Rare disease

Primary gastric Hodgkin's lymphoma: favourable outcome following multi-agent chemotherapy without surgical intervention

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Summary

The authors report the case of a 51-year-old man who presented with left-sided abdominal pain and weight loss associated with drenching night sweats. Preliminary blood tests yielded no specific cause for his symptoms, but abdominal ultrasound revealed multiple hepatic lesions and peripancreatic lymphadenopathy. Further imaging, including positron emission tomography (PET)/CT, revealed fludeoxyglucose 18F (FDG) avid uptake within lymphadenopathy above and below the diaphragm and also noted gastric thickening. Diagnosis was established with gastric biopsy and revealed gastric Hodgkin's lymphoma. He was started on and tolerated multi-agent chemotherapy. Repeated PET/CT and gastric biopsy showed complete metabolic and pathologic response to treatment.

BACKGROUND

Hodgkin's lymphoma (HL) predominantly occurs within lymph nodes but can also affect lymphoid tissue such as spleen, Waldeyer's ring and liver, and, in lesser degrees, the lymphatic and reticular framework of almost any organ of the body.¹ Primary gastric lymphomas (PGL) account for less than 5% of all gastric malignancies² and is the most common type of extra-nodal lymphoma, representing approximately 70% of all primary gastrointestinal lymphomas with the overwhelming majority of these being non-Hodgkin's lymphoma.³ Primary involvement of extra-nodal sites, including the gastrointestinal tract, is exceedingly rare with HL and only a few isolated case reports are to be found in the literature usually with systemic involvement.^{3, 4}

We report the case of a 56-year-old Caucasian man of Irish origin who presented with histopathological and radiological evidence of primary gastric Hodgkin's lymphoma (PGHL).

CASE PRESENTATION

A Caucasian man presented at 51 years of age with a 3-month history of left upper quadrant abdominal pain associated with nausea, loss of appetite and weight loss of 25 kg (approximately 30% of his body weight). He also had drenching night sweats but denied itching or other significant upper gastrointestinal symptoms. He denied any significant past medical illnesses. He gave a smoking history of 30 packs per year but had abstained for 6 weeks prior to his presentation and admitted to minimal alcohol usage.

On clinical examination, he was a pleasant and co-operative gentleman with an Eastern Cooperative Oncology

Group (ECOG) performance status of 1 with evidence of lymphadenopathy in his left supraclavicular fossa (SCF) and a mass in his epigastrium. His liver and spleen were not clinically enlarged. His preliminary and follow-up blood tests are shown below in table 1.

Abdominal ultrasound revealed multiple liver lesions, suggestive of metastases, and peripancreatic lymphadenopathy. CT imaging of the abdomen and pelvis revealed extensive peripancreatic lymphadenopathy extending down the mesentery, multiple hepatic lesions consistent with metastases up to 1.3 cm and marked thickening of the gastric antrum. Positron emission tomography (PET)/CT revealed fludeoxyglucose 18F (FDG) avid areas in the stomach, liver, abdominal para-aortic, mediastinal and bilateral cervical lymphadenopathy (shown in figure 1).

Upper gastrointestinal endoscopy was undertaken and noted antral thickening with a large malignant looking ulcer. Gastric biopsies were undertaken and revealed a classical HL that was CD15, CD30 positive, with focal positivity for fascin. Second opinion at another tertiary centre was undertaken and confirmed the findings. A further excision biopsy of the left SCF lymph node was performed and also confirmed HL, nodular sclerosing subtype that was CD15, CD30 and fascin positive, and morphologically resembled the gastric biopsy (shown in figure 2).

Bone marrow and trephine was performed and revealed normal cellular bone marrow with trilinear haematopoiesis and no lymphoid or other malignant infiltration seen.

TREATMENT

With a stage IV_{BE} PGHL, and given his good ECOG performance status, he was started on standard chemotherapy after discussion of the benefits and side effects;

Figure 1 Baseline positron emission tomography/CT scan.

Figure 2 Restaging positron emission tomography/CT.

eight cycles of chemotherapy (five cycles of adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) initially, then three cycles of EVAP due to toxicities encountered, which included etoposide, vinblastine, doxorubicin and prednisolone) were delivered every 4 weeks. There were no significant adverse events during the prescribed course other than pulmonary toxicity and neurotoxicity. His first cycle of chemotherapy was given as an inpatient, and the remainder were as an outpatient with no need for delays, blood product support or dose reductions. His mid assessment scan following four cycles of chemotherapy showed a favourable response and so he was allowed to complete his prescribed eight cycles.

OUTCOME AND FOLLOW-UP

On completion of his chemotherapy, his presenting symptoms have completely resolved and he underwent repeat upper gastrointestinal endoscopy, which revealed resolution of his previously noted gastric thickening and large ulcer. Random biopsies were taken and were all negative for malignancy. He also underwent restaging PET/CT scan, which revealed no FDG-avid areas, suggesting radiological resolution of his disease and a complete metabolic response to treatment (shown in figure 2).

He remains on regular follow-up in the Medical Oncology clinic and undergoes annual upper gastrointestinal endoscopies. Four years later, he continues in clinical remission.

Table 1 Summary of blood tests performed

Blood tests (fasting morning samples)	Normal range	Pre-treatment	Post-treatment (6 months)	Post-treatment (48 months)
Full blood count		All normal	All normal	All normal
Urea and electrolytes		All normal	All normal	All normal
Liver function tests		All normal	All normal	All normal
Erythrocyte sedimentation	5–15mm/h	91 mm/h	23 mm/h	12 mm/h
Lactate dehydrogenase	98–192 IU/l	170 IU/l	172 IU/l	168 IU/l
Hepatitis B and C serology		All negative	Not repeated	Not repeated
Cytomegalovirus serology		Negative	Not repeated	Not repeated
Epstein–Barr virus high avidity IgG		Positive	Not repeated	Not repeated
Varicella zoster virus IgG		Positive	Not repeated	Not repeated
HIV 1 + 2 serology		Negative	Not repeated	Not repeated

DISCUSSION

Gastric infiltration with malignancy is a relatively commonly encountered scenario observed in clinical practice with gastric adenocarcinoma (90% of cases) and PGL (less than 5% of cases and usually of the non-Hodgkin's variety) being the more prevalent histological considerations; however, PGHL remains a rare clinical entity, prior to confirmation by histology and immunohistochemistry, and is reported as being less than 1% of all PGLs.^{5–7} The demographic profile for patients with PGHL with mediastinal involvement in the literature shows a female preponderance and tends to occur in older patients; the median age listed in pooled data in the literature ranges from 27–50 years of age.⁸ Our case was a man presenting at 51 years of age with mediastinal involvement, which is not completely in keeping with the limited information available in the literature.

The presenting features for patients with PGHL may be very non-specific in nature.⁹ An abdominal mass was appreciated on clinical examination in 20% of cases in combined series and this was often associated with systemic symptoms such as fever.⁷ However, the most common clinical presentation finding, observed in 80% of cases in combined series, was inguinal, femoral or superficial iliac lymphadenopathy.⁷ Patients with PGHL may also present with involvement of the spleen, through either splenic rupture, abscess formation or asymptomatic splenomegaly; biochemical and haematological of haemolytic anaemia or immune thrombocytopaenia may also be seen rarely but can, however, serve as a 'penny-dropping' feature in patients with abnormal clinical, radiographic and endoscopic findings when a diagnosis of PGHL might be considered as these findings are linked to the activity of HL.⁸

Establishing this rare diagnosis, even with a good degree of clinical suspicion, is dependent upon confirmation by histological evaluation given the low incidence of this disease. Specialised review is always recommended, as was sought for this case, to reduce the likelihood for misinterpretation and, ultimately, under diagnosis. The major histological pattern seen in patients with HL is the detection of Reed–Steinberg cells by light microscopy, and by extension the same for diagnosing PGHL, and with a lower incidence of nodular sclerosing subtype, as compared to supradiaphragmatic HL, and more lymphocyte-predominant subtype seen.⁸ However, immunohistological assessment helps to clarify cases, which might not be overtly obvious initially, with the identification of CD15 and CD30 positive cells as seen in this case.¹⁰ For our patient,

his PGHL was of the nodular sclerosing subtype and was also CD15 and CD30 positive.

Given the low incidence of PGHL, upper endoscopic features are not helpful, as they are non-specific in nature, with observed findings such ulcerated and elevated lesions, with or without mucosal thickening.⁹ These are not distinct to PGHL, but should serve to raise suspicion of potential malignancy and a biopsy should be taken for evaluation. CT imaging is the most widely used means of evaluating malignancy and, as such, can play a vital role in potentially detecting PGHL; the radiological patterns seem to follow the gross pathological finding, where gastric wall thickening with smooth lobulated outer borders are noted.¹¹ The sensitivity and specificity of using PET/CT imaging in the evaluation of nodal and extranodal lymphomas is well-established;¹² the down side of the use of this modality, especially in our case for the investigation of PGHL, is that there is no statistically proven data in the literature on the evaluation of the treatment response in patients with lymphoma with gastrointestinal involvement.¹² CT imaging in our patient did elucidate abnormality within the gastric bed, as did repeated PET/CT imaging, which had shown a metabolic improvement with treatment; this was validated only with the reports of the repeat gastric biopsies that revealed no evidence of residual disease.

Treatment of most lymphoid malignancies involves the appropriate sequencing of radiotherapy and chemotherapy. However, there is no clear guidance for the management of PGHL as its prognosis is not fully understood. Ideally, potential surgical resection is the most suitable option to ensure complete removal of the malignancy, but for our patient there was also widespread nodal disease above and below his diaphragm and other poor prognostic features, including being older than 50 years and an elevated

Learning points

- ▶ The patient had clinical, radiological and histological features of PGHL.
- ▶ He responded favourably to systemic chemotherapy, with biochemical, radiological and histological regression of his disease without obvious ill effect and remains in continued remission 48 months later.
- ▶ Hopefully this case can offer further information on this rare condition and can enhance the information presently available in the literature.

erythrocyte sedimentation rate, so we elected to only offer standard multiagent chemotherapy for advanced stage HL.¹³ Most of the cases highlighted within the literature had undergone total or partial gastrectomy as part of their treatment plan and had, consequently, not required chemotherapy as the resection had been complete and there was no clear role for adjuvant treatment for PGHL.

Competing interests None.

Patient consent Not obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Quintyne KI, Mulcahy E, Wallis F, Wilson L, Gupta RK. Primary gastric Hodgkin's lymphoma: favourable outcome following multi-agent chemotherapy without surgical intervention. *BMJ Case Reports* 2011;**10**.1136/bcr.11.2010.3476, date of publication

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