal pain and mass, and recurrent fever for 1 month. She had no diabetes or hypertension history. Her physical examination revealed anemia of conjunctiva palpebrae and spleen enlargement. A blood routine test indicated thrombocytopenia and anemia (platelet count $15*10^9$/L, hemoglobin 61 g/L,). Abdominal computed tomography (CT) scan documented splenomegaly with hetero-

Editor: N/A.

The authors report no conflicts of interest

[a] Cardiovascular Division, [b] Hematology Division, [c] Nephrology Division, Xiangya Hospital, Central South University, Changsha, People's Republic of China.

[*] Correspondence: Hongya Xin, Hematology Division (e-mail: xinhongya@163.com); Tianlun Yang, Cardiovascular Division, Xiangya Hospital of Central South University, Xiangya Road, Kaifu District 410000, Changsha, Hunan Province, People's Republic of China (e-mail: tianluny@163.com).

Medicine (2019) 98:19(e15535)

Received: 13 February 2019 / Received in final form: 29 March 2019 / Accepted: 9 April 2019

http://dx.doi.org/10.1097/MD.0000000000015535

geneous enhancement. Positron emission tomography and computed tomography (PET-CT) scan indicated irregular fluorodeoxyglucose (FDG) avidity of spleen, with no abnormal avidity in other sites, demonstrating that there was no sign of metastasis. Bone marrow aspiration showed hypercellularity with increased numbers of megakaryocytes and erythroblasts. Bone marrow biopsy did not reveal abnormalities. Coombs test and Han's test were negative. Hepatitis B virus (HBV) and Epstein–Barr virus (EBV) deoxyribonucleic acid (DNA) tests for serum were negative. Human immunodeficiency virus (HIV) and hepatitis C virus (HCV) antibody tests were negative.

After admission, the patient received component blood transfusion, but the platelet and hemoglobin concentrations continued to decrease, and she had severe abdominal pain. She underwent splenectomy 10 days after admission. Spleen pathology revealed IDCS without splenic lymph nodes involvement. Her blood routine slightly improved after surgery.

Though it seemed that she would have a good outcome, the patient suffered from recurrent fever and thrombocytopenia 10 days after surgery. Imipenem was adopted considering bacterial infection which turned out to be effective. However, her platelet count was still dropping with no obvious bleeding. We administered one cycle of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) (adriamycin 25 mg/m^2, bleomycin 10 mg/m^2, vinblastine 6 mg/m^2, dacarbazine 375 mg/m^2) on day 1 with ifosfamide (1.2 g/m^2) on days 2 to 4 and oxaliplatin (85 mg/m^2) on day 2. Four days after chemotherapy her hepatic enzyme increased and gradually developed severe liver failure (alanine aminotransferase [ALT] 1080 u/L, aspartate transaminase [AST] 950 u/L, total bilirubin [TB] 650 umol/L, prothrombin time activity [PTA] 10%). She lost consciousness 2 weeks later. She was planned to be transferred to ICU for artificial liver support system, but her family rejected for the transfer. Eventually the patient died due to hepatic failure 1 month later after chemotherapy.

2.1. Pathology

Histologic sections of spleen revealed destruction of normal architecture, replaced by neoplastic cells infiltration with remaining lymphocytes around them (Fig. 1). Neoplastic cells represent with spindle and oval shapes, which contain spherical or oval nucleoli and occasional vesicular nucleoli. Nuclear groove and multinucleated forms can be observed (Fig. 2). Immunohistochemical analysis showed that neoplastic cells expressed S-100, vimentin, CD68, CD163, negative for CD21, CD23, Langerin, CD1a, CD34, CD30, HMB45, myeloperoxidase (MPO), CD20, Lysozyme, EMA, SMA, and EBER. Ki-67 proliferation was 30%.

3. Discussion

3.1. Etiology

Dendritic cells are a group of immune accessory cells present in lymphoid and nonlymphoid organs, include four types: follicular, interdigitating, Langerhans, and fibroblastic cells.[8] IDCS is a rare neoplasm originating from interdigitating cells. During the last four decades, only 134 cases reported in English literature. Epidemiologically, most IDCS patients are adult males with median age of 56.5 years, ranging from 1.8 to 88 years. Of the 40 cases, 40% were Asian, 20% Caucasian, 5% Hispanic, 28% white Americans, and 5% black Americans.[8] The etiology of

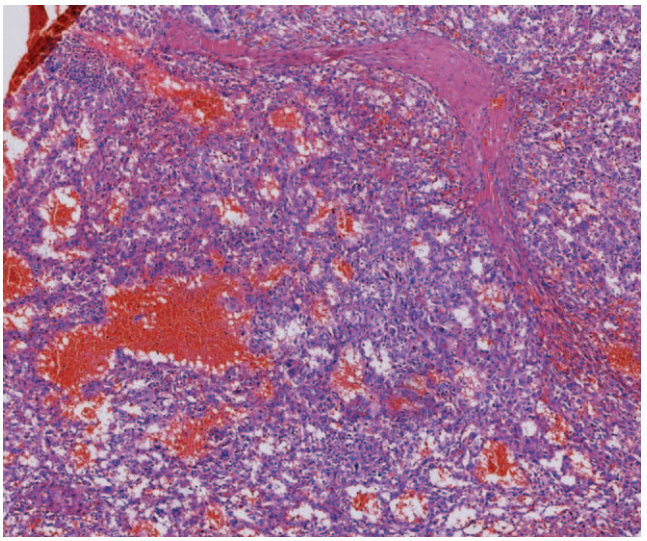

Figure 1. Low-power image of a histologic section of the patient's spleen. Infiltration by neoplastic cells is evident (H&E, ×40). H&E = hematoxylin and eosin stain.

IDCS remains unclear; researches implicated EBV as risk factor of FDCS,[8,9] but no reports revealed consequences between viral infection and IDCS. Our tests excluded the patient's infection of HBV, HCV, HIV, or EBV which supported previous findings. However malignant transformation after radiotherapy and chemotherapy might contribute to the pathogenesis of IDCS.[10]

3.2. Clinical presentation and pathological findings

The clinical presentation of IDCS is unremarkable. Saygin reported that most patients presented with nodal involvement, mainly in cervical lymph nodes.[8] Extranodal involvement

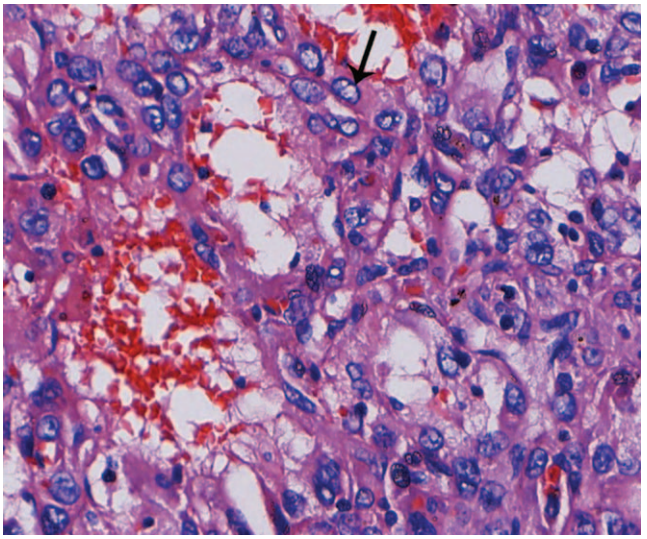

Figure 2. High-power image of a histologic section of the patient's spleen. The shape of neoplastic cells and the morphology of their nuclei and nucleoli is apparent (pointed by the arrow) (H&E, ×400). H&E = hematoxylin and eosin stain.

includes lung, skin, breast, bone, liver, spleen, and intestine.[1–5,11] Bone pain, hematuria, hemoptysis, dyspnea, cough, vaginal bleeding, and ataxia were observed in patients with different sites of extranodal involvement. In our case, the patient presented with spleen involvement accompanied by abdominal pain, fever, and thrombocytopenia.

Diagnosis of IDCS depends on pathological findings which can be challenging. Histologically, IDCS cells show oval to spindle cells, with a variety of patterns, including sinusoidal, nesting, fascicular, storiform, and Reed-Sternberg like giant cells. Lymphoplasmocytic infiltration and epithelioid cells could be seen in the tumors. Tumor cells are positive for S-100, vimentin, HLA-DR, CD163, and CD68. IDCS is negative for CD21, CD35, CD3, and CD20. The Ki-67 labelling index usually ranges between 10% and 20%.[4,8] The ultrastructure of tumor cells can be documented with certainty by electron microscopy. The cells had structure typical of interdigitating cells, with irregularly shaped nuclei displaying indentations and notches.[5] The neoplasm cells had characteristic interdigitating cellular junctions.[12] Abundant organelles were present in the cytoplasm, consisting mostly of mitochondria and clusters of the rough endoplasmic reticulum.[5,6] Desmosomal junctions and Birbeck granules were absent.[5] In our case, neoplastic cells presented as spindle-like and oval shapes and contained spherical and oval nucleoli which conformed to morphological characteristics of IDCS. Immunohistochemical analysis documented the expression of S-100 protein (100%), vimentin, CD68 and CD163, and the absence of B-cell markers, T-cell markers, smooth muscle actin (SMA), epithelial membrane antigen (EMA), MPO, Lagerin, CD30, CD34, CD1a, CD21, and CD35. On the basis of these determinations, we came to the diagnosis of IDCS. However, we did not succeed to apply electron microscopy in time for further characterization of cellular ultrastructure. Genetic data were not acquired in this case since the patient did not consent to next-generation sequencing of the spleen and peripheral blood.

The differential diagnosis of IDCS includes malignant melanoma, malignant fibrous histiocytoma, anaplastic large cell lymphoma, FDCS and Langerhans' cell sarcoma. Malignant melanoma may show nested growth patterns and positivity for markers of HMB45 and Melan-A.[12] Inflammatory myofibroblastic tumors contain a mixture of inflammatory cells and SMA-positive myofibroblasts.[13] Anaplastic large cell lymphoma can be easily identified by the expression of CD30 and CD20, and the absence of S-100.[14,15] FDCS is positive for CD21, CD35, and EMA.[16] Finally, Langerhans' cell sarcoma shows histologically Birbek granules and is positive for CD1a.[17]

3.3. Treatment

Treatment of IDCS has been a matter of discussion in recent years with no specific guidelines because of limited cases gathered. Most patients diagnosed as IDCS with local disease were recommended with surgical intervention, while adjuvant chemotherapy and radiotherapy post-surgery are controversial. It has been concluded that there was no statistically significant survival difference between patients treated with or without adjuvant radiotherapy or other modalities (including chemotherapy) postsurgery.[8] However, there are researches reported that adjuvant therapy was effective.[18] The standard post-surgery treatment of localized IDCS remains to be discussed.

Patients with metastatic disease were recommended with surgical intervention and chemotherapy. Until now, chemotherapy usually contains alkylating agent and anthracycline agent, for example, CHOP, ABVD, ICE, EPOCH, and DHAP have shown promising achievement.[8,16,18–20] Among them, CHOP and ABVD seem to top the others with more cases,[18,19] but still, lack evidence-based significance. In this case, we reviewed all cases and adopted ABVD chemotherapy, but due to its highly malignant form, we added ifosfamide and oxaliplatin, which showed no improvement in her symptom and caused liver disfunction. Unfortunately, the patient's liver function was damaged by chemotherapy which led to death.

3.4. Prognosis

Patients with localized disease have a two-year overall survival rate of 68.1% with median survival of 2 years, while patients with metastatic disease have a significant lower overall survival rate of 15.8% with median survival of 9 months.[8] Chemotherapy and radiotherapy may prolong patient surviving time but may lead to other life-threatening complications such as severe infection, and liver or renal damage.

Acknowledgment

This work was supported by the National Natural Science Foundation of China (81570334 H0206).

Author contributions

Conceptualization: Chengchen Zhao, Xiaohui Xie.
Data curation: Xiaohui Xie.
Formal analysis: Chengchen Zhao.
Investigation: Chengchen Zhao.
Methodology: Chengchen Zhao.
Project administration: Chengchen Zhao.
Supervision: Dengshu Wu, Hongya Xin.
Writing – original draft: Chengchen Zhao, Tianlun Yang.
Writing – review & editing: Chengchen Zhao, Xiaohui Xie, DongZheng Gai, Hongya Xin, Tianlun Yang.

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