



CASE RECORDS

HISTIOCYTIC SARCOMA: A CASE SERIES OF EXTRANODAL AND NODAL PRESENTATIONS

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ABSTRACT

Introduction: Histiocytic sarcoma is an aggressive malignancy of mature histiocytes which often carries a poor prognosis. Histiocytic sarcoma is defined in the World Health Organisation (WHO) classification of histiocytic and dendritic cell neoplasms.

Case Presentation: Case 1 depicts a 42 year old Malay gentleman with no premorbid presented to the haematology unit with a three month history of fever, night sweats, unintentional weight loss, left axillary and bilateral inguinal swellings which were progressively enlarging. Physical examination revealed a medium built gentleman with left axilla, bilateral inguinal lymphadenopathies and hepatosplenomegaly. Excision biopsies of the left axillary and inguinal lymph nodes were compatible with histiocytic sarcoma. He did not have any bone marrow infiltration. He was treated with 6 cycles of CHOP (Cyclophosphamide, doxorubicin, vincristine, and prednisolone) polychemotherapy but he subsequently succumbed to severe hemophagocytic syndrome shortly after his 6th CHOP chemotherapy. Case 2 describes a 55-year-old previously healthy Malay gentleman who presented with perianal swelling and weight loss for two months. Physical examination revealed a large perianal swelling measuring 10 cm with bilateral inguinal lymphadenopathies. Anorectal tissue histology was compatible with the diagnosis of histiocytic sarcoma. He underwent a transverse colostomy, which was subsequently reversed post chemotherapy. He completed 6 cycles of CHOP chemotherapy followed by upfront consolidation autologous stem cell transplant. He is currently 9 months in complete remission.

Conclusion: Histiocytic sarcoma remains a disease with poor treatment outcomes and high mortality. Understanding the pathogenesis and pathobiology of the disease will provide future to the development of novel therapies.

KEYWORDS : Histiocytic sarcoma, lymphadenopathies, hepatosplenomegaly, excision biopsy.

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INTRODUCTION

Histiocytic sarcoma is an extremely rare aggressive malignancy of mature histiocytes which often carries a poor and dismal prognosis. Histiocytic sarcoma is defined in the World Health Organization (WHO) 2016 classification of histiocytic and dendritic cell neoplasms [1]. This condition comprises of less than 1% of all hematolymphoid neoplasms. It can manifest as a primary malignancy of mature histiocytes which is derived from the mononuclear phagocyte system or as a secondary malignancy which could occur post cytotoxic chemotherapy for germ cell tumours. The mean age of diagnosis is 51 years with male predominance [2].

Patients with histiocytic sarcoma usually present with a painless mass at an extranodal site and have typical B symptoms such as fever, night sweats, or unintentional weight loss [2].

CASE PRESENTATION

Case 1 :

A 42 year old gentleman of Malay ethnicity with no premorbid presented to the haematology unit with a three month history of fever, night sweats and unintentional weight loss. He complained of left axillary and bilateral inguinal swellings which were progressively

worsening. There was no significant family history. He works as a chef with the Malaysian army. He is a non smoker and does not consume alcohol. He denies any indulgence with traditional or recreational drugs.

Physical examination revealed a medium built gentleman with stable parameters. There were multiple left axilla and bilateral inguinal lymphadenopathies measuring 5 x 6 cms in size the largest. His liver and spleen were palpable measuring 3 cm below the costal margin. He did not have any skin lesions or pruritus. Other systemic examinations were unremarkable.

His baseline staging whole body Computed Tomography (CT) imaging showed hepatosplenomegaly with intra-abdominal and inguinal lymphadenopathy, a small left lung nodule with left axillary lymphadenopathy. Axillary and inguinal lymph node histology (Image 1) showed malignant cells exhibiting large eccentric nuclei with vesicular chromatin and prominent irregular nucleolus. The malignant cells stained positive for CD 45, CD 68 and CD 123 which were compatible with histiocytic sarcoma.

The staging bone marrow biopsy showed no infiltration. His laboratory parameters revealed a haemoglobin of 10.2 g/dL, a total white cell count of $10.6 \times 10^9/L$ and a platelet count of $157 \times 10^9/L$. His lactate dehydrogenase (LDH) was elevated at 740 U/L. He had normal renal and liver functions. There were no demonstration of any hyperuricemia, hypercalcemia or hypereosinophilia. His HIV serology, Epstein Barr Virus (EBV) PCR and direct antiglobulin test (DAT) were all negative.

He was treated with 6 cycles of standard CHOP induction chemotherapy (Cyclophosphamide, doxorubicin, vincristine, prednisolone). Due to the natural history of the disease, he was scheduled for upfront consolidation high dose therapy-autologous stem cell transplant (HDT-ASCT). Shortly after his 6th cycle of CHOP chemotherapy, he developed severe hemophagocytic syndrome with led to multiorgan failure in which he succumbed at the intensive care unit a day later.

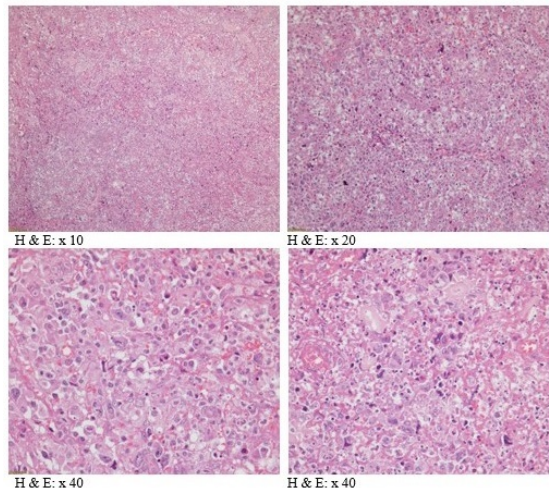


Image 1: Haematoxylin & Eosin (H & E) x 10, x 20 and x 40: Axillary and inguinal lymph node histology shows malignant histiocytic cells exhibiting large eccentric nuclei with vesicular chromatin, prominent irregular nucleolus and abundant eosinophilic cytoplasm.

Case 2:

A 55 year old gentleman of Malay ethnicity who was previously healthy presented to the haematology unit with perianal swelling of 2 months which was progressively worsening. He had bilateral inguinal swellings. He also complained of fever and progressive weight loss.

On examination, he was alert with stable vital parameters. There was a large perianal swelling measuring 10 cm associated with serous discharge. Bilateral inguinal swellings measuring 3 x 3 cm the largest were also seen. Liver and spleen were not palpable. Other systemic examinations were unremarkable.

His baseline whole body Computed Tomography (CT) imaging showed a large anorectal mass measuring 10 cm extending to the mid rectum with near obliteration of the bowel lumen and presacral space. Multiple enlarged pelvic, mesenteric, inguinal, aortocaval and para-aortic lymph nodes were seen. Other organ systems were not involved.

Anorectal tissue histology was compatible with histiocytic sarcoma with neoplastic cells expressing positivity for CD 45, CD 68 and Vimentin. They were negative for all B, T, Natural Killer (NK) lymphoid, plasma, epithelial, melanocytic, blast and myeloid markers.

Trephine showed no evidence of marrow infiltration.

A transverse colostomy was performed by the surgeon. He completed 6 cycles of standard CHOP chemotherapy followed by upfront consolidation high dose therapy-autologous stem cell transplant. 18-Fluorodeoxyglucose Positron Emission Tomography (18-FDG PET) imaging post therapy showed complete metabolic response. His transverse colostomy was subsequently reversed. He has been in complete remission for the past 9 months.

DISCUSSION

Histiocytic sarcoma is an extremely rare and aggressive neoplasm. Histiocytic Sarcoma was first described in 1939 by Scott and Robb Smith as histiocytic medullary reticulosis which then was designated in 1966 as malignant histiocytosis [3]. Following this, the term histiocytic sarcoma was coined in 1970 by Mathe et al [3].

Histiocytic sarcoma is often associated and may occur secondary to malignancies such as follicular lymphoma (FL), Diffuse Large B Cell Lymphoma (DLBCL), acute monoblastic leukaemia, hairy cell leukaemia (HCL), chronic lymphocytic leukaemia and chronic myelomonocytic leukaemia [4].

The lymph node appears to be the most common site of involvement in histiocytic sarcoma followed by the gastrointestinal tract, spleen, soft tissue, skin and central nervous system [5].

Histiocytic sarcoma often shows a diffuse architecture with a sinusoidal or paracortical pattern involving the nodal or extranodal tissue specimens [5]. The neoplastic cells are large and round with abundant eosinophilic cytoplasm and well-defined cellular borders [6]. The nuclei are large, eccentric and pleomorphic with one or more distinct nucleoli. Hemophagocytosis or emperipolesis by neoplastic cells can be present [6].

Immunohistochemistry staining usually show positivity for histiocyte-associated markers such as CD4, CD11c, CD 68, CD 163 or lysozyme [7]. Human leukocyte antigen-antigen D related (HLA-DR) and CD45 are often positive. S100 is often positive, but only in a minor subset of cells [7]. The tumour cells are usually negative for B-cell, T-cell and myeloid cell markers.

As to date, there is no standard chemotherapy regimen in the treatment of histiocytic sarcoma. Localised or unifocal disease are often treated with surgery/excision followed by adjuvant irradiation [8]. Advanced/metastatic disease will require systemic chemotherapy. CHOP chemotherapy appears to be the most commonly utilized chemotherapy regime. In the past, other regimens

including CHOP-E, BEAM and MEAM had been used. Most patients demonstrate limited response to these treatments and they follow a very aggressive clinical course [8].

Novel drugs in treatments such as thalidomide, alemtuzumab, vemurafenib, imatinib, sorafenib and bevacizumab have also been tried. The BRAF pathway may play a role in the carcinogenesis of histiocytic neoplasms giving hope for BRAF inhibitors such as vemurafenib [9].

AUTHORS' CONTRIBUTIONS

The participation of each author corresponds to the criteria of authorship and contributorship emphasized in the [Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals](#) of the [International Committee of Medical Journal Editors](#). Indeed, all the authors have actively participated in the redaction, the revision of the manuscript and provided approval for this final revised version.

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The loss of tumor suppressor genes such as PTEN and INK4a/ARF in mice causes premalignant expansion of biphenotypic myelolymphoid cells followed by the development of Histiocytic Sarcoma [10]. Larger randomized trials are required to assess the effectiveness of these therapies.

CONCLUSION

Histiocytic sarcoma remains a disease with poor treatment outcomes and high mortality. Understanding the pathogenesis and pathobiology of the disease will provide future to the development of novel therapies.

SPONSORSHIP

Declared none.

COMPETING INTERESTS

The authors declare no competing interests.

INFORM CONSENT

Consent obtained from the next of kin and the patient for publication.