CASE REPORT

Peripheral T-cell lymphoma in a patient with Crohn's disease

Srilakshmi Sudha Kollepara,¹ Mohammad Muhsin Chisti,^{2,3} Seerin Viviane Shatavi,⁴ Ishmael A Jaiyesimi⁴

¹Department of Internal Medicine, DMC Sinai Grace Hospital, Detroit, Michigan, USA

²Department of Internal Medicine, Hematology and Oncology, Oakland University William Beaumont School of Medicine, Royal Oak, Michigan, USA

³Department of Hematology and Oncology, Oakland University William Beaumont School of Medicine, Livonia, Michigan, USA

⁴Department of Hematology and Oncology, William Beaumont Hospital, Royal Oak, Michigan, USA

Correspondence to

Dr Mohammad Muhsin Chisti, drmohsinchisti@yahoo.com

SUMMARY

A 46-year-old man with a long-standing history of Crohn's disease who was treated with multiple therapies over a period of 9 years presented with oral lesions which on biopsy demonstrated peripheral T-cell lymphoma. Initially, the development of T-cell lymphoma was presumed to be secondary to prolonged immunosuppression but it did not respond to withholding immunosuppressive therapy. On treatment with CHOP (cyclophosphamide, hydroxydaunorubicin, oncovin and prednisone) chemotherapy, complete remission was achieved. Although development of malignancies in the immune-suppressed patient with Crohn's disease has been previously described but we present a rare case of T-cell lymphoma in a similar patient, which has not been reported before.

BACKGROUND

With the advent of novel immunosuppressive agents, balancing the risk–benefit ratio in the treatment of inflammatory disease remains a constant concern. Earlier studies have suggested an increase in the risk of malignancies especially lymphomas in patients with inflammatory disease.¹ However, this relationship remains controversial as it was not demonstrated in other population studies.² Furthermore, other studies have suggested an increased risk of lymphoma in patients treated with immunosuppressive agents.³ Previous literature predominantly in patients with transplant taking immunosuppressive agents demonstrated that the incidence of T-cell lymphoma is extremely rare.⁴ However, the occurrence of T-cell lymphoma limited to gastrointestinal tract in patients with inflammatory bowel disease treated with immunosuppressive agents has not been described before. We present a case of T-cell lymphoma in a patient with Crohn's disease treated with immunosuppression.

CASE PRESENTATION

A 46-year-old man who was diagnosed with Crohn's disease 9 years ago presented with oral lesions. He had similar lesions 2 years ago which on biopsy demonstrated non-specific inflammation. His treatment for Crohn's disease included sulfasalazine for 3 years followed by infliximab for 4 years and most recently on methotrexate for the past 2 years before this presentation. In between he was also briefly treated with 6-mercaptopurine as well as adalimumab for short duration of time because of intolerance. He was concerned about

increasing bowel movements and abdominal pain over the past few weeks before presentation.

INVESTIGATIONS

Biopsy of the oral lesions demonstrated a diffuse infiltrate of intermediate sized atypical lymphoid cells involving the mucosa and submucosa. Immunohistochemistry showed that these cells were positive for CD2, CD3, T-cell receptor β F1, granzyme B and T-cell intracellular antigen 1, but appear negative for other markers. In situ hybridisation for Epstein-Barr virus was negative. These findings supported peripheral T-cell lymphoma not otherwise specified (NOS). The tests were confirmed at Mayo Clinic, Rochester, Minnesota.

He subsequently underwent colonoscopy with biopsies that revealed pan colitis and similar findings of peripheral T-cell lymphoma NOS. Positron emission tomography (PET) scan showed mild uptake in colon, confirming colon limited T-cell lymphoma. There was lymphadenopathy noted on CT which was not PET avid. Other investigations including oesophagogastroduodenoscopy and bone marrow biopsy did not reveal any evidence of T-cell lymphoma.

TREATMENT

Evolution of peripheral T-cell lymphoma while a patient is on immunosuppressive therapy is a clinical challenge, since there is very less literature to suggest treatment options in this scenario. Case reports suggest either stopping immunosuppressive therapy or starting chemotherapeutic treatment. After detailed discussions with the patient, the decision was made to stop methotrexate. His symptoms did not improve despite withholding methotrexate and continuing prednisone for Crohn's disease maintenance. Subsequently, the patient was started on CHOP (cyclophosphamide, hydroxydaunorubicin, oncovin and prednisone) chemotherapy regimen based on standard non-Hodgkin's lymphoma protocol for six cycles.

OUTCOME AND FOLLOW-UP

His subsequent course was complicated by neutropenic fever as well as *Clostridium difficile* colitis which were managed with appropriate treatment. His symptoms of diarrhoea and abdominal pain improved after three cycles of chemotherapy. After completion of six cycles, a CT scan showed resolution of lymphadenopathy and a PET scan demonstrated no evidence of lymphoma (figure 1). This was also further confirmed by colonoscopy with biopsy.

To cite: Kollepara SS, Chisti MM, Shatavi SV, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-200606

Figure 1 (A) CT abdomen prior to initiation of therapy showing abdominal lymphadenopathy (peripancreatic lymph node 15 mm in short axis). (B) CT abdomen post-treatment showing resolution of lymphadenopathy.

DISCUSSION

Previous experience from patients with transplant helped us to understand that immunosuppressive therapy facilitates the genesis of cancer as well as accelerates their growth.⁵ Postulated mechanisms for this increased oncogenesis include decreased immunosurveillance, oncogenic effects of drugs⁵ as well as reactivation of latent oncogenic viruses.⁶

Earlier studies have demonstrated that there is a small increased risk of lymphoma in patients with Crohn's disease.⁷ Furthermore, the incidence of lymphoma as an adverse event associated with various immunotherapies for Crohn's disease remains an important concern for patients as well as physicians alike which is also reflected by the black box warning on the thiopurines and anti-tissue necrotic factor (TNF) agents used in the treatment of Crohn's disease regarding their potential to cause malignancy. Previous literature examining the number needed to treat so as to cause one additional lymphoma ranges from 400 to 4000 depending on the age group in patients treated with thiopurine analogues⁸ where as it is 2000 for anti-TNF medications.⁹

Hepatosplenic T-cell lymphoma risk has been previously well described. However, there is limited literature about the occurrence of peripheral T-cell lymphoma in patients with Crohn's disease.¹⁰ Recently Deepak *et al*¹¹ demonstrated that the risk of T-cell non-Hodgkin's lymphoma is increased with TNF α

inhibitor use in combination with thiopurines but not with TNF α inhibitors alone. Zheng *et al* previously described an interesting scenario in which a patient was presumptively treated with antituberculosis regimen and was subsequently diagnosed with Crohn's disease for which he received mesalazine. However, he was diagnosed with T-cell lymphoma within few months.¹² In contrast, our patient was on long-term immunosuppressants and presented with a clinical dilemma about the appropriate course of treatment.

Learning points

- ▶ Lymphoma should be considered in the differential diagnosis when patients with Crohn's disease presents with worsening symptoms in spite of being on appropriate treatment.
- ▶ T-cell lymphoma is a rare malignancy that occurs as a consequence of being on immunosuppressive therapy.
- ▶ Stopping immunosuppressive treatment is first modality of approach in treating these patients.
- ▶ In case of no response to withholding immunosuppression, the disease should be treated with standard chemotherapy.

Acknowledgements The authors would like to acknowledge William Beaumont Hospital, Oakland University William Beaumont School of Medicine.

Contributors All authors have been involved in writing the manuscript and contributed to this case report.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Palli D, Trallori G, Bagnoli S, *et al*. Hodgkin's disease risk is increased in patients with ulcerative colitis. *Gastroenterology* 2000;119:647–53.
- 2 Lewis JD, Bilker WB, Brensinger C, *et al*. Inflammatory bowel disease is not associated with an increased risk of lymphoma. *Gastroenterology* 2001;121:1080–7.
- 3 Ljung T, Karlen P, Schmidt D, *et al*. Infliximab in inflammatory bowel disease: clinical outcome in a population based cohort from Stockholm County. *Gut* 2004;53:849–53.
- 4 Bewtra M, Lewis JD. Update on the risk of lymphoma following immunosuppressive therapy for inflammatory bowel disease. *Expert Rev Clin Immunol* 2010;6:621–31.
- 5 Gutierrez-Dalmau A, Campistol JM. Immunosuppressive therapy and malignancy in organ transplant recipients: a systematic review. *Drugs* 2007;67:1167e98.
- 6 Caillard S, Lelong C, Pessione F, *et al*. Posttransplant lymphoproliferative disorders occurring after renal transplantation in adults: report of 230 cases from the French Registry. *Am J Transplant* 2006;6:2735e42.
- 7 Von Roon AC, Reese G, Teare J, *et al*. The risk of cancer in patients with Crohn's disease. *Dis Colon Rectum* 2007;50:839–55.
- 8 Kandiel A, Fraser AG, Korelitz BI, *et al*. Increased risk of lymphoma among inflammatory bowel disease patients treated with azathioprine and 6-mercaptopurine. *Gut* 2005;54:1121–5.
- 9 Siegel CA, Marden SM, Persing SM, *et al*. Risk of lymphoma associated with combination anti-tumor necrosis factor and immunomodulator therapy for the treatment of Crohn's disease: a meta-analysis. *Clin Gastroenterol Hepatol* 2009;7:874–81.
- 10 Bewtra M. Lymphoma in inflammatory bowel disease and treatment decisions. *Am J Gastroenterol* 2012;107:964–70.
- 11 Deepak P, Sifuentes H, Sherid M, *et al*. T-cell non-Hodgkin's lymphomas reported to the FDA AERS with tumor necrosis factor-alpha (TNF- α) inhibitors: results of the REFURBISH study. *Am J Gastroenterol* 2013;108:99–105.
- 12 Zheng S, Xu H, Ouyang Q, *et al*. A case of rapid growing colonic NK/T cell lymphoma complicated by Crohn's disease. *Cancer Res* 2013;25:119–23.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow