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 histocytes 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 premorbids 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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A 55 year old gentleman of Malay ethnicity who was previously healthy presented to the haematology unit with 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 staging whole body Computed Tomography (CT) imaging showed hepatosplenomegaly with intra-abdominal and inguinal lymphadenopathies, 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, CD 163 or lysozyme for histiocyte-associated markers such as CD4, CD11c, CD14, CD1a, CD 68, CD 163 or lysozyme.

Immunohistochemistry staining usually show positivity for 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

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.
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. 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 [8].

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.

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.

SPONSORSHIP
Declared none.

COMPETING INTERESTS
The authors declare no competing interests.

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