Epstein-Barr Virus Associated Lymphoepithelioma-like Carcinoma at the Lesser Curvature of the Upper Gastric Body: A Case Report

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ABSTRACT

Lymphoepithelioma-like gastric carcinoma (LELGC) is a rare neoplasm of the stomach with dense lymphocytic infiltration. More than 80% of LELGCs are positive for the Epstein-Barr virus (EBV). Here, we report a 64-year old Chinese man with swallowing discomfort while eating food. Endoscopy and computed tomography both showed a submucosal lesion at the lesser curvature of the upper gastric body. The first diagnostic impression was a gastrointestinal stromal tumour. Subsequently, the patient received a wedge resection of the stomach. On histopathological examination, the tumour was found to consist of small nests of neoplastic cells within dense lymphocytic infiltration. Additionally, most of the neoplastic cells were positive for cytokeratin and Epstein-Barr virus-encoded RNA (EBER). Subsequently, the diagnosis of LELGC was made. We believe that physicians should be aware of the diagnosis of submucosal gastric lesions, particularly in older male patients.

Keywords: Epstein-Barr virus, Epstein-Barr virus-encoded RNA, lymphoepithelioma-like gastric carcinoma

El Virus de Epstein-Barr Asociado al Carcinoma de Tipo Linfoepitelioma en la Curvatura Menor de la Parte Superior del Cuerpo Gástrico: Reporte de Caso

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RESUMEN

El carcinoma gástrico de tipo linfoepitelioma (CGLE) es una neoplasia rara del estómago con una infiltración linfocítica densa. Más del 80% de los CGLEs son positivos al virus de Epstein-Barr (EBV). Aquí reportamos el caso de un paciente chino de 64 años, que sentía malestar al efectuar la deglución de alimentos. Tanto la endoscopia como la tomografía computarizada mostraron una lesión submucosa en la curvatura menor de la parte superior del cuerpo gástrico. La primera impresión diagnóstica fue de un tumor del estroma gastrointestinal Posteriormente, al paciente se le hizo una resección en cuña del estómago. En el examen histopatológico, se halló que el tumor consistía de pequeños nidos de células neoplásicas dentro de una infiltración linfocítica densa. Además, la mayoría de las células neoplásicas eran positivas a la citoqueratina y al ARN codificado por el virus de Epstein-Barr (EBER). Posteriormente, se realizó el diagnóstico de CGLE. Creemos que los médicos deben tomar conciencia del diagnóstico de las lesiones submucosas gástricas, especialmente en los pacientes mayores hombres.

Palabras claves: Virus de Epstein-Barr, ARN codificado por el virus de Epstein-Barr, carcinoma gástrico de tipo linfoepitelioma

West Indian Med J 2014; 63 (1): 112

INTRODUCTION

Lymphoepithelioma-like gastric carcinoma (LELGC), which was described as poorly differentiated carcinoma with dense lymphocytic infiltration (1), is a rare neoplasm of the stomach. The incidence of this tumour is about 1–4% of all gastric car-

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DOI: 10.7727/wimj.2012.294

cinomas (2). More than 80% of LELGCs are positive for the Epstein-Barr virus (EBV), but the detailed mechanism by which EBV contributes to carcinogenesis is still unknown (2, 3). When the carcinoma invades the submucosa, it can be misdiagnosed as a gastrointestinal stromal tumour (GIST), lymphoma, or carcinoid tumour. Here, we describe a rare case of LELGC at the lesser curvature of the upper gastric body.

CASE REPORT

A 64-year old man came to the clinic on March 13, 2012, presenting with swallowing discomfort while eating food. His medical history was uneventful. Laboratory examinations (*eg* haemoglobin, albumin, alanine aminotransferase levels) and tumour markers (carcinoembryonic antigen, alpha-fetoprotein, carbohydrate antigen 19-9) were within the normal range. Ultrasonic endoscopy revealed a submucosal lesion (approximately 1.47 × 0.54 cm) at the lesser curvature of the upper gastric body with an active ulcer on the mucosal surface (Fig. 1). The diagnostic impression was a gastrointestinal stromal

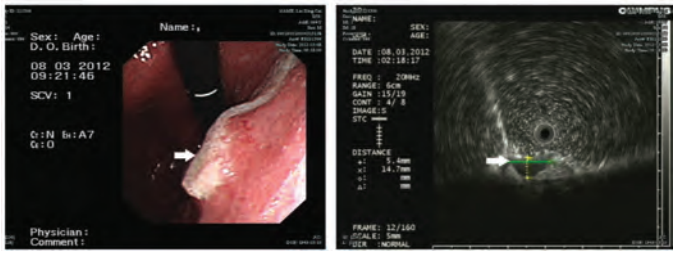

Fig. 1: Ultrasonic endoscopy shows a submucosal lesion with an active ulcer on the mucosal surface (arrow). The lesion is approximately 1.47 × 0.54 cm.

tumour with ulcer formation. Contrast-enhanced computed tomography (CT) showed a 1.6 × 1.1 cm lesion with contrast enhancement at the lesser curvature to the cardia. No evidence of perigastric infiltration, enlarged lymph nodes, or distant metastasis was found on CT (Fig. 2). Wedge resection of the

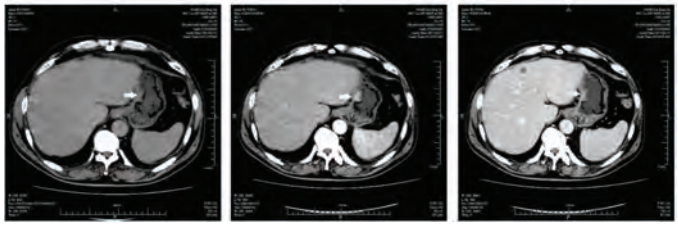

Fig. 2: Abdominal contrast-enhanced computed tomography scan showed a lesion at the lesser curvature near to the cardia (arrow). The lesion was 1.6 × 1.1 cm in size and was apparently enhanced.

stomach was performed to remove the lesion. Macroscopically, the tumour appeared as a 1.8 × 1.6 × 0.6 cm mass with superficial ulceration on the mucosa and a well-delineated margin. The diagnosis of intraoperative frozen section examination was lymphoma. However, on light microscopy, the tumour invaded the submucosa and consisted of nests of neoplastic cells within dense lymphocytic infiltration. The tumour cells were arranged primarily in tubular and oval patterns. Immunohistochemistry of the tumour cells showed positivity for cytokeratin (Fig. 3B). Additionally, the infiltrating lymphocytes were composed predominantly of $CD4^+$ T and $CD8^+$ T cells (Fig. 4). *In situ* hybridization revealed that most of the tumour cells stained positively for EBV-encoded RNA [EBER] (Fig. 3E). The surgical margins were free. Finally, the diagnosis of lymphoepithelioma-like gastric carcinoma was made.

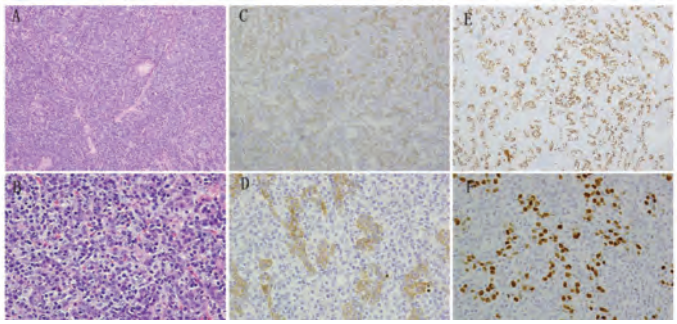

Fig. 3: Histopathological features of the lymphoepithelioma-like gastric carcinoma (LELGC). The tumour consisted of nests of neoplastic cells within a dense lymphocytic infiltration (A: ×100, B: ×400). Immunohistochemistry shows the tumour cells are positive for cytokeratin (C: ×100, D: ×400). *In situ* hybridization, most of the tumour cells stain positively for Epstein-Barr virus encoded RNA (E: ×100, F: ×400).

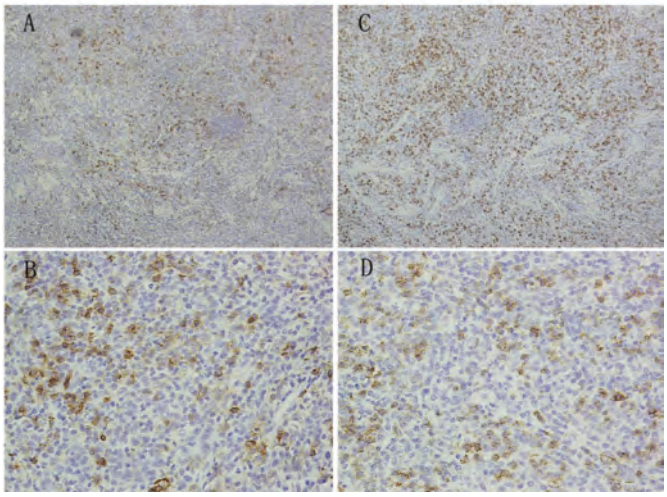

Fig. 4: Immunohistochemistry shows the infiltrating lymphocytes are composed predominantly of $CD4^+$ T cells (A: ×100, B: ×400) and $CD8^+$T cells (C: ×100, D: ×400).

DISCUSSION

Lymphoepithelioma-like carcinoma, which can originate from almost all anatomical sites of the body, shows similar histological characteristics to undifferentiated nasopharyngeal carcinoma. In 1976, Watanabe *et al* first described a gastric carcinoma with lymphoid stroma (4), which was subsequently named lymphoepithelioma-like gastric carcinoma; it is a rare type of gastric carcinoma with an incidence of 1–4% of all gastric carcinomas, and it is considered to display an older male predominance (5).

Lymphoepithelioma-like carcinoma demonstrates special histopathological characteristics that distinguish it from common gastric adenocarcinoma. Macroscopically, the carcinoma is an ulcerating tumour with a distinct borderline. Microscopically, the neoplastic cells, which are arranged in microalveolar or tubular patterns, are surrounded by abundant lymphoid stroma (6). The neoplastic cells are oval or polygonal, with prominent nucleoli and abundant eosinophilic cytoplasm (2). The lymphoid reaction consisted of lymphocytes and plasma cells, and infiltrating lymphocytes are composed predominantly of $CD4^+$ and $CD8^+$ cells (6). However, the detailed mechanism of abundant lymphocytic infiltration remains unclear. The Epstein-Barr virus and micro-satellite instability (MSI) are found to be related to lymphocyte-rich gastric cancers by some authors (7). Over 80% of LELGCs are positive for EBV infection. Interestingly, the neoplastic cells, unlike lymphocytes, uniformly express EBV. The cause may be that EBV infects the gastric epithelial cells through cell fusion between EBV-infected lymphocytes and epithelial cells before neoplastic transformation (2). Lymphocyte-rich gastric cancer correlating with MSI is due to defective repair of DNA replication by mismatched repair genes [hMLH1] (8).

Lymphoepithelioma-like gastric carcinoma has been reported to have a favourable prognosis compared with conventional gastric cancers, with the five-year survival rate being 83% (9). Some authors believe this better prognosis is ascribed to the lymphoid reaction of the body because abundant lymphocyte infiltration may prevent spread of neoplastic cells through the gastric wall to lymph nodes or adjacent tissue (10). Surgical operation is considered to be an important treatment option for LELGC. However, the operative procedure is inconsistent. Most cases are diagnosed as undifferentiated gastric cancers preoperatively, so the patient would receive subtotal or total gastrectomy with lymphadenectomy. For the submucosal lesion, endoscopic submucosal dissection may also be an appropriate choice (11). In the present case, the preoperative diagnosis was a GIST; thus, we performed a wedge resection of the stomach to remove the lesion. Because of the favourable prognosis, we believe that there is no need for reoperation.

In summary, LELGC is a rare gastric neoplasm with favourable prognosis. We believe that physicians should be aware of the diagnosis of submucosal lesions, particularly in older male patients. For imaging experts, understanding the correlations between imaging findings and clinical characteristics is important in the preoperative diagnosis. For oncologists, surgical operation and postoperative treatment need further study.

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