Case Report

Lymph node involvement in histiocytic sarcoma: A report of two cases with previous misdiagnoses

Santosh Kumar Mondal, Palash Kumar Mandal, Sankha Chatterjee, Shravasti Roy[1]

Department of Pathology, Medical College, Kolkata, [1]Department of Pathology, Saroj Gupta Cancer Centre and Research Institute, Kolkata, West Bengal, India

ABSTRACT

Histiocytic sarcoma (HS) is an unusual rare but controversial neoplasm. Here, we report two cases of HS initially misdiagnosed as other entities and with initial wrong treatment. The first case was a 29-year-old male with right cervical lymphadenopathy. The patient was misdiagnosed as nodular sclerosis variant of Hodgkin disease. The second case was a 12-year-old male child with axillary and mediastinal lymph nodes. This case was misdiagnosed as tuberculosis. Both these two cases were initially treated according to their primary diagnosis, but without any treatment success. Subsequently, repeat biopsies of these cases were done. Histopathologic examination showed these cases to be HS. The tumor cells were immunoreactive for CD68, CD163, and immunonegative for cytokeratin, epithelial membrane antigen, CD15, CD30, and other markers. Focal positivity of S-100 was noted in one case. Thus, confirmed diagnosis of HS was established. Patients were treated for HS and were kept well in 1-year follow-up period.

Key words: Histiocytic sarcoma, immunohistochemistry, misdiagnosis

INTRODUCTION

Histiocytic sarcoma (HS), formerly designated as true histiocytic lymphoma is a rare aggressive hematopoietic neoplasm, representing <1% of all nonHodgkin lymphomas.[1] HS can present as localized disease confined to lymph nodes, skin and intestinal tract, or as disseminated disease.[1]

Neoplasms originally classified as "reticulum cell sarcomas" and later as "histiocytic lymphomas" by Rappaport have encompassed a biologically heterogeneous group of disorders, most of them are now classified as high-grade T- or B-cell, nonHodgkin's lymphomas. The term "HS" was introduced by Mathé *et al*. which was based on histologic similarities of these cells, to macrophages.[2] Most of the patients of HS are adult males (median age 46 years). Awareness of HS is important, as the tumor mimics other nonHodgkin lymphomas in their clinical presentation and morphologic appearance.

Access this article online	
Quick Response Code:	Website: www.ccij-online.org
	DOI: 10.4103/2278-0513.149061

CASE REPORT

Case 1

A 29-year-old male presented with right cervical lymphadenopathy for last 3 months along with generalized weakness and low-grade fever. Histopathologic examination of the lymph node was made, and diagnosis of nodular sclerosis variant of Hodgkin lymphoma was given. The patient was treated with chemotherapy. But the patient's condition did not improve, and lymph node did not regress. A repeat biopsy was done for histopathologic examination. Microscopical examination revealed complete effacement of the lymph nodes and composed of diffuse proliferation of large round to oval cells with pleomorphic vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm [Figure 1]. Mitotic figures and large multinucleated cells were also noted. Immunohistochemistry (IHC) showed tumor cells were positive for CD68, CD163, NSE, and vimentin. The tumor cells were immunonegative for CD30, CD43, epithelial membrane antigen (EMA), CD21, CD35, cytokeratin, CD1a, CD99, SMA, CD117, Melan A, and HMB45. Weak positivity seen for CD4, S-100, and CD45. Reactive lymphocytes but not the tumor cells were positive for CD3, CD4, CD8, and to a lesser degree for CD20. After morphologic examination and IHC evaluation, a final diagnosis of HS was established.

Address for correspondence: Dr. Santosh Kumar Mondal, Teenkanya Complex, Flat 1B, Block B, 204 R N Guha Road, Dumdum, Kolkata - 700 028, West Bengal, India. E-mail: dr_santoshkumar@hotmail.com

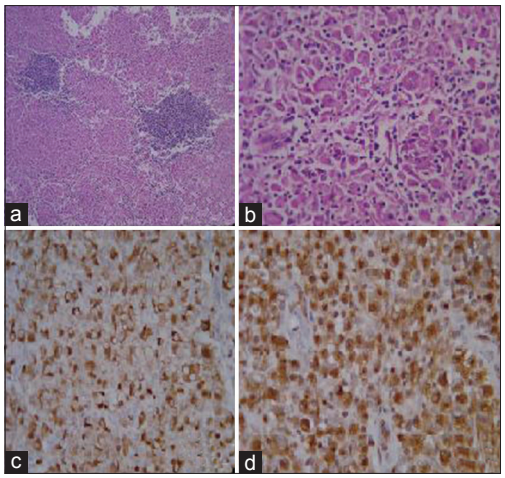

Figure 1: (a) Microphotograph showing effacement of the lymph node. The tumor is composed of large pleomorphic cells with eccentric nuclei. Occasional clusters of residual lymphoid cells are seen (H and E, ×100). (b) High power view showing the large tumor cells having eccentric vesicular nuclei, prominent nucleoli, and abundant eosinophilic cytoplasm. Binucleated cells are also present (H and E, ×400). (c) Immunohistochemistry showing CD68 positivity among tumor cells (×400). (d) Immunohistochemistry showing the vimentin positivity among tumor cells (×400)

Case 2

A 12-year-old male child presented with axillary and mediastinal lymph node enlargement. The boy was also suffering from fever, loss of weight, and generalized weakness. Histopathologic examination of axillary lymph nodes was done, and diagnosis of tuberculous lymphadenitis was made. The patient was given anti-tuberculous drug for 6 months but of no use. Then a repeat biopsy from axillary lymph nodes was done and specimen sent for histologic diagnosis. Morphologic examination and IHC showed almost similar results as in case 1. But in this case, necrosis was present unlike case 1. Hence, a final diagnosis of HS was rendered.

Modified CHOEP-14 chemotherapy was administered intravenously in both these patients (cyclophosphamide 750 mg/m^2 day 1, doxorubicin 50 mg/m^2 day 1, vincristine 1.4 mg/m^2 day 1, etoposide 100 mg/m^2 day 1, and prednisolone 50 mg/m^2 days 1-5 followed by Rh G-CSF [filgrastim] at a dose of 300 μg/day) along with intravenous heparin to prevent disseminated intravascular coagulation. A total of six cycles of chemotherapy was employed at an interval of 2 weeks. Local radiotherapy in a dose of 40 Gy was given to the cervical and axillary lymph nodes after chemotherapy. Both the patients showed improvement and 1-year follow-up period is uneventful.

DISCUSSION

Histiocytic sarcoma is a rare malignant neoplasm that occurs in lymph nodes, skin, and the gastrointestinal tract.[1,3] Many previously published cases may have been misdiagnosed examples of nonHodgkin lymphoma. In the WHO classification, HS was defined as a malignant proliferation of cells showing similar morphologic and immunophenotypic features as in mature histiocytes. Hence, diagnosis of HS rests on morphologic features of the histiocytic lineage among the tumor cells and exclusion of other differential diagnosis by IHC. Differential diagnoses of HS include diffuse large B-cell lymphoma, Langerhans cell sarcoma, anaplastic large cell lymphoma (ALCL), metastatic carcinoma, and melanoma. In our cases, the tumor cells showed the histiocytic lineage by IHC (CD68, CD163) but negative for CD21, CD35, CD1a (dendritic cell and Langerhans cell marker), CD20/CD79a (B-cell marker), CD30, EMA (ALCL marker), cytokeratin/EMA (carcinoma marker), and HMB45/S-100 (melanoma marker). This matched with other workers' findings.[4,5] Thus, the diagnosis of HS was established.

Immunohistochemistry is a key to the diagnosis of HS. Immuno-markers once thought to be specific for histiocytic differentiation, like alpha-1-antichymotrypsin, alpha-1-antitrypsin, lysozyme have been shown to have low specificity and may be positive in many other neoplasms, including other nonHodgkin's lymphomas.[6] The recent characterization of CD163, a hemoglobin scavenger receptor protein, has offered a means of identifying histiocytic neoplasm with greater specificity.[7,8]

Histiocytic sarcoma can present at extranodal sites such as skin, gastrointestinal tract, spleen, bone marrow, and central nervous system.[8] Some patients may have systemic manifestations, with features of malignant histiocytosis. Most of the cases of HS demonstrate high proliferative rate and extranodal spread.[1] Stage of disease and possibly tumor size are considered prognostic factors as in most other lymhomas.[1] But both our cases presented with lower clinical stage and there was no extranodal spread. Our patients responded to therapy and were kept well in the 1st year follow-up period, unlike in other studies where patients succumbed to the disease early.

Histiocytic sarcoma may also be associated with other hematological disorders such as acute leukemia and myelodysplasia.[9] Genetic or epigenetic inactivation of PTEN, p14ARF, and p16INK4A has been observed in HS, which provides insight into the pathogenesis of this neoplasm.[10]

Primary treatment of HS consists of radical surgery with wide surgical margins, frequently combined with elective radiotherapy. With no evidence-based data, several

chemotherapeutic regimens have been added to surgery and radiotherapy, primarily for local control of the disease.[11] Recently, thalidomide and allogenic hematopoietic stem cell transplantation showed some success in therapy.[12] Pileri *et al*. reported that among 12 cases treated with chemotherapy with or without radiotherapy, only two cases maintained complete remission and seven patients died of HS.[13] Recent data have shown promising results with the addition of etoposide to conventional CHOP chemotherapy on complete remission with increase in survival rate in patients suffering from aggressive lymphoma under 60 years old.[14] In our patients also, modified CHOP or CHOEP-14 was administered.

CONCLUSION

Optimal management of HS is still debated due to limited chemotherapeutic trials in a small number of cases and poor survival. Whatever be the final outcome with newer drugs, correct diagnosis at an early stage can only prolong patient's disease free survival.

REFERENCES

1. Jaffe ES, Harris NL, Stein H, Vardiman JW, editors. Pathology and Genetics of Tumors of Haematopoietic and Lymphoid Tissues. Lyon: IARC Press; 2001. p. 273-90.
2. Mathé G, Gerard-Marchant R, Texier JL, Schlumberger JR, Berumen L, Paintrand M. The two varieties of lymphoid tissue "reticulosarcomas", histiocytic and histioblastic types. Br J Cancer 1970;24:687-95.
3. Sundersingh S, Majhi U, Seshadhri RA, Tenali GS. Multifocal histiocytic sarcoma of the gastrointestinal tract. Indian J Pathol Microbiol 2012;55:233-5.
4. Hornick JL, Jaffe ES, Fletcher CD. Extranodal histiocytic sarcoma: Clinicopathologic analysis of 14 cases of a rare epithelioid malignancy. Am J Surg Pathol 2004;28:1133-44.
5. Alexiev BA, Sailey CJ, McClure SA, Ord RA, Zhao XF, Papadimitriou JC. Primary histiocytic sarcoma arising in the head and neck with predominant spindle cell component. Diagn Pathol 2007;2:7.
6. Soini Y, Miettinen M. Alpha-1-antitrypsin and lysozyme. Their limited significance in fibrohistiocytic tumors. Am J Clin Pathol 1989;91:515-21.
7. Graversen JH, Madsen M, Moestrup SK. CD163: A signal receptor scavenging haptoglobin-hemoglobin complexes from plasma. Int J Biochem Cell Biol 2002;34:309-14.
8. Vos JA, Abbondanzo SL, Barekman CL, Andriko JW, Miettinen M, Aguilera NS. Histiocytic sarcoma: A study of five cases including the histiocyte marker CD163. Mod Pathol 2005;18:693-704.
9. Sohn BS, Kim T, Kim JE, Bae E, Park CJ, Huh J, *et al.* A case of histiocytic sarcoma presenting with primary bone marrow involvement. J Korean Med Sci 2010;25:313-6.
10. Carrasco DR, Fenton T, Sukhdeo K, Protopopova M, Enos M, You MJ, *et al.* The PTEN and INK4A/ARF tumor suppressors maintain myelolymphoid homeostasis and cooperate to constrain histiocytic sarcoma development in humans. Cancer Cell 2006;9:379-90.
11. De Vos FY, Gerding MN, Arends JW, Wegman JJ. Histiocytic sarcoma localised in the thyroid: A case report. Ann Hematol 2008;87:681-2.
12. Abidi MH, Tove I, Ibrahim RB, Maria D, Peres E. Thalidomide for the treatment of histiocytic sarcoma after hematopoietic stem cell transplant. Am J Hematol 2007;82:932-3.
13. Pileri SA, Grogan TM, Harris NL, Banks P, Campo E, Chan JK, *et al.* Tumours of histiocytes and accessory dendritic cells: An immunohistochemical approach to classification from the International Lymphoma Study Group based on 61 cases. Histopathology 2002;41:1-29.
14. Yoshida C, Takeuchi M. Histiocytic sarcoma: Identification of its histiocytic origin using immunohistochemistry. Intern Med 2008;47:165-9.

Cite this article as: Mondal SK, Mandal PK, Chatterjee S, Roy S. Lymph node involvement in histiocytic sarcoma: A report of two cases with previous misdiagnoses. Clin Cancer Investig J 2015;4:93-5.

Source of Support: Nil, **Conflict of Interest:** None declared.