Netherlands
The Journal of Medicine

CASE REPORT

# Failure of CHOP with rituximab for lymphomatoid granulomatosis

**S.F. Oosting-Lenstra*, M. van Marwijk Kooy**

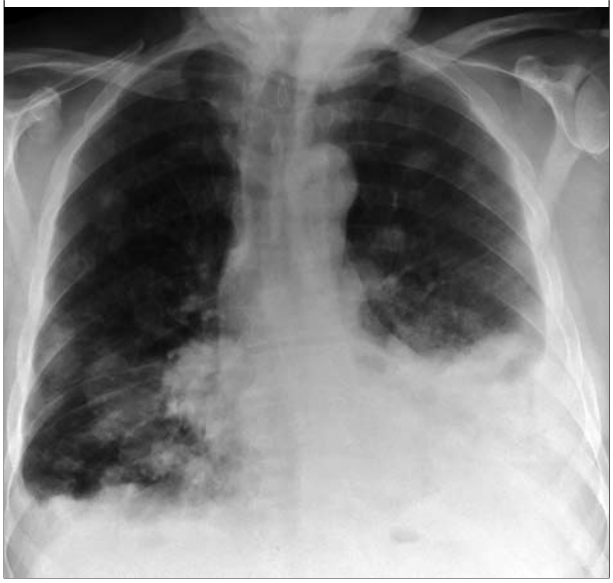
Department of Internal Medicine, Isala Clinics, Zwolle, the Netherlands, *corresponding author (currently: Department of Medical Oncology, University Medical Centre Groningen, Groningen, the Netherlands): fax: +31 (0)50-361 48 62, e-mail: s.oosting@int.umcg.nl

## ABSTRACT

**We present a 66-year-old male patient with pulmonary lymphomatoid granulomatosis.**

**The patient had progressive disease after three courses of CHOP and rituximab and, therefore, treatment with interferon-α2b 5 x $10^6$ IE three times a week was started. This resulted in stable disease for five months. Subsequently, progression occurred and the patient died 12 months after initial presentation. Lymphomatoid granulomatosis is a rare, poor-risk, Epstein-Barr virus related, B cell lymphoproliferative disease. There is no standard treatment but promising results have been reported with rituximab, either as monotherapy or in combination with chemotherapy. This case demonstrates that lymphomatoid granulomatosis is still a chemotherapy-resistant disease in some patients despite addition of rituximab. A review of the literature regarding aetiology, clinical features, diagnosis and treatment options is presented.**

**Figure 1.** *Chest X-ray on presentation*



## KEYWORDS

Epstein-Barr virus, interferon, lymphomatoid granulomatosis, lymphoproliferative disease, rituximab

## CASE REPORT

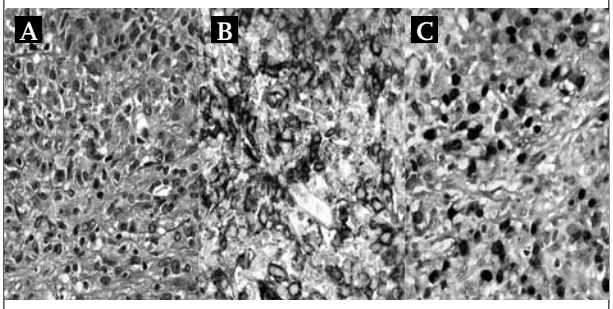
A 66-year-old man presented with superficial thrombophlebitis of his left leg. A routine chest X-ray showed multiple round nodules, predominantly in the lower lung fields (*figure 1*). The patient had a history of diabetes, hypertension, hypercholesterolaemia, claudication and a temporary paralysis of the facial nerve. He had lost 10 kg of weight in the previous six months and suffered from night sweats. During analysis he developed chills and fever with a productive cough and shortness of breath. On lung auscultation he had crackles and rales on both sides and diminished breath sounds over the lower left lung. There was no evidence of lymphadenopathy, hepatomegaly or splenomegaly. Laboratory tests showed a high sedimentation rate, a microcytic anaemia, a mild leucocytosis and thrombocytosis and an elevated alkaline phosphatase and γ-glutamyl transferase (*table 1*). A transbronchial lung biopsy was inconclusive and an open lung biopsy was performed. A small wedge resection containing a 3.5 cm white mass was removed. Histology showed necrotic tissue surrounded by a polymorphous infiltrate of lymphoid cells. Large CD20 positive B cells were present in a background of small CD3 positive T cells. This infiltrate was concentrated

**Table 1.** *Laboratory results*

| Test | Result | Test | Result |
|---|---|---|---|
| ESR | >120 mm/h | Base excess | -0.7 mmol/l |
| Haemoglobin | 5.9 mmol/l | $pO_2$ | 7.9 kPa |
| Haematocrit | 0.29 l/l | Urea | 9.9 mmol/l |
| MCV | 78 fL | Creatinine | 81 µmol/l |
| Leucocytes | 11.6 x $10^9$/l | Sodium | 134 mmol/l |
| Eosinophils | 0.25 x $10^9$/l | Potassium | 4.0 mmol/l |
| Basophils | 0.07 x $10^9$/l | AP | 193 U/l |
| Neutrophils | 9.58 x $10^9$/l | γGT | 234 U/l |
| Lymphocytes | 0.5 x $10^9$/l | ASAT | 39 U/l |
| Monocytes | 1.18 x $10^9$/l | ALAT | 33 U/l |
| Platelets | 415 x $10^9$/l | LDH | 395 U/l |
| pH | 7.45 | Albumin | 29 g/l |
| $pCO_2$ | 4.3 kPa | Bilirubin | <5 µmol/l |
| $HCO_3$ | 22.4 mmol/l | ANCA | Negative |

**ESR = erythrocyte sedimentation rate; MCV = mean corpuscular volume; AP = alkaline phosphatase; γGT = gamma glutamyl-transferase; ASAT = aspartate aminotransferase; ALAT = alanine aminotransferase; LDH = lactate dehydrogenase; ANCA = antineutrophil cytoplasmic antibodies.**

**Figure 2.** *(A) Polymorphic tumour cells in a background of small lymphocytes (H&E); (B) CD20 immunostain with a membranous positivity of large tumour cells; (C) most nuclei of the tumour cells are stained by EBER (EBV RNA in situ hybridisation)*




**Original magnification: 40X. Courtesy of Dr James E Boers, Isala Clinics, Zwolle.**

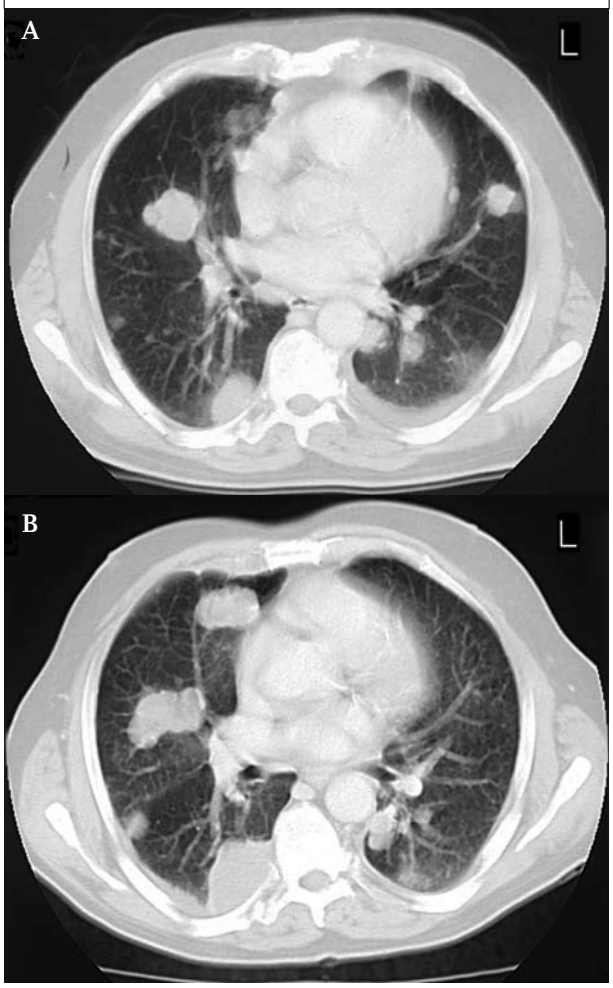
around the blood vessels. No yeast, fungi or acid-fast bacilli were detected but *in situ* hybridisation for Epstein-Barr virus (EBV) was strongly positive (*figure 2*). The diagnosis of lymphomatoid granulomatosis grade III was made. We treated him with intensified CHOP and rituximab every two weeks (*table 2*). After the third cycle a CT scan of the chest showed progressive disease (*figure 3*). The number as well as the size of the lesions had increased. Our patient was subsequently treated with interferon-α2b. Due to side effects, the maximum tolerated dose was 5 million IE three times a week. On this regimen he was stable for five months, but died 12 months after initial presentation due to progressive disease.

**Table 2.** *Chemotherapy regimen*

| | | | |
|---|---|---|---|
| Cyclophosphamide | 750 mg/m² | IV | Day 1 |
| Doxorubicin | 50 mg/m² | IV | Day 1 |
| Vincristine | 1.4 mg/m² (max 2.0 mg) | IV | Day 1 |
| Prednisone | 100 mg | PO | Day 1-5 |
| Rituximab | 375 mg/m² | IV | Day 3 (cycle 1-2)*, day 1 (cycle 3-6) |
| G-CSF (pegfilgrastim) | 6 mg | SC | Day 2 |

**Cycle duration 14 days. Rituximab was given on day 3 during cycle 1 and 2 in this protocol in order to prevent tumour lysis syndrome. G-CSF = granulocyte-colony stimulating factor; IV = intravenous; PO = per os; SC = subcutaneous.**

**Figure 3.** *CT scan of the chest (A) before start of treatment; (B) after three cycles CHOP with rituximab*




## INTRODUCTION

Lymphomatoid granulomatosis is a rare lymphoproliferative disease. It was first described in 1972 by Liebow *et al.* during their studies of patients with Wegener's granulomatosis.[1] Lymphomatoid granulomatosis was

described as an atypical angiocentric and angiodestructive lymphoproliferative disease, predominantly located in the lungs but sometimes present at other extranodal sites. After this first description there has been a lot of controversy regarding the concept and the nature of lymphomatoid granulomatosis. An overview of the literature about lymphomatoid granulomatosis, clinical and histological features and effectivity of different treatment modalities is presented.

## HISTORY OF THE CONCEPT

It has long been recognised that immunocompromised patients are predisposed to develop lymphomatoid granulomatosis. The disease has been reported in patients with primary immunodeficiency as well as in patients with secondary immunodeficiency. Furthermore, Sordillo *et al.* found that four of five lymphomatoid granulomatosis patients were unresponsive to common skin test antigens and that the fifth patient showed partial anergy.[2] Fauci *et al.* reported that three out of six lymphomatoid granulomatosis patients were anergic in response to common skin tests.[3] Due to clinical and histological similarities, it was suggested that lymphomatoid granulomatosis and polymorphic reticulosis (nasal and nasal type natural killer (NK) T cell lymphoma) were part of the same disease.[4] Together these diseases were called angiocentric immunoproliferative lesions (AIL).[5] A staging system for AIL, based on histological characteristics, was developed and proved to have prognostic value in small series of patients.[6] Nichols *et al.* postulated that lymphomatoid granulomatosis was a T-cell lymphoma because the majority of the lymphocytes consisted of T cells and this was the leading opinion for more than a decade.[7] Pisani *et al.* suggested that lymphomatoid granulomatosis was not a clinicopathological entity but a histological response to different stimuli, such as haematological malignancies, solid tumours, viral infections and autoimmunity.[8] This was, however, not a widely held opinion. In their initial description Liebow *et al.* suggested a relationship between lymphomatoid granulomatosis and EBV infection.[1] This relationship was confirmed in 1990 when EBV DNA was found in tissue samples of 21 out of 29 patients with lymphomatoid granulomatosis.[9] Guinee *et al.* combined *in situ* hybridisation for EBV with immunohistochemistry in tissue samples from ten patients with lymphomatoid granulomatosis.[10] In each case EBV was only present in the B cells. In six out of nine patients tested, immunoglobulin heavy chain rearrangement showed a monoclonal pattern. Wilson *et al.* confirmed that the EBV expression was restricted to B cells, in four patients. In analogy to post-transplant lymphoproliferative disease (PTLD), they also demonstrated two B cell clones in one patient and three B cell clones in another.[11]

These findings led to the current opinion that lymphomatoid granulomatosis is an EBV-associated B cell lymphoproliferative disease. The majority of the infiltrating cells are reactive T lymphocytes recruited in response to EBV infection. Cellular immunodeficiency probably prohibits EBV elimination in the majority of patients. In the WHO classification system lymphomatoid granulomatosis is grouped together with PTLD as 'B cell lymphoproliferative disorders with uncertain malignant potential'.

## CLINICAL FEATURES AND HISTOPATHOLOGY

Two large and three smaller series of patients with lymphomatoid granulomatosis have been described.[3,8,9,12,13] The largest series consists of 152 cases that were identified in Liebow's consultation files. Lymphomatoid granulomatosis has been diagnosed in patients from 4 to 85 years of age, but generally patients are between 40 and 60 years of age. Men are more frequently affected than women with male: female ratios ranging from 2:1 to 3:1. Most patients present with pulmonary symptoms such as cough, shortness of breath or chest pain and the majority of patients have systemic symptoms such as weight loss, fever and night sweats. Of the patients, 20 to 40% develop skin manifestations, either an erythematous rash or, less frequently, skin nodules. Almost a third of the patients develop neurological symptoms such as confusion, ataxia, hemiparesis or seizures, mostly due to mass lesions in the central nervous system (CNS). Cranial nerve palsies and peripheral polyneuropathy have also been described. The disease is typically located in the lungs. Localisation in the liver and kidneys occurs in approximately one third of patients but is generally asymptomatic. Hepatomegaly and splenomegaly are present in less than 20% of the patients and lymphadenopathy is even less common at presentation (7-8%). Pisani *et al.* detected bone marrow localisation in one of 19 patients and Fauci *et al.* in five of 15 patients.[8,3] Bone marrow investigation was not described in the two largest series.

Laboratory investigation shows nonspecific abnormalities at initial presentation. Erythrocyte sedimentation rate is either normal or elevated. White cell count is normal in 50%, elevated in 30% and decreased in 20% of patients. Mild anaemia is sometimes present and during disease progression, pancytopenia caused by the haemophagoytic syndrome occasionally develops. The majority of the patients have atypical abnormalities in immunoglobulin concentrations and about a third have mild elevations in liver enzyme levels.

Chest X-rays show bilateral lesions in 71 to 92% of patients. Multiple nodules are most frequently seen while diffuse,

reticular or nodular infiltrates are less often described. Rarely, lymphadenopathy, pleural effusions, cavitations or solitary masses are present. Mortality of patients with lymphomatoid granulomatosis ranges from 38 to 65% in the different studies. In patients who die from their disease, the median survival is 11.3 months and death is generally caused by massive pulmonary destruction. Older studies suggest that leucopenia, fever, anergy in reaction to common skin test antigens, young age and localisation in the CNS are poor prognostic signs.[3,11,12]

Diagnosis should be made on a dominant noncutaneous lesion. Transbronchial biopsy is not recommended since it is diagnostic in only 27% of cases while open lung biopsy specimens are uniformly positive.[8] Histology typically shows a polymorphous infiltrate predominantly consisting of lymphocytes although plasma cells, histiocytes and immunoblasts can also be present. The majority of the lymphocytes are T cells and CD4 positive as well as CD8 positive subsets, without malignant features, are present. Immunoblasts are large atypical CD20 positive B cells. Populations of B cells are either monoclonal, oligoclonal or polyclonal and most B cells contain EBV DNA. The infiltrate is concentrated around small arteries and veins and causes destruction of the vessels. Necrosis develops due to direct T cell invasion, causing infarction, and due to destruction of the vessels resulting in fibrinoid necrosis. The latter may be mediated by EBV latent membrane protein which can cause upregulation of both IP-10 (interferon-γ inducible protein) and Mig (monokine induced by interferon-γ), which have been shown to cause endothelial and vascular damage.[14] Skin lesions often lack EBV-positive B cells and resemble vasculitis. In 1979, it was already suggested that higher numbers of atypical lymphoreticular cells are associated with poor outcome.[12] Guinee *et al*. demonstrated a negative correlation between the amount of EBV-positive B cells and survival.[10] They suggested a grading system in which grade I lesions contain few, if any, EBV-positive B cells, grade II lesions show more EBV-positive B cells but less than 100 per high power field and grade III lesions consist of infiltrates with more than 100 EBV-positive B cells per high-power field.

In patients at risk for PTLD, serial quantitative polymerase chain reaction (PCR) analyses of EBV DNA in plasma has been shown to have predictive value for development of PTLD although there is considerable overlap between patients with symptomatic EBV reactivation without PTLD and patients with PTLD.[15] Response to treatment in patients with PTLD is accompanied by a prompt decline in viral copy number.[16,17] To our knowledge there are no data available about the value of determination of EBV load for diagnosis and guidance of therapy for patients with lymphomatoid granulomatosis. It is tempting, however, to hypothesise that serial measurements can be used to evaluate response to treatment.

## TREATMENT

Because lymphomatoid granulomatosis is a rare disease, very few treatment studies have been conducted and there is no standard treatment. Depending on severity at presentation most patients are treated with corticosteroids, either as single agent or combined with cyclophosphamide, or with other chemotherapeutic agents as CHOP or COP regimens. Radiotherapy has been used for CNS and orbital localisations.[2,12] The largest series described is a retrospective analysis of different treatment strategies in 147 patients.[12] Patients were classified according to treatment as follows: group I: corticosteroids (n=67), group II: corticosteroids combined with chemotherapy (n=42), group III: chemotherapy (n=13), group IV: antibiotics or no treatment (n=21), and group V: miscellaneous (n=4). Mortality varied from 64 to 69% and durable complete remission ranged from 24 to 27%. No significant differences were found between the groups.

Fauci *et al*. treated 15 patients prospectively with cyclophosphamide (2 mg/kg/day orally) and prednisone (1 mg/kg/day orally).[3] This protocol was based on treatment regimens for Wegener's granulomatosis. Two patients only received prednisone and died of progressive disease before diagnosis was clear. Seven patients achieved complete remission and remained disease free after a median follow-up of 5.2 years. Six patients treated with prednisone and cyclophosphamide died of progressive disease. Three of these six patients received combination chemotherapy without success.

Raez *et al*. treated a 51-year-old patient with lymphomatoid granulomatosis with PRoMACE-MOPP, a multiagent chemotherapeutic regimen for aggressive lymphomas.[18] The patient responded but disease recurred one month after completion of six cycles of the chemotherapy. The patient subsequently received cyclosporin-A and achieved complete remission within eight weeks. After discontinuing maintenance therapy two years later, disease recurred within three weeks. A third remission was achieved after restarting cyclosporin-A and the patient remained in remission for a follow-up of four years after diagnosis.

Wilson *et al*. treated four patients with interferon-α2b which has antiviral, antiproliferative and/or immunomodulatory effects, based on the assumption that lymphomatoid granulomatosis is related to PTLD.[11]

Three patients received interferon as first-line treatment and one patient received interferon after an early relapse on six cycles of CHOP chemotherapy. All four patients had responded by three months, three were in complete remission and remained disease free after 36 to 60 months of follow-up. One patient died after discontinuation of treatment.

The same investigators set up a phase II study with dose-adjusted interferon-α for patients with lymphomatoid granulomatosis grades I and II and EPOCH chemotherapy

(infusional etoposide, vincristine, doxorubicin, with bolus cyclophosphamide and oral prednisone) for lymphomatoid granulomatosis grade III. Interferon is started at 5-10 x $10^6$ IE three times a week and the dose is escalated until disease regression or tolerance is achieved. Accrual is still ongoing and preliminary results were published in 1999.[19] Of twelve evaluable patients on interferon, eight were in remission for a median duration of 19 months, four rapidly progressed to grade III lymphomatoid granulomatosis. Five evaluable patients were treated with chemotherapy, three achieved complete remission, two partial remission. Three of these five patients developed lower grade lymphomatoid granulomatosis and were subsequently treated with interferon, in two with good results. For the third patient follow-up was too short for evaluation. Two further cases of lymphomatoid granulomatosis were reported for first-line treatment with interferon. One patient relapsed on discontinuation after three months; the other patient was treated for 18 months with a good result.[20,21]

In 1986 Bernstein *et al*. described a 19-year-old patient with lymphomatoid granulomatosis with recurrent disease after COP chemotherapy.[22] The patient received a bone marrow transplant from his HLA-compatible brother and remained in remission during a follow-up of more than three years.

To our knowledge no patients have been reported for treatment with nonmyeloablative allogeneic stem cell transplantation. This might be an interesting treatment option for restoring the presumed underlying immunocompromised status while reducing toxicity compared with myeloablative allogeneic stem cell transplantation.

In two case reports, successful treatment of lymphomatoid granulomatosis with autologous stem cell transplantation has been described after failure of combination chemotherapy.[23,24] The patients were in remission for 12 months and eight years respectively. The last patient received maintenance therapy with interferon for almost four years.

Rituximab has been recognised as a promising treatment option in lymphomatoid granulomatosis over the last few years. Six patients were treated with rituximab monotherapy and three patients had durable complete remission,[25-27] one patient had a major response after four courses but died of haemoptysis[28] and two patients had progressive disease.[29,30] Two patients with lymphomatoid granulomatosis treated with CHOP in combination with rituximab have been described.[31,32] One patient was still in complete remission after 18 months of follow-up.[32] The other patient concomitantly received systemic and intrathecal methotrexate for CNS localisation.[31] He had a partial response of pulmonary lesions and stable CNS lesions two months after starting therapy; however, CNS lesions were progressive after six months. He then received radiation therapy and four courses of rituximab monotherapy with partial response of CNS lesions.

## DISCUSSION

This is the first description of failure of the combination of CHOP chemotherapy with rituximab to induce a response in lymphomatoid granulomatosis.

Many patients with lymphomatoid granulomatosis have been treated with CHOP chemotherapy but data on efficacy are lacking. Nevertheless, CHOP was the recommended treatment for patients with aggressive grade I and II disease and for all patients with grade III disease before rituximab became available.[33]

Anti-CD20 immunotherapy is a rational treatment option for several reasons. Firstly, the neoplastic cell population in lymphomatoid granulomatosis consists of CD20 positive B cells. Secondly, the addition of rituximab to CHOP chemotherapy for diffuse large B cell lymphoma has been shown to improve response rate, progression free and overall survival.[34] Furthermore, rituximab is an important drug for treating PTLD, a disease closely related to lymphomatoid granulomatosis.

In two earlier reports a complete and a partial response with CHOP with rituximab for lymphomatoid granulomatosis were described. Our patient, however, had progressive disease on three treatment cycles.

This case shows that lymphomatoid granulomatosis is still a chemotherapy-resistant disease in some patients despite the addition of rituximab.

Since promising results of interferon for lymphomatoid granulomatosis have been described in a limited number of patients we treated our patient with interferon. He was stable for five months on interferon 5 x $10^6$ IE, three times a week; however, he finally succumbed to progressive disease 12 months after initial presentation. Stable disease during interferon treatment in our patient should be considered a response because the patient had rapidly progressive disease before starting treatment. Unfortunately we were not able to increase the dose because of side effects. Otherwise an objective response might have been possible, as in one of the patients described by Wilson *et al*. who had complete remission after gradual dose increases of interferon up to 40 x $10^6$ IE three times a week.[11] Haematopoietic stem cell transplantation has successfully been used in refractory lymphomatoid granulomatosis. We did not consider our patient to be a candidate for transplantation because of infectious problems, substantial comorbidity and poor condition.

## NOTE

This case was presented at the Autumn Conference of the Netherlands Society of Haematology, (NVvH) in Lunteren on 4 November 2004.

## ACKNOWLEDGEMENT

We thank Dr L.F. Verdonck and Dr M. Jalving for critically reading the manuscript and their thoughtful suggestions, and Dr J.E. Boers for kindly providing the histological figures.

## REFERENCES

1. Liebow AA, Carrington CRB, Friedman PJ. Lymphomatoid granulomatosis. Hum Pathol 1972;3:457-558.
2. Sordillo PP, Epremian B, Koziner B, et al. Lymphomatoid granulomatosis: an analysis of clinical and immunologic characteristics. Cancer 1982;49:2070-6.
3. Fauci AS, Haynes BF, Costa J, et al. Lymphomatoid granulomatosis: prospective clinical and therapeutic experience over 10 years. N Engl J Med 1982;306:68-74.
4. DeRemee RA, Weiland RH, McDonald TJ. Polymorphic reticulosis and lymphomatoid granulomatosis: two diseases or one? Mayo Clin Proc 1978;53:634-40.
5. Jaffe ES. Pathologic and clinical spectrum of post-thymic t-cell malignancies. Cancer Invest 1984;2:413-26.
6. Lipford EH, Margolick JB, Longo JL, et al. Angiocentric immunoproliferative lesions: a clinicopathologic spectrum of post-thymic t-cell proliferations. Blood 1988;72:1674-81.
7. Nichols PW, Koss M, Levine AM, et al. Lymphomatoid granulomatosis: a T-cell disorder? Am J Med 1982;72:467-71.
8. Pisani RJ, DeRemee RA. Clinical implications of the histopathologic diagnosis of pulmonary lymphomatoid granulomatosis. Mayo Clin Proc 1990;65:151-63.
9. Katzenstein AL Peiper SC. Detection of Epstein-Barr virus genomes in lymphomatoid granulomatosis: analysis of 29 cases by the polymerase chain reaction technique. Mod Pathol 1990;3:435-41.
10. Guinee D, Jaffe E, Kingma D, et al. Pulmonary lymphomatoid granulomatosis. Am J Surg Pathol 1994;18:753-64.
11. Wilson WH, Kingma DW, Raffeld M, et al. Association of lymphomatoid granulomatosis with Epstein-Barr viral infection of B lymphocytes and response to interferon-α2b. Blood 1996;87:4531-7.
12. Katzenstein AA, Carrington CB, Liebow A. Lymphomatoid granulomatosis: a clinicopathologic study of 152 cases. Cancer 1979;43:360-73.
13. Koss MN, Hochholzer L, Langloss JM, et al. Lymphomatoid granulomatosis: a clinocopathologic study of 42 patients. Pathology 1986;18:283-8.
14. Teruya-Feldstein J, Jaffe ES, Burd PR, et al. The role of Mig, the monokine induced by interferon-gamma, and IP-10, the interferon-gamma inducible protein-10, in tissue necrosis and vascular damage associated with Epstein-Barr virus-positive lymphoproliferative disease. Blood 1997;90:4099-105.
15. Weinstock DM, Ambrossi GG, Brennan C, et al. Preemptive diagnosis and treatment of Epstein-Barr virus-associated post transplant lymphoproliferative disorder after hematopoietic stem cell transplant: an approach in development. Bone Marrow Transplant 2006;37:539-46.
16. Esser JWJ, Niesters HGM, Van der Holt B, et al. Prevention of Epstein-Barr virus-lymphoproliferative disease by molecular monitoring and preemptive rituximab in high-risk patients after allogeneic stem cell transplantation. Blood 2002;99:4364-9.
17. Greenfield HM, Gharib MI, Turner AJ, et al. The impact of monitoring Epstein-Barr virus PCR in paediatric bone marrow transplant patients: can it successfully predict outcome and guide intervention? Pediatr Blood Cancer 2006;47:200-5.
18. Raez LE, Temple JD, Saldana M. Successful treatment of lymphomatoid granulomatosis using cyclosporine - A after failure of intensive chemotherapy. Am J Hematol 1996;53:192-5.
19. Wilson WH, Gutierrez M, Raffield M, et al. Lymphomatoid granulomatosis: phase II study of dose-adjusted interferon-α or EPOCH chemotherapy [Abstract]. Blood 1999;94(10 Pt1):A-2668, 599a.
20. Richter C, Schnabel A, Müller KM, et al. Lymphomatoide granulomatose – Remissionsinduktion mit interferon-α2b. Dtsch Med Wschr 1997;122:1106-10.
21. Ören H, Irken G, Kargi A, et al. A pediatric case of lymphomatoid granulomatosis with onset after completion of chemotherapy for acute myeloid leukemia. J Pediatr Hematol Oncol 2003;25:163-6.
22. Bernstein ML, Reece ER, de Chadarévian J, et al. Bone marrow transplantation in lymphomatoid granulomatosis: Report of a case. Cancer 1986;58:969-72.
23. Lemieux J, Berbier V, Martel N, et al. Autologous hematopoietic stem cell transplantation for refractory lymphomatoid granulomatosis. Hematology 2002;7:355-8.
24. Johnston A, Coyle L, Nevell D. Prolonged remission of refractory lymphomatoid granulomatosis after autologous hemopoietic stem cell transplantation with post-transplantation maintenance interferon. Leuk Lymphoma 2006;47:323-8.
25. Sebire NJ, Haselden S, Malone M, et al. Isolated EBV lymphoproliferative disease in a child with Wiskott-Aldrich syndrome manifesting as cutaneous lymphomatoid granulomatosis and responsive to anti-CD20 immunotherapy. J Clin Pathol 2003;56:555-7.
26. Zaidi A, Kampalath B, Peltier WL, et al. Successful treatment of systemic and central nervous system lymphomatoid granulomatosis with rituximab. Leuk Lymphoma 2004;45:777-80.
27. Jordan K, Grothey A, Grothe W, et al. Successful treatment of mediastinal lymphomatoid granulomatosis with rituximab monotherapy. Eur J Haematol 2005;74:263-6.
28. Jaffre S, Jardin F, Dominique S, et al. Fatal haemoptysis in a case of lymphomatoid granulomatosis treated with rituximab. Eur Respir J 2006;27:644-6.
29. Polizzotto MN, Dawson MA, Opat SS. Failure of rituximab monotherapy in lymphomatoid granulomatosis. Eur J Haematol 2005;75:172-3.
30. Hochberg EP, Gilman MD, Hasserjian RP. Case 17-2006: A 34-year-old man with cavitary lung lesions. N Engl J Med 2006;354:2485-93.
31. Rao R, Vugman G, Leslie WT, et al. Lymphomatoid ganulomatosis treated with rituximab and chemotherapy. Clin Adv Hematol Oncol 2003;1:658-60.
32. Hagberg H. Review on lymphomatoid granulomatosis treated with rituximab and chemotherapy. Clin Adv Hematol Oncol 2003;1:660.
33. Jaffe ES, Wilson WH. Lymphomatoid granulomatosis: pathogenesis, pathology and clinical implications. Cancer Surv 1997;30:233-48.
34. Coiffier B, Lepage E, Briere J, et al. CHOP Chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-b-cell lymphoma. N Engl J Med 2002;346:235-42.