SIGNET RING LYMPHOMA: THE IMPORT OF IMMUNOHISTOCHEMISTRY IN RESOLVING DIAGNOSTIC DILEMNAS

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ABSTRACT

Signet ring cell lymphomas are a rare subtype of non Hodgkin lymphoma characterised by malignant lymphoid cells with cytoplasmic inclusions that displace the nucleus and imparts a "signet ring" appearance.This poses a diagnostic challenge as it can be mistaken for an adenocarcinoma or any other epithelial malignancy.A 54yr old male presented with a 6month history of generalised lymphadenopathy. Examination of excision biopsy of the lymph nodes show effacement of architecture by sheets neoplastic cells with abundant cytoplasm distended by eosinophilic amorphous substances. Immunohistochemistry with a panel of three monoclonal antibodies [LCA, CD20, and CD3] confirmed these cells to be of lymphoid origin.

KEY WORDS: Non Hodgkin Lymphoma; Signet Ring, Immunohistochemistry

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INTRODUCTION

Signet ring cell lymphoma [SRCL], an extremely rare variant of non Hodgkin lymphoma was first described in 1978.[1] It is widely regarded as a variant of follicular lymphoma because signet ring cells are occasionally seen in the germinal centre and a follicular architecture is recapitulated by several signet ring cell lymphomas. It is characterized by the proliferation of atypical lymphoid cells containing abundant eosinophilic intracytoplasmic deposits which push the nuclei to the edge, hence producing a signet ring morphology commonly seen in mucinous adenocarcinomas.[2]

CASE REPORT

We present the case of a 54 year old male presented with a 6month history of generalized lymphadenopathy and splenomegaly, who presented to the General surgery unit of Jos University Teaching Hospital. A working diagnosis of Non Hodgkin Lymphoma was made, and an excision biopsy of the left cervical lymph node was performed. Review of the microscopic slides at the Histopathology Unit of the same hospital revealed effacement of nodal architecture by sheets of pleomorphic cells containing and interspersed by abundant homogenous eosinophilic material. The intracellular accumulations displaced the nuclei of these cells rendering an eccentric / signet ring appearance. Initial impressions of a plasmacytoma, metastatic medullary carcinoma and metastatic signet ring adenocarcinoma were entertained. However web-based, inter-institutional consultations with centres in Europe and Asia were carried out followed by immunohistochemistry. A positive expression by the lesional cells of CD45 and CD20 [Figures 2 and 3] and negative staining with CD3 helped confirm the lymphoid nature of these cells as well as their B cell lineage. Subsequently a definitive diagnosis of a Signet Ring B cell lymphoma [SRBCL] was made.

DISCUSSION

This is the first reported case of Signet Ring Cell lymphoma in this center and the authors are not aware of any other case reported within the country / region. In 1978, Kim et al made the first documentation of signet ring lymphomas. He described seven cases of non Hodgkin's lymphoma in which the neoplastic cells contain an abundant vacuolated cytoplasm and peripheral nuclei. More than 50 cases have been described since then.[2,3] Most cases are nodal, the fewer

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cases that are extra nodal occur predominantly in the bone marrow.[2]

The diagnostic dilemma it poses is significant, it can has been mistaken for mucin producing adenocarcinomas and in some rare instances a liposarcoma. In a case report in Manchester, United Kingdom, the vacuoles within the neoplastic cells were on first impression, thought to be fixation artefacts.[1] However examination of touch preparations, use of special stains such as PAS, Oil Red O, Immunohistochemsitry and gene analysis help confirm the actual diagnosis. The nature of the vacuoles has been debated. Some workers suggest they are linked to the smooth endoplasmic reticulum, others the rough endoplasmic reticulum. Nonetheless the consensus is that they are membrane bound accumulations of intracellular immunoglobulin.

Signet ring lymphomas are mostly B cell lymphomas, although a few cases of T cell lineage / origin have been reported.[3,4] Cell lineage has been confirmed / demonstrated via expression of surface markers such as CD45, CD20 and CD3, positive staining for cytoplasmic immunoglobulin and demonstration of re arrangement of immunoglobulin genes.[2]

In conclusion the unique and enigmatic morphology of this rare lymphoma type requires assessment with a high index of suspicion. Equally, ancillary techniques have been once more demonstrated to be indispensable in the handling of specimens of a lymphoid nature. Difficulty in delineating close differentials equally arises when the size of the tissue biopsy is inadequate, as the likelihood of missing this diagnosis is higher with core needle biopsies.

Conflicting Interests: The authors declare that there is no conflict of interest regarding the publication of this paper.

The Authors describe a case of "signet-ring cell" lymphoma. This entity, although rare, is well known. In this case study there is nothing new: the dilemma announced in the title does not exist on the light of immunohistochemistry. Already in Henry and Symmers, Systemic Pathology, third edition,1992, pag. 659-660, two varieties of this lymphoma are described , in particular paying attention to the different content of the vacuoles. In this case study this content is not analyzed. Also, the ultrastructural characteristics of the cytoplasmic organelles are not mentioned

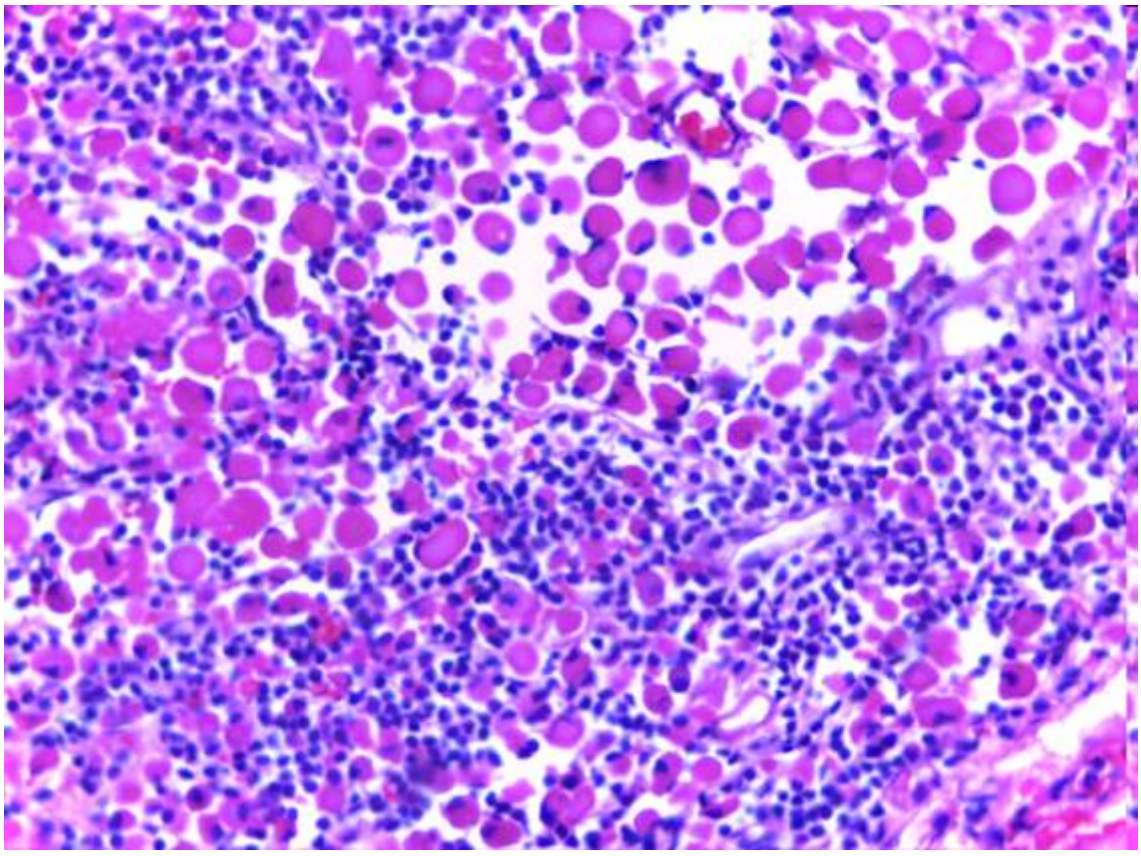

Figure 1:Photomicrograph of paraffin section of signet ring cell lymphoma showing neoplastic cells filled with abundant eosinophilic material, displacing the nuclei. Hematoxylin and Eosin x100

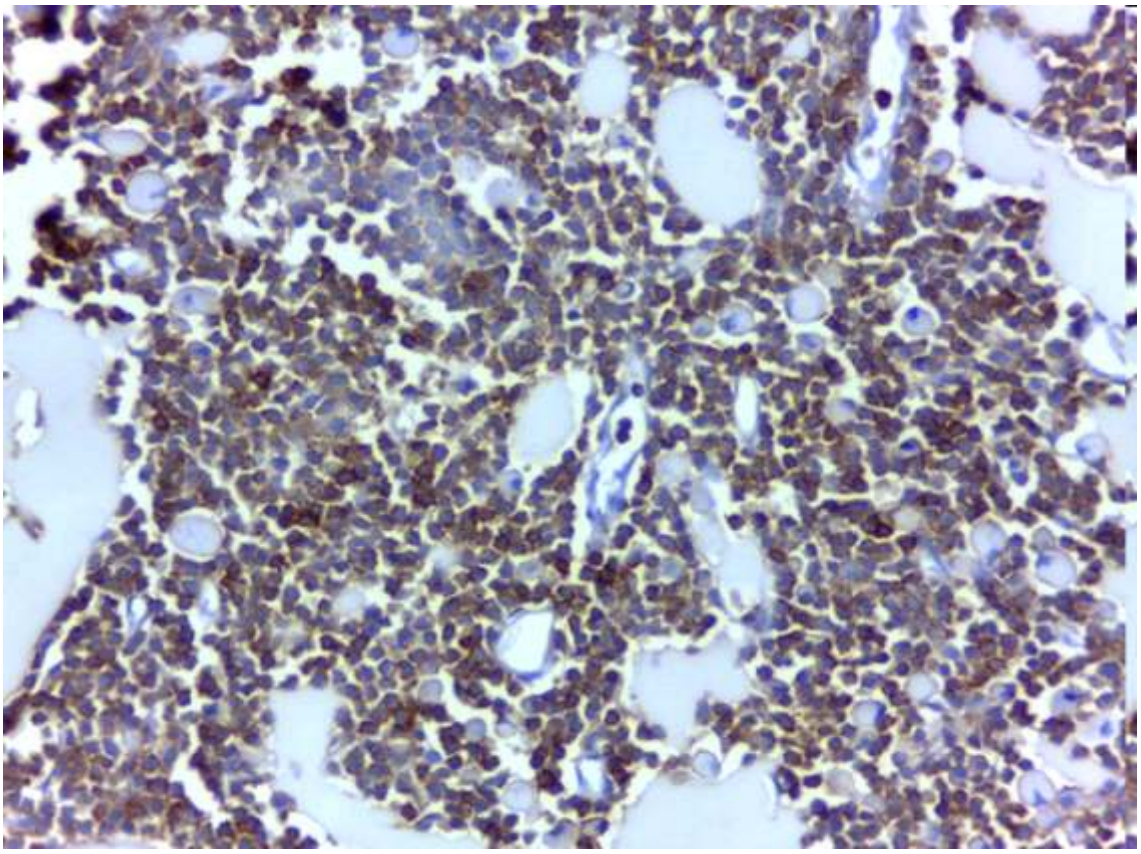

Figure 2: Photomicrograph of paraffin section of Signet ring lymphoma showing Leucocyte Common Antigen expressing cells of hematolymphoid origin. Indirect Immunoperoxidase x 100

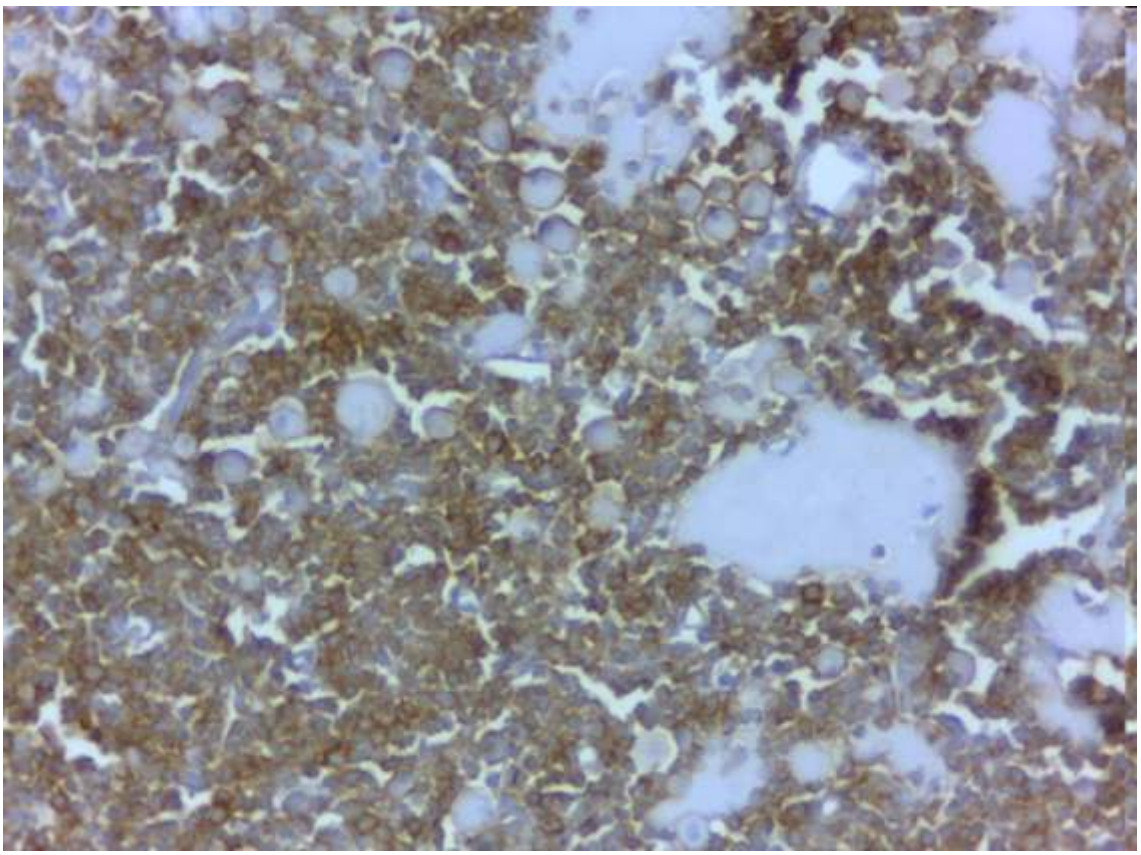

Figure 3: Photomicrograph of paraffin section of Signet ring lymphoma showing CD20 expressing B cells with eccentric nuclei. Indirect Immunoperoxidase x100

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