CASE REPORT

Rare synchronous primary large B-cell gastric lymphoma and huge retroperitoneal liposarcoma with inguinal hernia in chronic hepatitis B patient

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ABSTRACT

Multiple primary neoplasms with synchronous or metachronous presentation are rare, although the incidence has recently increased because of several factors. We present the case of a 53-year-old patient with chronic hepatitis B who presented with abdominal mass, mild abdominal pain, and inguinal hernia. Computed tomography imaging demonstrated diffuse thickening of the gastric antral wall, together with a huge heterogeneous abdominal mass with predominant fat attenuation with septa that showed mild enhancement on contrast-enhanced scans. Distal gastrectomy and wide resection of the retroperitoneal mass was performed. Pathology exam led to a diagnosis of diffuse large B-cell gastric lymphoma with retroperitoneal liposarcoma. This is a rare case of a primary gastric lymphoma with another primary (sarcomatous) malignancy occurring synchronously in same patient.

KEY WORDS

Multiple primary neoplasms, primary gastric lymphoma, liposarcoma, synchronous, metachronous

1. INTRODUCTION

Synchronous occurrence of two primary malignancies presenting as lymphoma and sarcoma is rare, although a few cases of secondary malignancy presenting in that fashion have been reported after treatment or in immunosuppression. To our knowledge, the case described here is the first to be reported of synchronous occurrence of primary gastric lymphoma and retroperitoneal liposarcoma in an immunocompetent patient.

2. CASE REPORT

A 53-year-old man was referred to our hospital in February 2008 with a 2-year history of abdominal pain. During the most recent 2 months, his symptoms had been persistent and increasingly severe. He had noticed progressive distension of the abdomen, with swelling in the right inguinal region and scrotum. The patient had been diagnosed with hepatitis B in 1976, which had been treated with the antiviral agent lamivudine for 1 year in 1996 and which was not subsequently followed up.

Physical examination of the abdomen revealed a firm, non-tender mass occupying almost all of the abdomen. The inguinal region demonstrated a complete indirect inguinal hernia with cystic consistency. The markers for chronic hepatitis B virus (HBV) were positive, including hepatitis B surface antigen, anti–hepatitis B e-antibody, and anti–hepatitis B core antibody, with a HBV DNA level of 7.56×10^3 copies per millilitre. Liver function tests and a hematologic profile were within normal limits.

Esophagogastroduodenoscopy demonstrated a deformed antrum, with a deep ulcer (approximately 4 cm, with an irregular margin) at the lesser curvature and a few bleeding points. Histopathology of an endoscopic biopsy specimen of the lesion was inconclusive. Biopsy material was negative for Helicobacter pylori. Computed tomography (CT) imaging of the whole abdomen revealed marked circumferential gastric antral wall thickening, with a lobulated inner surface and a smooth well-defined outer wall [Figure 1(A)]. After intravenous contrast, the thickened wall showed minimal homogeneous enhancement, with preservation of the perigastric fat plane [Figure 1(B)]. Few perigastric lymph nodes were noted. A huge, well-defined heterogeneous abdominal mass measuring 26×12×26 cm with predominant fat attenuation and no calcification occupied the retroperitoneum, extending from the infrapancreatic level to the pelvis. This tumour also had thickened, irregular septa with nodular components whose attenuation approximated that of skeletal muscle [Figure 1(C)]. The mass displaced the bowel loops laterally and superiorly. Post-contrast imaging showed moderate enhancement of the septa of the retroperitoneal mass.
mass measured approximately 28 cm, with complete capsule formation and no invasion to surrounding structures. The tumour had also herniated through the right deep inguinal ring, reaching the scrotum. Gastrectomy specimen showed invasion to the deeper layer and ulcer formation, and on histopathology, a growth pattern of large cells with pleomorphic nuclei suggestive of diffuse large B-cell lymphoma (DLBCL) was observed [Figure 2(A)].

Figure 1 (A) Pre-contrast computed tomography image demonstrates the thickened gastric antral wall and lobulated inner wall with relatively smooth outer surface (arrow). (B) Contrast-enhanced image demonstrates heterogeneous enhancement of the gastric antral wall (arrow). (C) Imaging of lower abdomen shows a huge heterogeneous retroperitoneal mass, with predominant fat attenuation. Multiple septae (black arrow) are seen, which enhanced moderately on contrast-enhanced scan. The mass is seen displacing the bowel laterally. (D) Coronal multiplanar reconstruction image shows the thickened gastric antral wall (black arrow). An area of globular non-adipose tissue (white arrow) is seen within the retroperitoneal mass.

The patient underwent a distal gastrectomy, together with wide resection of the retroperitoneal mass and inguinal hernia repair. The retroperitoneal mass abutted the major vessels (abdominal aorta and inferior vena cava) with preserved fat plane. No retroperitoneal lymphadenopathy or ascites was present. Liver and spleen were characteristically normal. Imaging of the thorax did not show any abnormality.

Posteriorly, the mass abutted the major vessels (abdominal aorta and inferior vena cava) with preserved fat plane. No retroperitoneal lymphadenopathy or ascites was present. Liver and spleen were characteristically normal. Imaging of the thorax did not show any abnormality.
Immunohistochemistry revealed CD20+ [Figure 2(B)], CD10+ [Figure 2(C)], CD5− [Figure 2(D)], and CD79a−, CD3−, and CD43− (not shown). Histopathology of the resected retroperitoneal mass showed variably sized adipocytes in a background of haphazardly arranged spindle-shaped cells [Figure 2(E)]. Immunohistochemistry examination of the resected abdominal mass was positive for vimentin and S100 (not shown). Immunostaining performed at a referral hospital was positive for MDM2 and CDK4.

Postoperatively, the patient was treated with chemotherapy in the form of CHOP (cyclophosphamide–doxorubicin–vincristine sulphate–prednisolone), which led to complete remission. Follow-up investigations ruled out any relapse, and the patient was disease free at the time of writing.

3. DISCUSSION AND CONCLUSIONS

Multiple primary neoplasms constitute approximately 2%–10% of all carcinoma cases reported in the literature. Various factors have been considered for the pathogenesis of multiple primary cancers at anatomically distinct sites. These include carcinogenic substances such as tobacco, alcohol, and dyes; genetic predisposition; immune suppression; various infections; and the sequelae of treatments such as radiotherapy, chemotherapy, or organ transplantation. Multiple primary neoplasm is diagnosed based on rules set out by the International Classification of Diseases for Oncology, which recognizes that the existence of 2 or more primary cancers does not depend on time; that a primary cancer is one that originates in a primary tissue site and that is not an extension, recurrence, or metastasis; and that only 1 tumour is to be recognized as arising in an organ or a pair of organs or a tissue.

The gastrointestinal tract is the most common extranodal site to be involved by non-Hodgkin lymphoma (NHL), accounting for about 4%–20% of all cases and about 30%–45% of all extranodal cases. The stomach is the most common of the gastrointestinal sites to be involved (60%–75%), followed by small bowel, ileum, cecum, and rectum. Gastric lymphoma comprises 3%–5% of all malignant tumours of the stomach. Although the incidence of gastric carcinoma has been markedly declining, the incidence of gastric lymphoma has been increasing. Our patient fulfilled the Dawson criteria for a diagnosis of primary gastric lymphoma. The clinical symptoms for gastric lymphoma are nonspecific, which is reflected in the late diagnosis.

The various radiographic patterns observed in double-contrast upper gastrointestinal studies may indicate ulcer, polypoid mass, thickened fold, mucosal nodularity, or infiltrating lesion, and thus are not conclusive, posing a diagnostic challenge for differentiating other malignant and benign lesions. Pathology confirmation is therefore required. Preservation of gastric distensibility and pliability despite extensive infiltration with gastric fold thickening is a finding more suggestive of lymphoma. At CT imaging, gastric wall thickening has been noted to be much less severe in low-grade lymphoma than in high-grade lymphoma, and abdominal lymphadenopathy is less common in low-grade lymphoma. Transpyloric spread and extension of lymphadenopathy below the renal hilum and presence of bulky lymph nodes are more suggestive of lymphoma than of carcinoma. The various observed patterns of gastric involvement can be segmental or diffuse infiltration and localized polypoid form. Tumour infiltration is usually homogeneous, although areas of low attenuation may be present in larger tumours. Diffuse infiltration (involving more than 50% of the length of the stomach) and segmental infiltration are the most common CT features found in gastric NHL. Our patient showed diffuse gastric wall thickening, with relative preservation of the adjacent fat plane and with no invasion to surrounding structures. This finding of preservation of the fat plane may be suggestive of lymphoma, but it is not specific.

Lymphomas constitute a heterogeneous group of diseases with epidemiologic associations. The causes of the common types remain elusive, although various risk factors such as chronic infection, immunosuppression, environmental radiation exposure, and hereditary factors have been implicated in some types. Lymphomagenesis in chronic infection has been understood to occur primarily by direct viral effects, as evidenced by Epstein–Barr virus in Hodgkin lymphoma and Burkitt lymphoma, or by chronic triggering of the immune system, as seen with the association between H. pylori in gastric mucosa and mucosa-associated lymphoid tissue (MALT) lymphoma, and between hepatitis C virus and splenic and extranodal marginal zone lymphomas. Although H. pylori has been implicated in the development of most MALT lymphomas, the exact mechanism is not fully understood. The suggestion is that a chronic inflammation enhances the probability of malignant transformation through B-cell proliferation in response to H. pylori, mediated by tumour-infiltrating T cells. A similar mechanism and role for H. pylori in the development of DLBCL is still very speculative, although a few studies have shown complete remission with H. pylori eradication therapy alone. Despite our patient’s H. pylori status being negative on biopsy, past infection by H. pylori and its role in the development of DLBCL cannot be fully refuted.

Another important issue to consider here is the chronic HBV infection in the patient. Various studies, including one in a large cohort of patients in Korea, have suggested that people positive for the HBV surface antigen have an increased risk of developing NHL. Similar studies have shown that infection with HBV is linked to the development of B-cell NHL.
**Figure 2** (A) Photomicrograph of the gastrectomy specimen shows a diffuse growth pattern, with predominant large neoplastic cells having pleomorphic nuclei, vesicular chromatin, and irregular nuclear membrane with prominent nucleoli. Right lower corner shows the neoplastic lymphocytes infiltrating between smooth muscle cells. Occasional inflammatory cells are seen. Hematoxylin and eosin stain, 400× magnification. (B) CD20+ staining of cells, consistent with B-cell origin (400×). (C) CD10 immunohistochemical expression in neoplastic cells of diffuse large B-cell lymphomas (400×). (D) Negative staining for CD5 immunohistochemical expression in the neoplastic cells (400×). (E) Photomicrograph of the retroperitoneal mass shows variable-sized adipocytes in the background of haphazardly arranged spindle-shaped cells. Occasional lipoblasts with vacuolations are seen. At the lower left corner, a lipoblast shows multinucleation with scalloped nuclear margins. Hematoxylin and eosin stain, 200×.)
We can thus suggest a role for HBV infection in the development of gastric lymphoma in our patient. Although many immunosuppressive drugs used for the various complications related to HBV can predispose to certain types of cancer, no such role is evident in our patient, who received only the antiviral agent lamivudine.

The DLBCLs are a heterogeneous group of tumours that are clinically, histologically, immunophenotypically, cytogenerically, and molecularly highly variable. They are classified into 3 subgroups—germinal-centre B-cell-like, activated B-cell-like, and primary mediastinal DLBCL—according to the pattern of gene expression, with each having a different prognosis. The most commonly seen translocations are t(14;18)(q32;q21) with BCL2 rearrangement, t(3;14)(p27;q32) with BCL6 rearrangement, and t(8;14)(q24;q32) with MYC rearrangements. The DLBCLs express B-cell–associated antigens (CD19, CD20, CD22, and CD79a). Variability has been observed in CD45, CD5, and CD10 expression; CD10 expression in particular has been noted as a prognostic indicator.16

Retroperitoneal sarcomas are relatively rare tumours, accounting for approximately 12% of all soft-tissue sarcomas.17 Retroperitoneal liposarcoma is an uncommon but highly heterogeneous malignant tumour, with, in the high-grade or poorly differentiated type, aggressive potential for recurrence and metastasis.18 Most patients present with an abdominal mass, and in almost half, vague abdominal pain may be the only presentation. As in our case, the location of the tumour may allow it to attain a considerable size before diagnosis, because of almost unrestricted growth and mobility of the anterior infra-abdominal organs.19 Correlation of imaging findings with histologic subtype has been attempted, with the CT patterns varying depending on the amount and distribution of adipose and non-adipose tissue in the tumour.

Differentiation by imaging techniques of well-differentiated and myxoid liposarcomas from the round cell and pleomorphic types has great significance for therapeutic approach in addition to marked prognostic value. In our patient, radiologic features suggested a rather indolent variant. Characteristic features that help to distinguish well-differentiated liposarcoma from other lesions such as lipoma include the presence of thickened septa, nodular or globular areas of non-adipose tissue within the lesion, associated non-adipose masses, and a total amount of non-adipose tissue exceeding 25% of the lesion.20 The other 3 histologic subtypes generally contain less than 25% fat, with some demonstrating no fat at all on radiologic examination. Compared with other subtypes, myxoid liposarcoma is usually well-defined and homogeneous, occasionally appearing as cystic-like masses. Pleomorphic and round liposarcomas often do not contain fat; they are usually heterogeneous and indistinguishable from one another and (when they contain no fat) from other malignant soft-tissue lesions.21

Well-differentiated liposarcomas are highly variable on immunohistochemistry, with markers being nonspecific. Cyogenetically, most well-differentiated liposarcomas are characterized by supernumerary ring and giant marker chromosomes, with amplification of the murine double-minute type 2 (MDM2) gene, derived, in most cases, from the 12q13–15 region, and of cyclin-dependent kinase 4 (CDK4) on fluorescent in situ hybridization and quantitative polymerase chain reaction.22

Liposarcoma and NHL may be related to unidentified familial diseases, or spurious associations may be present.23 In our patient, development of DLBCL suggests a potential role for HBV. However, a link to the same causative factor for development of liposarcoma cannot be established. Further studies into whether there is a definite association, common risk factors, or just chance occurrence are needed. Multiple primary neoplasms pose diagnostic and therapeutic challenges because of increased incidences of complications and development of subsequent malignant neoplasms, which may be therapy-related, in long-term survivors.24

CONFLICT OF INTEREST DISCLOSURES

The authors declare that they have no financial conflicts of interest.

REFERENCES


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