CASE REPORT

A Case of Synchronous Diffuse Large B Cell Lymphoma and Gastrointestinal Stromal Tumour

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ABSTRACT

The occurrence of gastrointestinal stromal tumours (GIST) synchronous with lymphoma is rare. The diagnosis may be overlooked if the lesion is mistaken for the same primary pathology. We report the case of a 66-year-old man who presented with a swelling of the left parotid gland for six months. Histopathology of the parotid gland revealed diffuse large B-cell lymphoma (DLBCL), activated B-cell subtype. Staging positron emission tomography with fluorodeoxyglucose (FDG) and computed tomography (PET-CT) revealed a hypermetabolic left intraparotid lesion, a hypermetabolic mass at the lesser curvature of the stomach with enlarged cervical and bilateral inguinal nodes. Given the persistent FDG avidity on interim PET/CT, fine needle aspiration cytology of the gastric mass with endoscopic ultrasound was performed, confirming GIST. In summary, it is important to recognise patterns of discordant response to treatment leading to re-evaluation of the diagnosis. Early diagnosis of both tumours is essential for immediate treatment to improve prognosis. It would be interesting to clarify whether there is a common mechanism between the co-occurrence of GIST and lymphoma. *Malaysian Journal of Medicine and Health Sciences (*2024) 20(4): 389-391. doi:10.47836/mjmhs20.4.47

Keywords: Synchronous, Lymphoma, Gastrointestinal stromal tumour, Discordant, Co-occurence

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INTRODUCTION

A systematic review and population-based study reported that the incidence of patients with GIST having a second malignancy is 4.5-33%, which may be either synchronous or metachronous lesions [1, 2]. Nevertheless, little is known about the exact mechanism or pathophysiology leading to this occurrence. The incidence of non-Hodgkin's lymphoma (NHL) was significantly increased in patients with GIST, which could be detected before, during or after the diagnosis of GIST [1].

GISTs are the most common mesenchymal tumours that occur throughout the gastrointestinal tract, with the stomach being the most common site. They have positive immunostaining for DOG1 and CD117 [3]. For resectable GIST without metastasis, treatment consists of complete resection without tumour rupture and achieving negative margins, while cases that are not resectable benefit from imatinib as an adjuvant or treatment [3]. Although it is sometimes impossible to biopsy all lesions at initial presentation, this is worth considering so that synchronous or metachronous lesions are not missed. Early diagnosis of both tumours is essential for prompt treatment.

CASE REPORT

A 66-year-old Chinese man with type 2 diabetes mellitus and hypertension presented with a swelling of the left parotid gland that had persisted for six months and had become progressively larger and harder. Examination revealed a hard mass in the area of the parotid gland above the angle of the mandible. Initial computed tomography (CT) of the neck showed multiple metastatic nodal lesions over the left intraparotid, subparotid and bilateral cervical lymphadenopathy. Histopathological examination (HPE) of the left cervical lymph node revealed sheets and nests of malignant cells exhibiting moderate to marked nuclear polymorphism with enlarged vesicular nuclei, prominent nucleoli and moderate to abundant cytoplasm. The malignant cells were strongly

positive for CD45, CD20, CD30 and MUM1, with a focal expression of p63. They were negative for panCK, CK7, CD10, BCL6, CD3 and CD68 with Ki67 proliferative index of 90%. These findings were consistent with diffuse large B-cell lymphoma (DLBCL), activated B-cell-like (ABC) subtype (Figure 1). His peripheral blood film showed no leukoerythroblastic picture or abnormal lymphoid cells. Bone marrow aspiration revealed 1% abnormal lymphoid cells. Cytogenetic examination revealed male chromosomes and no evidence of clonal abnormality in any of the cells analysed.

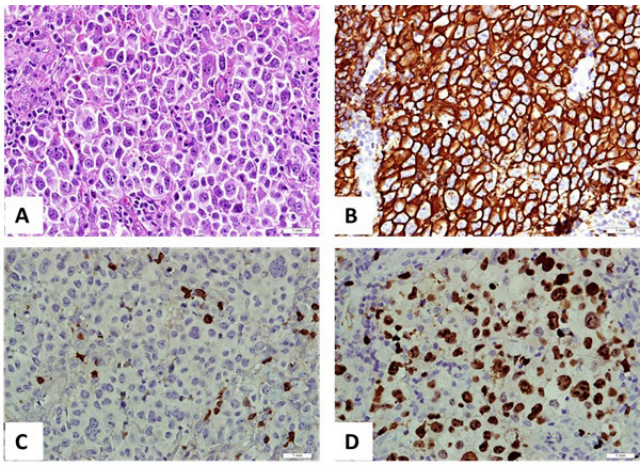

Figure 1 (A) Photomicrograph of left cervical lymph node biopsy showing sheets of malignant large lymphoid cells displaying enlarged pleomorphic nuclei with prominent nucleoli (haematoxylin and eosin, 40x magnification); (B) Immunochemistry staining for CD20 showing positivity (40x magnification); (C) immunochemistry staining negative for CD3 (40x magnification); (D) high Ki67 proliferative index (40x magnification)

18F-fluorodeoxyglucose positron-emission tomography with computed tomography (PET-CT) showed a hypermetabolic left intraparotid lesion, a hypermetabolic mass at the lesser curvature of the stomach, likely a gastrohepatic node, with enlarged cervical and bilateral inguinal nodes. (Figure 2A). Therefore, he had stage IIIe DLBCL, ABC subtype, with an International Prognostic Index score of 4. He underwent three cycles of immunochemotherapy consisting of rituximab, cyclophosphamide, vincristine, and doxorubicin given intravenously and oral prednisolone (R-CHOP). After three cycles of R-CHOP, the interim PET-CT showed a marked reduction in the size and metabolic activity of all cervical nodes, with all nodes being PET-negative, except for a few left cervical lymph nodes with Deauville 3-4. However, there was increased metabolic activity of the mass on the lesser curvature of the stomach, which remained similar in size (Deauville 4) (Figure 2B).

An oesophagogastroduodenoscopy (OGDS) was performed, which showed an external compression in the direction of the small curvature of the stomach. Endoscopic ultrasonography (EUS)-guided fine needle aspiration (FNA) cytology was performed which revealed a 5x4 cm lesion outside the lesser curvature. Cytological examination of the mass revealed a gastrointestinal

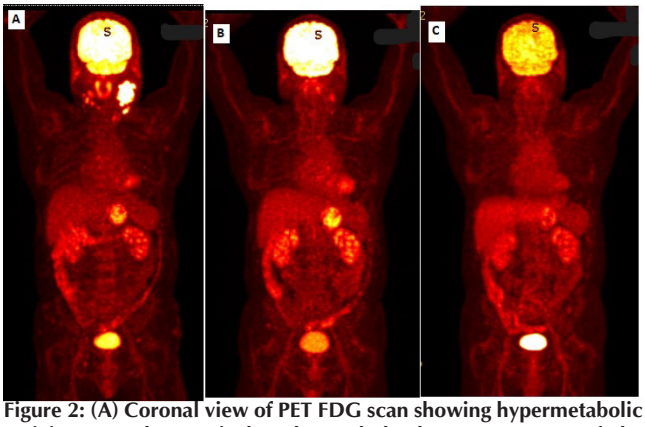

Figure 2: (A) Coronal view of PET FDG scan showing hypermetabolic activity over the cervical nodes and the lesser curvature of the stomach at the time of diagnosis; (B) reduction of metabolic activity and size of cervical lymph nodes with increased metabolic activity over the lesser curvature of the stomach and similar in size after three cycles of R-CHOP; (C) Complete metabolic response over all cervical lymph nodes with similar activity over the lesser curvature after six cycles of R-CHOP

stromal tumour (GIST) (Figure 3). At a multidisciplinary team meeting, it was decided to complete six cycles of R-CHOP followed by surgical resection of the GIST.

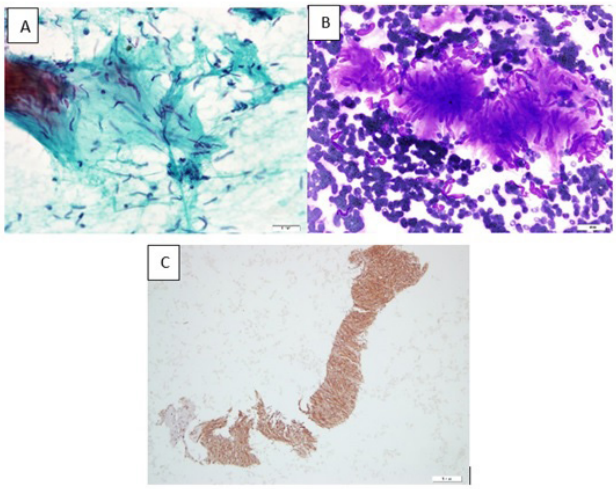

Figure 3: Fine needle aspiration cytology of tumour at lesser curvature using (A) Papanicolaou smear (pap), 40x magnification; and (B) May-Grunwald-Giemsa (MGG) stain, 40 x magnification showing moderate cellularity with the presence of multiple clusters of spindle cells and singly distributed bare nuclei. The cells exhibit spindle to oval wispy nuclei, smooth nuclear membrane, and fine chromatin pattern with inconspicuous nucleoli. The cytoplasm is elongated with indistinct cytoplasmic membrane. (C) Immunohistochemistry study for CD 117, 10x magnification, showing positive staining

His end-of-treatment response evaluation using PET-CT after six cycles of R-CHOP treatment showed complete metabolic response of all cervical nodes; with the lesion over the lesser curvature of the stomach remained the same (Figure 2C). Four months after the diagnosis of GIST, he underwent a partial gastrectomy to resect the tumour at the lesser curvature. The cut sections showed a submucosal mass of 55mm x 50mm x 45mm with variegated surface. Immunohistochemical staining of the tumour showed positivity for CD117, CD34, DOG1 and SMA (focal) and negativity for S100 and desmin.

Therefore, the TNM staging was pT3 N0. He is currently well, and the latest CT of the abdomen did not show any tumour recurrence.

DISCUSSION

In our case, GIST was diagnosed incidentally after the persistent lesion was detected at the interim PET-CT following three cycles of R-CHOP immunochemotherapy. The International Association of Cancer Registries and the International Agency for Research on Cancer (IACR/IARC) defined synchronous multiple primary malignancies as two or more primary malignancies diagnosed within six months [4]. In our case, differential diagnoses of the FDG-avid lesion at the lesser curvature of the stomach include gastric carcinoma, lymphoma, carcinoid tumour and GIST. Therefore, a tissue biopsy or at least a sample for cytological examination is crucial to support the diagnosis. It is often difficult to obtain a histological diagnosis of a GIST compared to a gastric carcinoma by endoscopic biopsy because the mucosa covering a GIST appears normal [3].

In a population-based study by Murphy et al., NHL is one of the malignancies with a significantly increased incidence both before and after diagnosis of GIST [1]. Although there are few published cases of NHL and GIST, it is not known where the association comes from, whether it is coincidental or whether there is a common aetiological factor, such as genetic factors, mutations or molecular pathways, and what the prognosis of this association is. The increased incidence of NHL and GIST may be due to closer surveillance or monitoring of the NHL itself by imaging studies during interim and final stages of treatment.

The standard of care treatment for DLBCL is R-CHOP immunochemotherapy, which consists of rituximab, cyclophosphamide, vincristine and doxorubicin administered intravenously, together with oral prednisolone (R-CHOP), with a complete response rate of up to 80% [5]. The presence of lesions with inconsistent response to treatment warrants re-evaluation of the site. EUS is the safest and most useful modality to differentiate subepithelial lesions suspected to be GIST and appearing as hypoechoic solid masses from other lesions such as lipomas, cysts, varices and extra-gastrointestinal compression [3]. EUS-guided FNA is currently an established method of tissue sampling of subepithelial lesions for diagnostic purposes [3]. The decision to defer treatment for GIST until completion of chemoimmunotherapy was primarily due to the fact that GIST did not cause any obstructive or compressive symptoms in our patient with the absence of metastatic spread and the DLBCL was at stage IIIe. Surgical resection is the standard treatment of a GIST without metastasis, as illustrated in our case, and it is essential to prevent tumour rupture with negative margins. A GIST with metastasis is usually treated by tyrosine kinase inhibitors, such as imatinib [3].

CONCLUSION

We report here a case of synchronous stage IIIe DLBCL and stomach GIST during the treatment of DLBCL that exhibits a unique and interesting clinical course. It is of utmost importance to recognise patterns of inconsistent response to treatment that lead to a re-evaluation of the diagnosis. Early diagnosis of NHL, especially DLBCL and GIST, is essential for prompt and timely treatment to improve the prognosis of both malignancies. Future studies elucidating the common mechanism between the co-occurrence of GIST and other malignancies could be conducted to fill the knowledge gap.

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