Follicular immunoblastic lymphoma: a clinicopathologic and immunohistochemical study of a case

HE Xuanqiu1, YANG Lei2*, DING Yanqing2*

First Clinical Medical College1, Department of Pathology, Nanfang Hospital2, Southern Medical University, Guangzhou 510515, China

Abstract: Primary follicular immunoblastic lymphoma (FIBL) is an extremely rare lymphoma. The positive expression of CD10 suggests the lymphoma originating from germinal centers (GC) and CD138-positive expression generally indicates plasmablastic or plasmacytic differentiation. We report such a rare case in a Chinese female patient and analyze the clinicopathologic and immunohistochemical features of this disease. PET-CT examination was performed to detect signs of systemic lymph node metastasis. We also discussed the differential diagnosis of FIBL from follicular lymphoma (FL) and reactive follicular hyperplasia (RFH). As a rare variant of human follicular lymphoma, FIBL is featured by a neoplastic overgrowth of intrafollicular immunoblasts. Compared with FL, FIBL has a greater chance to evolve into diffuse large B-cell lymphoma with therefore a poorer prognosis.

Key words: follicular lymphoma; immunoblasts; immunophenotype; PET-CT

INTRODUCTION

Follicular lymphoma (FL) of the germinal center (GC) origin is the most common type of indolent non-Hodgkin’s lymphomas1,2, defined as a lymphoma of follicle center B-cells (centrocytes and centroblasts) with at least a partial follicular pattern1. In malignant lymphomas, such as diffuse large B-cell lymphoma (DLBCL), B-immunoblasts grow predominantly in a diffuse form3. However, several cases were reported to show immunoblastic neoplasm growth in a complete or partial follicular growth pattern accompanied by a few of plasmablast cells4-6. Such neoplasms were presumed to represent a rare variant of FL, known as follicular immunoblastic lymphoma (FIBL) or follicular immunoblastic-plasmablastic lymphoma (FIPL) based on their distinct cell morphologies. FIBL is characterized by the predominance of immunoblasts in the cellular composition in the follicles. These immunoblasts can be considered as the neoplastic counterpart of the intrafollicular immunoblasts. Even till now the epidemiological and clinical data of FIBL remain scarce regarding its incidence, diagnosis and optimal treatment. In this report, we describe a case of primary FIBL in a Chinese female patient, who showed no representative clinical symptoms. We analyzed the clinical characteristics, histopathology, immunohistochemistry and differential diagnosis of this disease to provide better insights into this rare clinical entity.

CASE REPORT

Clinical data

A 39-year old female patient with no remarkable medical history was presented to our hospital with the symptoms of back pain and abdominal pain for half a month, which was irregular and irrelevant with diet. The patient did not report fever or appetite disorder. Weight loss was not found. On admission, routine blood test showed a low hemoglobin (HGB) level of 89 g/L (normal, 110-150 g/L) with an elevated lactate dehydrogenase (LDH) level of 508 U/L (normal, 100-300 U/L). The other test results were normal. A palpable lymph node was detected in the left submandibular area, measuring 2.0 cm in diameter, and several flexible and non-tender enlarged lymph nodes were found in the bilateral inguinal regions. Computed tomography (CT) revealed multiple abdominal and retroperitoneal lymph node enlargement. Positron emission computed tomography (PET-CT) showed numerous nodular high metabolic lesions in the bilateral parotids, bilateral submaxillary areas, bilateral supraclavicular and subclavian fossas, bilateral axillaries, left posterior mediastinum, deep surface of the diaphragm, retroperitoneal area, adjacent areas in the bilateral common and external iliac arteries and bilateral inguinal regions. PET-CT also detected high metabolic lesions in the bilateral parotids and enlarged spleen, suggesting lymphoma infiltration of both organs. In addition, the metabolism of bone marrow showed a diffuse slight elevation while bone marrow biopsy reported no abnormal cell invasion. An excision biopsy of the right inguinal lymph nodes was performed, which revealed the presence of an undifferentiated neoplasm. Histopathological and immunohistochemical studies of the specimen revealed infiltration by a non-Hodgkin B cell lymphoma, predominantly of the...
follicular type with characteristics of immunoblastic cells.

Pathological findings

Under light microscope, the normal nodal architecture of the lymph nodes was completely effaced by a large number of homogeneous large lymphocytes, which formed an abnormal shape of the follicles. These follicles lay adjacent to each other with a little interposed lymphoid tissue and a few small lymphocytes coming from the surrounding follicular zones (Fig. 1A, B). The homogeneous large cells possessed prominent oval to indented nuclei with vesicular chromatin and single centrally placed nucleoli. The cytoplasm, moderate in amount or abundant, was basophilic by HE staining. Mitoses were frequently seen (6-7 cell per high power field) (Fig. 1C). In addition, scattered plasma cells and tingible-body macrophages were found within the follicles to produce a starry-sky appearance (Fig. 1D).

The immunophenotypes of the lymphoma cells were CD20+ (Fig. 2A, B), CD10+ (Fig. 2C), CD30+ (Fig. 2D), MUM1+ (Fig. 2E), CD138+ (Fig. 2F), CD38+ (Fig. 2G), Ki-67 (80%) (Fig. 2H), CD3, CD5, CD21, CD45RO, CD68, CD79a, Bcl-2, Bcl-6, Cyclin D1, and PAX-5+. Based on the clinical, morphological and immunophenotypic results, a diagnosis of primary FIBL of the GC origin was made after professional consultation.

DISCUSSION

FL is characterized by follicular structures composed of neoplastic cells. The normal GC of follicles contain mainly small cleaved cells (centrocytes) and large cells (centroblasts) in varying proportions and rarely immunoblasts [9]. B-immunoblasts are precursors of plasma cells and occur commonly in the extrafollicular sites of the lymphoid tissue [10]. The de novo FIBL was first described by Chan et al in 1990 [11], when no definite WHO nomenclature of FIBL was made among FL classification in human. Chan presumed the tumor as
FIBL based on the predominant cell constitution by neoplastic cells. Even by now, FIBL has not been listed as a distinct clinical neoplasm in the WHO lymphoma classification and does not fall into the category of FL.

In the present case, which represents the first case of FIBL reported in China, the majority of tumor cells possessed abundant plasmacytoid cytoplasm, irregular nuclei and large nucleoli. The cytoplasmic features were the most important indication to identify B-immunoblastic lymphoma compared to centroblastic (large noncleaved follicle center cell) lymphoma, although the dividing line between them was not always clear. Immunohistochemically, the FIBL in this case showed a diffuse positive expression of CD10, indicating a possible GC origin of the tumor; the positivity for CD30 and MUM1 was related to B-cell activation. Möller et al reported that CD30 was expressed on a subset of terminally differentiated plasma cells as an activation antigen [7]. MUM1 (multiple myeloma oncogene 1), as a reliable associated marker CD10 usually do not express GC through the node were devoid of mantle zones of follicles. The extensive follicles densely distributed throughout the node were devoid of mantle zones of small lymphocytes. For RFH, the cell polarity existed in the GC with marginal zone lymphomas (MZL), which usually do not express GC-associated marker CD10 [13-14]. As for plasma cells, demonstrated by CD138 [9, 15], they were present mostly in the interfollicular areas in RFH, but not in the intrafollicular regions in FIBL. Based on these conspicuous features, we established the diagnosis of FIBL, which can be interpreted as an entity of neoplastic overgrowth of intrafollicular immunoblasts and possibly as a neoplastic counterpart of FL.

Immunoblastic differentiation is a terminal maturation and accordingly, immunoblastic lymphoma was reported as a diffusely growing neoplasms [5-16-17]. For this reason, FIBL may progress from a follicular to a diffuse architectural pattern and has a greater chance than FL of evolving into DLBCL. FIBL can be more aggressive and is associated with a poorer prognosis than centroblastic lymphoma. On the other hand, along with the immunoblastic, plasmablastic or plasmacytic differentiation and maturation, FIBL might assume a follicular growth pattern rather than the more typical diffuse growth pattern. In addition, bone marrow involvement was common in FL (occurring in about 70% of patients overall) [18], but in our case, abnormal cell invasion was absent in bone marrow biopsy. Because of financial reasons, the patient chose to have Chinese traditional treatment and no progressive symptoms were found in the follow-up for two years. Currently there is no established therapeutic paradigm for this rare disease, and its optimal treatment still awaits further investigation.

**ACKNOWLEDGEMENTS**

We gratefully acknowledge ZHU Meigang, MD, at the Department of Pathology, Nanfang Hospital and Southern Medical University, for pathological consultation.

**REFERENCES**

何选秋1,杨磊1,丁彦青2
南方医科大学1第一临床医学院，2南方医院病理科，广东 广州 510515

摘要: 原发性滤泡性免疫母细胞淋巴瘤（FIBL）是种极少见的淋巴瘤，其免疫表型CD10阳性提示起源于生发中心，而CD138阳性说明伴有浆母/浆细胞分化。为了更好地诊疗此病，本文从临床病理和免疫表型的特点方面报道国内首例女性患者，行PET-CT检查明确全身淋巴结的累及情况，并分别与滤泡性淋巴瘤、反应性滤泡增生作鉴别诊断。FIBL作为滤泡性淋巴瘤的罕见变异型，表现为滤泡内的肿瘤性免疫母细胞过度增生，向弥漫性大B细胞淋巴瘤的转化率略高于滤泡性淋巴瘤，预后较差，应予重视。

关键词: 滤泡性淋巴瘤; 免疫母细胞; 免疫表型分型; PET-CT

收稿日期:2013-02-04
作者简介:何选秋,南方医科大学临床医学八年制,E-mail: lmsh815@163.com
通信作者:杨磊,副教授,E-mail: youth_md@163.com;丁彦青,教授,E-mail: dyq@fimmu.com