CASE REPORT

Lymphomatoid granulomatosis with pulmonary and gastrointestinal involvement

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SUMMARY

We present a rare case of grade II lymphomatoid granulomatosis (LYG) with pulmonary and gastrointestinal involvement. LYG is considered an Epstein-Barr virus-driven lymphoproliferative disorder that often presents with multiple nodular lesions in the lungs and sometimes involvement of skin and the central nervous system. Although the aetiology is unknown, it is associated with the use of immunosuppressives. Involvement of other organ systems is very rare. We successfully treated our patients with 6 cycles of R-CHOP and autologous stem cell transplantation with a major response at 20 months follow-up.

BACKGROUND

Lymphomatoid granulomatosis (LYG) is a rare Epstein-Barr virus (EBV)-driven lymphoproliferative disorder that often presents with multiple nodular lesions in the lungs. Sometimes, skin and the central nervous system are also affected by the disease.^{1–9} Involvement of other organ systems is extremely rare. We present a case of a patient with pulmonary and gastrointestinal involvement of LYG.

CASE PRESENTATION

A Caucasian female aged 66 years with a history of chronic obstructive lung disease and Crohn's disease (CD) presented with a cough, fever, 6 kg weight loss and night sweats. She used mercaptopurine 25 mg/day since 2012 for her CD. Her pulmonary function test showed a mild obstruction

Figure 2 Histopathological slide showing necrosis (large circle) and lymphocytic infiltration with atypical and enlarged cells (small circles).

and she had a normal high-resolution CT 3 months before presentation.

Physical examination and laboratory studies (including complete blood count, metabolic panels, immunological markers and immunoglobulins) showed no abnormalities. A new chest X-ray showed unilateral nodular lesions (figure 1). Chest CT showed multiple nodules in the right lower lobe of various sizes with possible central necrosis (figure 2). No intrabronchial abnormalities were seen at bronchoscopy and all cultures were sterile.

Histopathological slides from transthoracic biopsies showed areas of necrosis with infiltration by CD3-positive T-lymphocytes and CD20-positive and EBV-positive B-lymphocytes (figure 3). The EBV titre in blood was 1.9×10^4 . LYG was diagnosed and was, because of the level of B-cell

Figure 1 (A) Chest X-ray with multiple nodular lesions in the right lung. (B) Chest CT showed multiple nodules in the right lower lobe, various sizes and with the suggestion of central necrosis.

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Figure 3 (A) CD3-positive T-cell infiltration, (B) CD20-positive B cells and (C) Epstein-Barr virus-positive EBER staining.

infiltration, classified as grade II disease.^{10 11} The mercaptopurine was discontinued with follow-up of the lesions ('watchful waiting'). Her CD remained stable.

Four weeks later, she presented with a collapse after haematemesis. Her haemoglobin level dropped from 8.7 to 5.7 mmol/L. Gastroscopy showed an ulcerated lesion in the proximal stomach (figure 4). Coiling by the intervention radiologist stopped the bleeding. Histopathological evaluation showed LYG grade II, similar to the lung, present in the gastric ulcer. Because of progression of the disease outside the lung with a bleeding LYG lesion in the stomach, treatment was started.

TREATMENT

Before initiating treatment, a PET scan was performed that showed no other involvement apart from the lung and stomach. Bone marrow investigation showed no abnormalities. She was treated with six cycles of R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone) every 3 weeks according to standard non-Hodgkin protocol. The lesions of the lung decreased in size and control gastroscopy showed disappearance of the gastric lesion. After two cycles, EBV-PCR in the blood became negative. After six cycles of R-CHOP, it was decided to treat her with an autologous stem cell transplantation (ASCT) after BEAM-induction (carmustine, etoposide, Ara-C and melphalan) chemotherapy, because of worsening of her prognosis due to other (extrapulmonary) lesions.

OUTCOME AND FOLLOW-UP

The R-CHOP treatment and ASCT resulted in a major response with regression of the disease at 20 months follow-up.

Figure 4 Bleeding lymphomatoid granulomatosis lesion in the stomach.

DISCUSSION

We present a rare case of grade II LYG with involvement of the lung and the stomach. Apart from lung involvement, which is almost always present in LYG,³ skin and the central nervous system are often affected.^{1–8} Gastrointestinal involvement is only found in a very limited number of cases.^{12 13} LYG often presents between the fourth and sixth decade and is seen more often in men than in women.¹⁴

LYG, a rare EBV-driven lymphoproliferative disease, was first described by Liebow *et al* in 1972.⁹ Currently, it is classified by the WHO as a B-cell proliferation of uncertain malignant potential.^{10 15} An abnormal response to an EBV infection in an immunodeficient state results in LYG rather than clearing of the virus.¹⁶ LYG has been reported in patients using various immunosuppressive drugs such as azathioprine and methotrexate.^{17–19} Infiltrative nodular lesions consisting of abnormal cells accumulate in the affected organs. Subsequently, a T-cell response results in destruction of blood vessels and tissue damage.¹⁴ The differential diagnosis includes other EBV-positive lymphomas, necrotising vasculitides (like granulomatosis with polyangiitis and eosinophilic granulomatosis with polyangiitis), sarcoidosis and Mycobacterial and fungal infections. In contrast to, for example, EBV-related post-transplantation lymphoma, LYG is characterised by the triad; necrosis, T-lymphocytes and various degree of EBV-positive B-cell lymphocyte infiltration. LYG is divided into three grades that are based on an increasing proportion of enlarged atypical EBV-positive B cells and necrosis.^{10 11} It is important to distinguish grade III from grades I and II since grade III lesions are targeted therapeutically like diffuse large B-cell malignancies, while in grade I and II disease, a policy of discontinuations of immunosuppressive medications with follow-up of the lesions is indicated.^{10 15}

During the entire course of the disease, our patient had a grade II LYG. Initially, only the mercaptopurine was stopped, with no flare-up of her CD. However, because of the potential life-threatening gastrointestinal bleeding, it was decided to treat

Learning points

- ▶ Lymphomatoid granulomatosis (LYG) is an Epstein-Barr virus-driven lymphoproliferative disease that can affect multiple organs including the gastrointestinal tract.
- ▶ Complications of organ involvement, such as gastrointestinal bleeding, can be an indication to treat LYG according to lymphoma protocols.
- ▶ R-CHOP and autologous stem cell transplantation can be an effective treatment for LYG.

her as an aggressive lymphoma with R-CHOP and stem cell transplantation. To the best of our knowledge, this is the first case presented in the literature with pulmonary and intestinal involvement of LYG that was treated because of gastrointestinal bleeding. Successful treatment using R-CHOP in LYG is reported anecdotally, but no progression-free survival data are available.²⁰ Our patient showed a major response to R-CHOP treatment followed with ASCT with regression of the disease at 20 months follow-up.

Contributors JHK is responsible for writing the paper and literature study. HCTvZ is responsible for treatment patient, review paper and literature study. AJPvT is responsible for treatment patient and review paper. AR is responsible for treatment patient, review paper and guidance of process.

Competing interests None declared.

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