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Case Report

A Case of Disseminated Extranodal Interdigitating Dendritic Cell Sarcoma Arising from Parotid Gland

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귀밑샘에서 기원한 림프절 외 수지양 가지 세포 육종이 전신에 파종된 증례

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Interdigitating dendritic cell sarcoma (IDCS) is an extremely rare tumor derived from professional antigen presenting cell and primarily found in lymph nodes, with rarer case report about extranodal presentation of IDCS. A 71-yr-old man was admitted with progressively enlarging and painless mass in the right parotid area for 2 months. Computed tomography of the neck and chest revealed enhancing mass in right parotid gland, multiple lymphadenopathies around neck and mediastinum, and an osteolytic metastasis at thoracic spine. Morphological and immunohistochemical analysis of an excisional biopsy specimen from parotid mass were consistent with a diagnosis of IDCS. Palliative chemotherapy with 6 cycles of CHOP (cyclophosphamide, adriamycin, vincristine, and prednisolone) regimen and 2 cycles of ABVD (adriamycin, bleomycin, vinblastine, and dacarbazine) regimen plus radiotherapy on parotid mass failed in tumor reduction. We describe a rare case of disseminated extranodal IDCS arising from parotid gland.

Key Words: disseminated, interdigitating dendritic cell sarcoma, parotid gland

Dendritic cells are professional antigen presenting cells and a heterogeneous group of cells that includes Langerhans' cell, dermal dendrocytes, follicular dendritic cells (FDCs), and interdigitating dendritic cells (IDCs).[1] IDCs are found in the T-cell area of lymphoid tissues including lymph node, thymic medulla and spleen in responsible for stimulating resting T-cells in the primary immune response. Interdigitating dendriti ccell sarcoma (IDCS) is a rare dendritic cell neoplasm, with only 100 cases reported to date.[1] The etiology and pathogenes is of IDCSare currently poorly understood, although a viral etiology such as Epstein-Barr virus and human herpes virus 8 has been suggested in the development of the closely related follicular dendritic cell sarcoma (FDCS).[1] IDCS occurs usually in lymph nodes, and approximately one-third of cases manifested extranodal presentation.[2] The sites of extranodal sites included liver (27%), spleen (18%), skin (15%), lung (12%), nasopharynx, small intestine, tonsil, bone marrow, chest wall, salivary gland, urinary bladder, and

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breast.[2] Among extranodal sites, the occurrence of IDCS in the parotid gland is low. Here we present a case of disseminated extranodal IDCS arising from parotid gland.

CASE REPORT

A 71-year-old man visited the outpatient clinic with a 2-month history of progressively enlarging painless mass in the right parotid area. He had no relevant previous medical history. On physical examination, multiple non-tender masses were palpable around right parotid and left submandibular area. There were no enlargement of liver and spleen. Laboratory test including liver function test, renal function test, and serum lactate dehydrogenase levels (199 IU/L) showed no abnormal findings except mild anemia (serum hemoglobin 12.7 mg/dL).

Computed tomography (CT) of the neck revealed multiple enhancing masses in right parotid gland with adjacent streaky fat infiltration and fascia thickening (Fig. 1), and multiple enlarged lymph nodes in both sides of neck level I to V. CT scan of chest showed a nodule in the left lower lobe measuring 0.6 cm and multiple mediastinal lymphadenopathies as well as an osteolytic lesion at thoracic spine (T1). No evidence of metastasis was found in CT scan of abdomen and pelvis. Positron emission tomography-computed tomography (PET-CT) scan showed hypermetabolic lesions at the right parotid area (maximum standardized uptake value [SUVmax] = 16.09) and lymph nodes in both side of neck. In addition, abnormal hypermetabolic lesions at several tiny nodules in both lung fields, multiple mediastinal lymph nodes (right lower paratracheal, subcarinal, and both hilar lymph nodes),

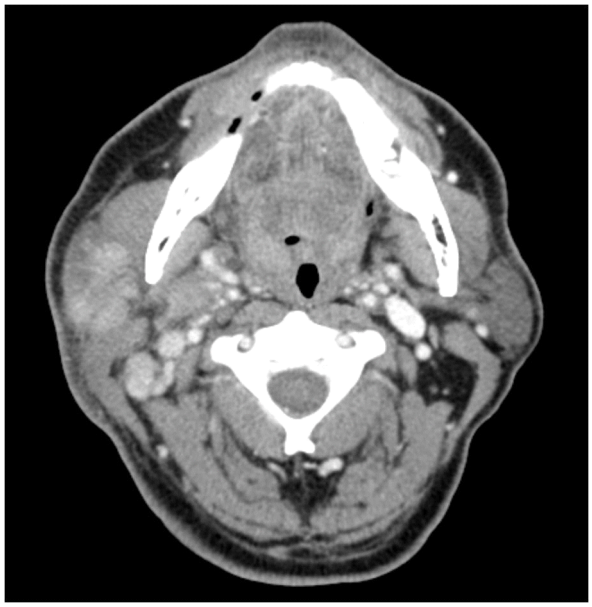

Fig. 1.

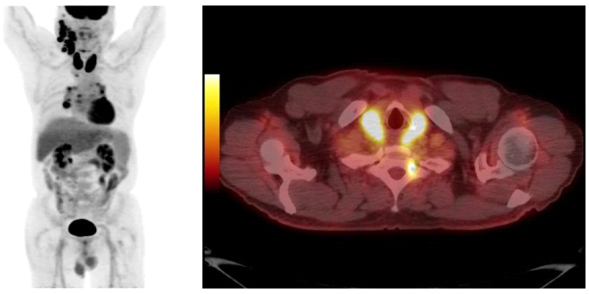

Fig. 2.

and thoracic spine (T1 area) which was suspicious of metastasis were noted on PET-CT scan (Fig. 2). Excisional biopsy was performed from lymph node in the right parotid gland.

Microscopically, the specimen from excisional biopsy included a linear piece of fibrovascular/fibromuscular connective tissue with infiltration of large atypical mononuclear cells with frequent mitotic figures. Immunohistochemical staining showed strong positive reaction for S100, CD68 and vimentin (Fig. 3), but negative reaction for CD21, CD23, CD35, CD1a, CD3, CD20, HMB45 and CD34. In situ hybridization for

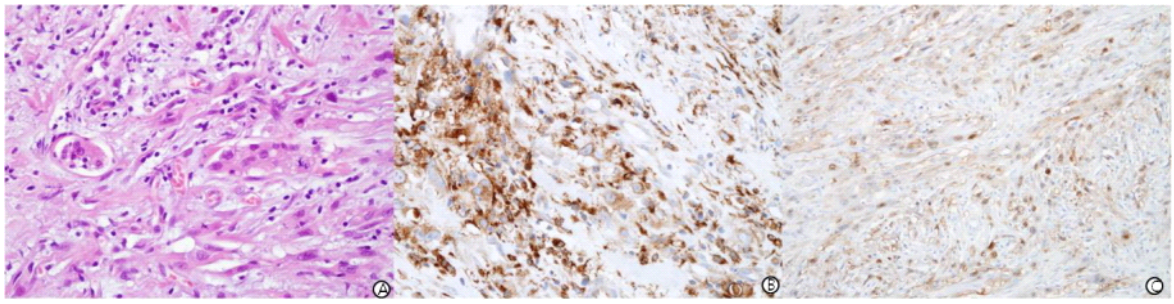

Fig. 3.

EBV was negative.

Bone marrow showed no tumor deposit. Under a diagnosis of IDCS, the patient was treated with combination chemotherapy consisting of cyclophosphamide (750 ㎎/㎡ of body surface area [BSA]), doxorubicin (50 ㎎/㎡ of BSA), vincristine(1.4 ㎎/㎡ of BSA), and prednisone (100 ㎎/day for 5 days) (CHOP). After 3 cycles of CHOP chemotherapy, a follow-up CT scan of neck showed slightly decreased size of the right parotid gland mass and multiple lymph nodes in both sides of neck. During chemotherapy, no significant complications were noted. After 6 cycles of CHOP chemotherapy, follow-up magnetic resonance image (MRI) of neck revealed increased size of parotid mass with in filtration of inflammatory cells and metastatic lymphadenopathies in both cervical areas. A salvage regimen was opted according to the previously reportof successful treatment of IDCS with ABVD chemotherapy. He received the 2 cycles of ABVD consisting of doxorubicin (25 ㎎/㎡ of BSA), bleomycin (10 ㎎/㎡ of BSA), vinblastine (6 ㎎/㎡ of BSA), and dacarbazine (375 ㎎/㎡ of BSA) on day 1 and 15 every 4 weeks. Radiotherapy was delivered to the parotid mass at a total of 1,800 cGy for the relief of pain, quite short of planned dose at 6,000 cGy, because of poor compliance as well as performance. During supportive care such as pain control, the parotid mass and multiple cervical lymphadenopathies got aggravated. Eventually, the patient died of progressive disease 7 month after diagnosis of IDCS.

Discussion

IDCS is an extremely rare neoplasm with currently only 100 cases reported in English literature. In a pooled analysis of 100 cases, affected patients displayed isolated nodal disease (47%), combined nodal and extranodal disease (28%), and isolated extranodal disease (25%).[1,2] Cervical and axillary lymph nodes were the most common sites of nodal involvement. However, the disease has been reported in a wide variety of extranodal sites. Until now, 5 cases of IDCS have been reported in Korea.[3-7] Demographic and clinical features of 100 reported and 5 Korean cases are summarized in Table1. Han et al.[3] described an IDCS with extranodal involvement of the pleura. Kim et al.[4] presented a localized IDCS patient (tonsil involvement) treated with chemotherapy and adjuvant radiotherapy, with an early complete response, and Lee et al.[5] reported a case of successfully treated disseminated IDCS using ABVD chemotherapy. For parotid gland involvement, there have been 3 cases in English literature[8] and no report

so far in Korea. To our knowledge, our report is the first case of disseminated IDCS involving the parotid gland and bone in Korea.

Majority of the cases manifested with a painless lump, but systemic signs and symptoms, including fever, weight loss, night sweat and fatigue have been reported in 11 cases, 9 of whom had both nodal and extranodal disease.[2] In addition, depending on the location and extension of disease involvement, patients present with various manifestations such as bone pain, hematuria, hemoptysis, vaginal bleeding and ataxia. In our case, patient present with painless mass around parotid gland without systemic symptoms despite of having extranodal involvement such as bone metastasis.

Differential diagnosis of IDCS includes Langerhans cell sarcoma, FDCS, non-Hodgkin's lymphoma (diffuse large B-cell lymphoma, peripheral T-cell lymphoma, and anaplastic large cell lymphoma), metastatic carcinoma, and melanoma.[1,9] Not only extreme rarity of IDCS, but its histopathologic similarity to other tumor arising from reticular cells makes difficulty in differential diagnosis. There are no specific histologic feature suggesting IDCS. Dendritic cell neoplasm is composed of spindle to ovoid cells forming fascicles, whorls, diffuse sheets or nodules.[9] Epithelioid cells and giant cells are rarely observed and

Table 1. Demographic and clinical features of reported and Korean cases.

	Reported cases (N = 100)	Korean cases (N = 5)
Age		
Median (range), yr	56.5 (1.8 – 88)	57 (32 – 73)
Sex		
Male:female (ratio)	58:42 (1.38:1)	2:3 (1:1.5)
Presentation[a]		
Localized	59% (45/76)	20% (1/5)
Locally advanced	5.3% (4/76)	40% (2/5)
Metastatic	35.6% (27/76)	40% (2/5)
Involved sites (number of cases)		
Lymph nodes		
Cervical	41	2
Axillary	22	2
Mediastinal	9	-
Intraabdominal	18	-
Exrtanodal sites		
Tonsil	3	1
Nasopharynx	3	2
Soft tissue	1	1
Bone	5	1
Pleura	3	1
Treatment (number of cases)[a]		
Surgery alone	21/76	-
Surgery plus adjuvant therapy	18/76	1/5
Radiation therapy alone	6/76	1/5
Chemotherapy alone	26/76	2/5
Chemotherapy plus radiation therapy	2/76	1/5
No treatment	2/76	-
Unknown	1/76	-

[a]Data obtained from 76 out of 100 reported cases were analyzed.

lymphoplasmacytic infiltration present frequently in tumor tissue.[9] Therefore, immunohistochemical markers are important for correct diagnosis of dendritic cell tumor. Tumor cells displayed a heterogeneous immunophenotype which are strong expression for S100, vimentin, HLA-DR, and fascin, variable staining has been reported for CD68, CD43, CD4, CD123, and lysozyme, but negative for CD20, CD3, CD5, cytokeratin, myeloperoxidase, CD1a, CD21, CD23, CD35, and CD34.[1,9] On the contrary, positive immunohistochemical markers for follicular dendritic cells are CD21, CD23, CD35 ; CD1a and S100 for Langerhans'cellsarcoma ; positive CD 3 for T-cell ; positive CD20 for B-cell ; positive HMB 45 for melanoma ; positive CD34 for myeloid stem cell.[1] In our case, immunohistochemistry results of the tumor cells obtained from right parotid area were positive for S100, CD68, and vimentin, but negative for T cell, B cell, FDCS, epithelial, melanoma, and myeloid markers, which led us to make a diagnosis of IDCS.

Due to the rarity of disease, no consensus has been established on the optimal treatment strategy for localized or advanced IDCS. Various therapeutic approaches, including surgery, radiation therapy, chemotherapy and combination of these modalities have been applied with various outcomes.[1] In a localized disease, surgery has been known as the mainstay of treatment, though it has been reported that a recurrence rate was substantial up to 40%.[10] The role of adjuvant therapy after surgery remains unclear. In other studies, localized IDCS patients treated with surgery and non-surgical modalities did not show a statistically significant difference in overall survival.[1,10] Therefore, radiotherapy may be preferred for treatment of localized IDCS, particularly when surgical resection is not feasible. Sometimes, a good response to chemotherapy has been reported in an advanced case without surgery.[2] Because of a lack of clinical data, the chemotherapy regimens designed for non-Hodgkin's lymphoma or Hodgkin's disease has been used for chemotherapeutic regimen for IDCS treatment. There are case reports of employing CHOP or/and ABVD chemotherapy regimens for treatment for IDCS, especially disseminated type.[2,5,10] Although Lee et al.[5] reported that disseminated IDCS of inferior nasal concha was successfully treated after 8 cycles of ABVD chemotherapy, the response to chemotherapy has been unpredictable in general . Several chemotherapeutic agents have been tried including DHAP (dexamethasone, cisplatin, high-dose cytarabine), ICE(ifosfamide, carboplatin, etoposide), and cisplatin/epirubicin, with limited response.[1] Radiation therapy has also been used in the treatment, but it showed little benefit in this type of sarcoma.[1] In our case, after 3 cycles of CHOP chemotherapy, the patient stayed at stable disease. A total of 6 cycles of CHOP chemotherapy resulted in disease progression. Switching to ABVD regimen as second-line chemotherapy plus palliative radiotherapy on parotid area for pain relief also failed.

Most patients with IDCS displayed an extremely aggressive clinical behavior, widespread metastasis, and poor response to therapy.[1] The median duration of overall survival was 10 months. In a study of 18 patients who received palliative chemotherapy, 3 achieved completere mission, 6 had no response, and 7 died of disease.[11] In an other study of 4 patients with disseminated IDCS, all failed to get the improvement from chemotherapy and died from disease within 0.5 to 14 months after diagnosis.[12] Moreover, lack of

reliable prognostic factors makes outcome unpredictable. Even though several factors such as young age and localized form seem to predict relatively good prognosis, histologic features such as high mitotic activity, the presence of necrosis and nuclear pleomorphism do not show association with prognosis.[1,2,13] In this case, the fact that this patient was already 71-year-old and initially diagnosed as disseminated form predicted poor outcome and he died of disease progression 7 month after diagnosis of advanced IDCS.

In summary, the subtle onset and extremely low incidence of IDCS often result in delayed diagnosis and hence in fatal outcome because of the aggressive clinical course. We described a rare case of disseminated extranodal IDCS arising in parotid gland, based on microscopic features and immunohistochemical markers suggesting IDCS such as the strong expression of for S100, CD68 and vimentin.

Conflict of interest

Conflict of interest relevant to this article was not repor ted.

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