# Systematic Review of Spinal Lymphomatoid Granulomatosis Cases

*Naotaka Iwamoto[1,2], Kyongsong Kim[3], Rinko Kokubo[3], Toyohiko Isu[4], Daijiro Morimoto[1], Tomoko Omura[3], Koji Saito[5], Yoshinao Kikuchi[5], Yasunori Ota[5], Akira Matsuno[2], Akio Morita[1]*

**Key words**
- CNS lymphomatoid granulomatosis
- Lymphomatoid granulomatosis
- Spinal intramedullary tumor

**Abbreviations and Acronyms**
CNS: Central nervous system
EBV: Epstein-Barr virus
HIV: Human immunodeficiency virus
LYG: Lymphomatoid granulomatosis
MRI: Magnetic resonance imaging

*From the [1]Department of Neurosurgery, Nippon Medical School Hospital, Tokyo; [2]Department of Neurosurgery, Teikyo University School of Medicine, Tokyo; [3]Department of Neurosurgery, Chiba Hokuso Hospital, Nippon Medical School, Chiba; [4]Department of Neurosurgery, Kushiro Rosai Hospital, Hokkaido; and [5]Department of Pathology, Teikyo University School of Medicine, Tokyo, Japan*

*To whom correspondence should be addressed: Naotaka Iwamoto, M.D., Ph.D. [E-mail: 4649nao-iwamoto@nms.ac.jp]*

*Citation: World Neurosurg. X (2021) 11:100106. https://doi.org/10.1016/j.wnsx.2021.100106*

*Journal homepage: www.journals.elsevier.com/world-neurosurgery-x*

*Available online: www.sciencedirect.com*



**Lymphomatoid granulomatosis (LYG) is a rare Epstein-Barr virus—associated systemic angiocentric and angiodestructive lymphoproliferative disorder. It commonly involves the lungs and can also affect the skin, liver, kidney, and central nervous system. It can rarely occur in the spine, however, the details are unclear. We performed a systematic review of published cases (including our 1 case) of spinal LYG.**

**We performed a systematic search of studies in English on spinal LYG, focusing on its clinical features, imaging, and treatments, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines on the PubMed database. We identified 14 patients from the literature. We also found 1 case of isolated cervical LYG (grade 3) who was treated with steroid and radiation therapy for the spinal lesion after pathologic diagnosis. We performed a pooled analysis of these 15 cases.**

**The mean age was 43.4 years, and 13 of the 15 patients were male. Brain lesions were present in 11 of 12 intramedullary spinal lesions, and only 1 was an isolated spinal LYG case. Regarding the diagnostic methods, 1 case was not described. Of the 14 cases described, 12 patients underwent biopsies (7 brain, 4 lung, and 1 spinal cord lesion) and 2 underwent surgical removal for an extramedullary lesion. In the overall prognosis from a mean follow-up period of 21.6 months, 4 patients died despite several treatments.**

**Spinal LYG, particularly isolated spinal LYG, is rare. Thus further accumulation of cases may be necessary to better understand its characteristics.**

## INTRODUCTION

The Epstein-Barr virus (EBV) is associated with several neoplasms. Lymphomatoid granulomatosis (LYG) is a rare EBV-associated systemic angiocentric and angiodestructive lymphoproliferative disorder that commonly involves the lungs (the initial site of manifestation in >90% of patients), skin (40%–50% of patients), liver, kidney, and central nervous system (CNS).[1–4]

CNS LYG accounts for approximately 30% of all LYG cases.[1] In most of these cases, the site of CNS LYG is in the brain, and LYG occurring in the spinal cord is rare.[5] However, the details on CNS LYG are unknown. Hence the characteristics and therapeutic strategy for spinal LYG need to be clarified. Because there has been no systematic review on this disease entity to date to the best of our knowledge, we performed a systematic review of published cases on EBV-associated spinal LYG.

## MATERIALS AND METHODS

We performed a systematic literature search according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Two reviewers (NI and KK) independently screened and selected cases, and disagreement was resolved by discussion or independent review by a third author (RK).

Published studies were retrieved from PubMed databases until April 2020. The initial search was performed by combinations of the terms "lymphomatoid granulomatosis" AND "central nervous system" OR "CNS" OR "intramedullary" OR "spine" OR "spinal" OR "spinal cord." For investigation of the craniocervical junction, the initial search was also performed by combinations of the terms "lymphomatoid granulomatosis" AND "brain" OR "cerebral" OR "intracranial." The duplicated retrievals were deleted. The exclusion criteria were non-English articles, nonspinal lesion cases, and cases not diagnosed by magnetic resonance imaging (MRI).

## ADDITIONAL CASE ILLUSTRATION

The patient's consent for publication of all materials was obtained in writing. This was a case of an 85-year-old man who had hypertension, diabetes mellitus, and angina pectoris and suffered from gradual worsening of his left hemiparesis and gait disturbance over a few months. On admission, he had left hemiparesis (McCormick grade 4) and pain around the left scapula

and ulnar side of the upper left limb. Cervical MRI revealed an intramedullary tumor with cord swelling around the C6 level of the cervical spine (Figure 1). Brain MRI and chest and abdominal CT revealed no abnormal lesion. We considered the primary intramedullary tumor of the cervical cord. The patient underwent lesion biopsy with C5-7 laminectomy under general anesthesia. On pathologic examination, hematoxylin-eosin staining showed various infiltrations of plasma cells, macrophages, and lymphocytes. In immunohistochemistry analysis, lymphocytes were found in both CD3-positive T cells and CD79a-positive B cells, and B cells were also positive in EBV-encoded small ribonucleic acid in situ hybridization staining showing EBV gene expression. The pathologic diagnosis was LYG grade 3 (Figure 2). Postoperatively, intravenous steroid pulse treatment (1000 mg of methylprednisolone for 3 days) and radiation therapy on the spinal lesion of C3/4-C7/T1 (24 Gy overall; 1.5 Gy × 16 days, once daily) were performed. His left hemiparesis partially improved. Twenty-five months postoperatively, his McCormick grade improved from 4 to 2 and cervical MRI revealed a slight intramedullary T2 hyperintensity lesion without any gadolinium-enhancing effect, suggesting no tumor recurrence (see Figure 1).

## SYSTEMATIC REVIEW OF RESULTS

### Study Selection

From the systematic literature search, 132 articles were identified for full-text screening. By further application of strict inclusion and exclusion criteria, 14 articles were included in our final analysis (Figure 3).[1,2,5–16] In this study, 15 cases, including our 1 case, were investigated (Table 1).

### Investigated Patient Characteristics

The mean age was 43.4 ± 19.7 (range: 4–85). The 13 cases were male, and the male-to-female ratio was 6.5:1. Regarding immunosuppressing diseases, there was only 1 case with a human immunodeficiency virus (HIV) infection and there was no patient who underwent transplantation. There were 2 cases of treatment history that may have affected immune function: 1 with chemotherapy for acute lymphocytic leukemia (case 6) and 1 with corticosteroid administration for hypersensitivity pneumonia (case 12). Three cases had treatment history for other diseases as follows: tuberculosis and syphilis (case 3), well-controlled asthma and atopic dermatitis (case 9), and hypertension, diabetes mellitus, and angina pectoris (case 15).

Out of 14 cases where other organs were involved, 5 cases had only brain lesions (isolated CNS-LYG) and 9 cases involved other organs; 6 cases in the lung, 6 in the brain, 2 in lymph nodules, 2 in the bone marrow, 2 in the spleen, 1 in the liver, and 1 in the kidney. Brain lesions were present in 11 of 12 intramedullary spinal lesions, and only 1 was an isolated spinal LYG case. Meanwhile, 3 cases of extramedullary lesions did not have brain lesions.

### Clinical Symptoms

On admission, 12 patients had spinal cord symptoms, such as paralysis, sensory disturbance, and bladder-rectal dysfunction. Gait disturbance was present in all 12 cases; 9 had paralysis in both legs, 1 had unilateral leg paralysis, and 2 had hemiparesis. Upper limb paralysis was noted in 4 cases, 2 were hemiparesis, and 2 were unilateral arm paralysis accompanied by dual leg paresis. The other 3 had brain symptoms without spinal cord symptoms. Of the former 12 cases, their chief complaints were

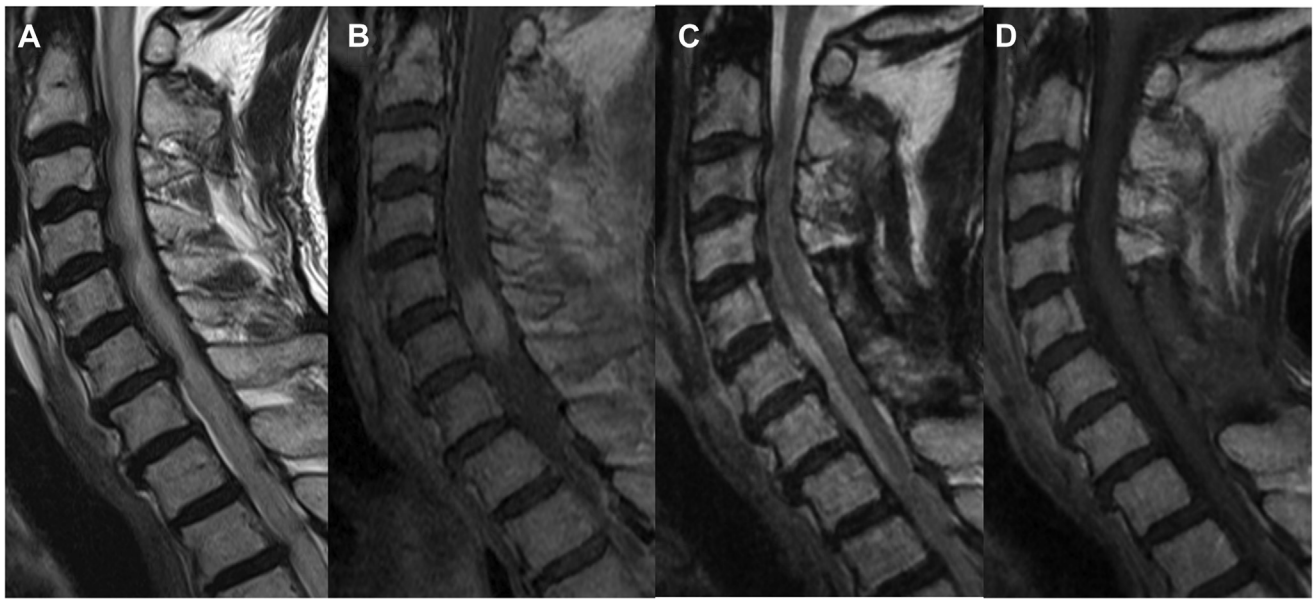


**Figure 1.** Cervical magnetic resonance imaging sagittal view, preoperatively (**A** and **B**) and 25 months postoperatively (**C** and **D**). (**A**) T2-weighted imaging shows extensive intramedullary signal changes and cord swelling. (**B**) T1-weighted imaging–gadolinium enhancement reveals diffuse massive enhancement in the C6 vertebral level. (**C**) T2-weighted imaging shows decreasing of intramedullary signal changes and cord swelling. (**D**) T1-weighted imaging–gadolinium enhancement reveals disappearance of abnormal enhancement.

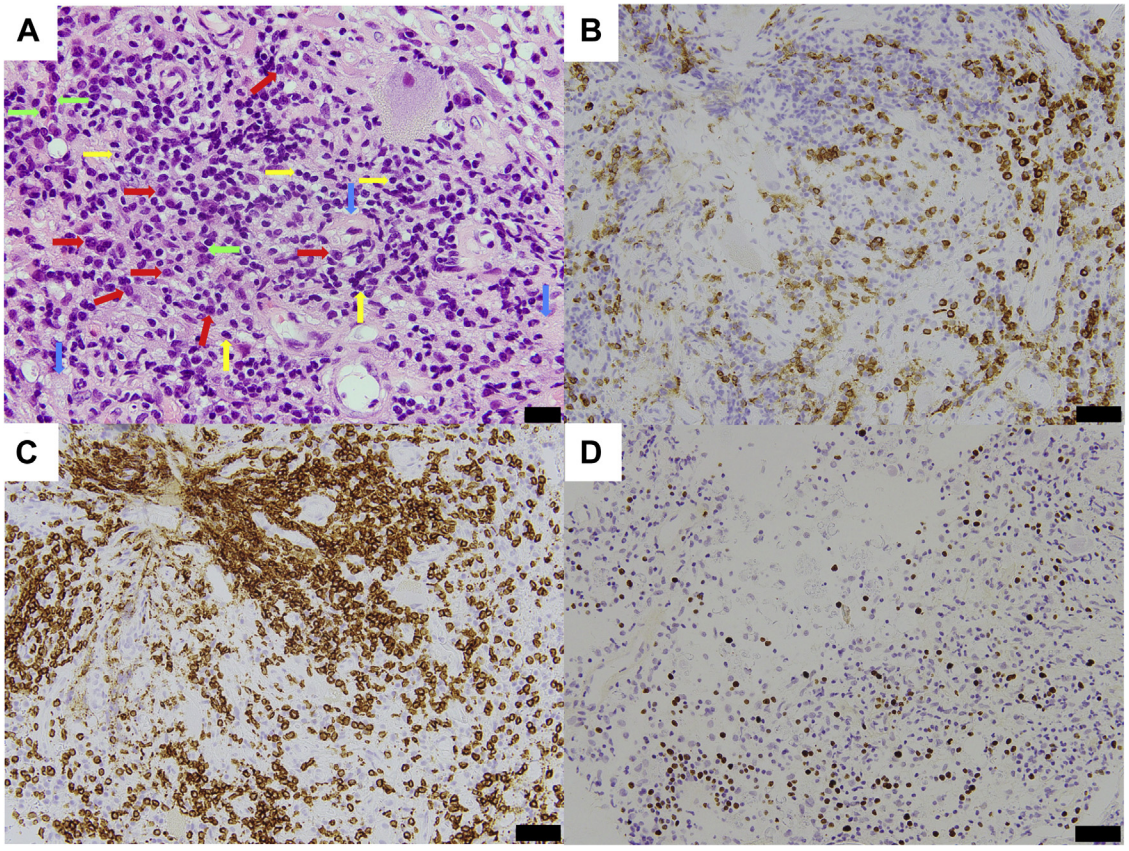


**Figure 2.** Pathologic examination. (**A**) Hematoxylin-eosin staining shows various infiltration of plasma cells (*green arrow*), macrophages (*blue arrow*), normal T cells (*yellow arrow*), and atypical B cells (*red arrow*). Bar: 20μm. (**B**–**D**) Immunohistochemical staining. Bar: 50μm. (**B**) CD79a staining detects positive B lymphocytes. (**C**) CD3 staining detects positive T lymphocytes. (**D**) Epstein-Barr virus–encoded small ribonucleic acid in situ hybridization shows multiple positive cells.

spinal cord symptoms, 6 had only spinal cord symptoms, 4 had systemic symptoms such as fever, cough, nausea, and body weight loss, and 2 had brain symptoms such as cranial nerve palsy, headache, cognitive impairment, ataxia, epilepsy, and tremor.

### Imaging

MRI of the spine showed multiple and single lesions in 4 cases and 10 cases, respectively (the number was not described in 1 case). The lesion levels were cervical in 11 cases, thoracic in 8 cases, and lumbar in 1 case with some that overlapped. Regarding the gadolinium-enhancing effect, all described 13 cases had an enhanced effect. In the enhancement characteristics, 2 cases with extramedullary lesion were heterogeneous, 3 were diffuse massive, 3 were punctate, 1 was linear, 1 was punctate and linear, and 1 was diffuse (the enhancement characteristic was not described in 2 cases). No cases had hemorrhage within the lesion.

### Diagnosis, Histopathology, Treatment, and Outcomes

Diagnosis was mainly based on biopsy (12 cases, which were described according to diagnostic methods). In cases 6 and 7, surgical removal was performed for compression myelopathy due to extramedullary lesions. Biopsy was performed in 4 cases in the lung, 7 in the brain, and 1 in the spinal cord, and 3 cases had bone marrow diagnosis (there is some overlap). LYG grading was described in 10 cases as follows: 4 cases were grade 1, 1 case was grade 1/2, 2 cases were grade 2, and 3 cases were grade 3. EBV infection was evaluated in 10 cases, of which 5 were positive, although serum EBV was present in 1 negative case.

All 12 cases with described treatment were given drug treatment as follows: rituximab in 3 cases (combined with steroid in 2 cases), cyclophosphamide with steroid in 6 cases (combined with doxorubicin and vincristine in 1 cases), interferon-α in 2 cases (combined with steroid in 1 cases), and steroid only in 2 cases (1 case with isolated spinal cord lesion was provided radiotherapy). Moreover, one of the HIV-positive cases was provided antiretroviral therapy. The overall prognosis after mean 21.6 ± 18.6 months (1–72 months) was described in 12 cases. Eight patients survived (5 had improved symptoms), although 4 died.

## DISCUSSION

### Patient Characteristics of Spinal Lymphomatoid Granulomatosis

LYG is a rare EBV-associated angiocentric/angiodestructive lymphoproliferative disease.[1–4] It commonly involves the lungs, and it can also occur in the skin, liver,

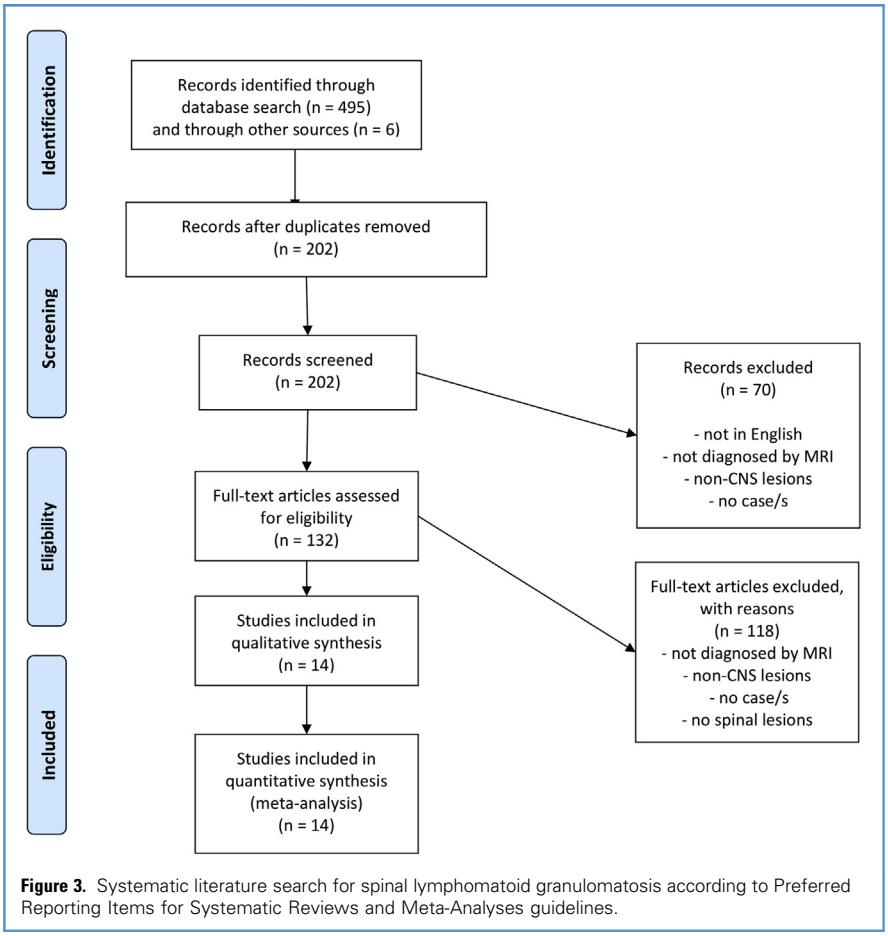


**Figure 3.** Systematic literature search for spinal lymphomatoid granulomatosis according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.

kidneys, and CNS. However, CNS LYG accounts for approximately 30% of all LYG cases, LYG that occur only in CNS is rare.[1–4] On that account, data on spinal lesion involvement remain limited. Hence we investigated many articles up to April 2020 and included only 15 cases of spinal lesion. These results suggest that spinal LYG is rarer than brain LYG. Spinal LYG was found to be more prevalent in men than in women in this study (6.5:1.0) than in previous reports (systemic LYG; 2:1[13] and isolated CNS LYG; 2.3:1.0[2]). Moreover, the lung lesion is the most common LYG lesion, although only 42.9% had lung lesions and 6 cases were isolated CNS LYG cases in our series. Previous studies reported that cerebral LYG frequently occurred in the brain parenchyma,[2] and spinal lymphoma, which is the same hematopoietic neoplasm as LYG, frequently involved intramedullary.[17] In this study, many of the spinal CNS LYGs were intramedullary lesions; similary, all 6 isolated CNS LYGs and 6 of 9 systemic CNS LYGs were intramedullary lesions (2 and 1 were extramedullary and epidural lesions, respectively). Hence, our result may be consistent with previous reports. In this series, of the 12 cases with intramedullary lesions, brain lesions were observed in all but 1 case. In addition, an intraaxial spinal lesion may be easy to concur with a brain lesion, and an isolated spinal LYG is extremely rare.

Furthermore, spinal lesion symptoms were indefinite. Most of which were myelopathy, and all cases had gait disturbance. In 12 cases with intraspinal cord lesions, the clinical symptoms were significant and 6 cases had only symptoms due to spinal lesions. Meanwhile, brain lesions were present in 11 cases. Symptoms may likely occur with the presence of spinal lesions. However, it is undeniable that the spine may not be examined, and asymptomatic cases may be overlooked as LYG is known to rarely occur in the spine. Although the lung is the initial manifestation site in >90% of patients, only 4 cases had symptoms other than CNS, such as fever and cough in this series. Hence the absence of these symptoms does not exclude spinal LYG.

## Imaging

In this series, spinal lesions were frequent in the cervical to upper thoracic and the prevalence of single lesion is relatively high at 71%. It was enhanced by gadolinium in all cases, such as in brain LYG lesions.[2,12] In the MRI of CNS-LYG, punctate or linear enhancement[1,18] is a relatively characteristic feature.[1] Regarding the enhancement characteristics of spinal medullary lesions, one-third was diffuse massive, one-third was punctate, and one-third was the others. In a previous report, microhemorrhage by hypointensity of T2*-weighted MRI is another characteristic feature of CNS LYG,[19] although there was no clear spinal lesion hemorrhage in our series. This result may be attributed to the difference between the brain and spine or may be because spinal microbleeding has not been examined in detail by T2*-MRI.

## Diagnosis, Histopathology, Treatment, and Outcomes

Lymphomatoid granulomatosis is a rare Epstein-Barr virus–associated B cell lymphoproliferative disorder, first described in 1972 by Leibow et al.[3] Histologically, LYG is polymorphous angiocentric and angiodestructive lymphoproliferative disease characterized by EBV-positive B cell proliferation associated with a predominantly T cell reaction.[2] LYG is characterized by small lymphocytes, plasma cells, histiocytes, and atypical lymphocytes along with areas with varying degrees of necrosis and vasculitis.[1] Because of the presence of predominant T cell infiltration, this disorder was initially thought to be a T cell disorder.[2] Subsequently, EBV-encoded small ribonucleic acid expressed by atypical large B cells were identified by immunohistochemistry and combined immunohistochemistry with in situ hybridization. Additionally, LYG was redefined as a B-lymphocyte disease and related to the EBV infection.[2,20,21] According to the World Health Organization Classification of Lymphoid Neoplasms revised in 2016, LYG is

**Table 1.** Characteristics of 15 Cases of Spinal Lymphomatoid Granulomatosis

| | | | | | | | Spinal Lesion | | | Clinical Lesion | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Authors (Reference Number) | Age/Sex | History | Immune System Status | Systemic Lesion of LYG | Brain Lesion | Number | MRI Enhancement | Level | Other Than CNS | Brain | Spine | LYG Grade/EBV | Surgery | Therapy | Follow-up | Prognosis |
| 1 | He et al.[2] | 22/Male | — | — | — | + | Multiple | Punctate and linear | C4, T4 | — | + | — | NL/− | BB | CY, ST | 1 | Death |
| 2 | Costiniuk et al.[8] | 35/Male | — | HIV | K, LN, S | + | Multiple | Linear | C~T | — | + | + | I/− (serum +) | BB | RI, ST HIV treatment | 34 | Improved |
| 3 | Kim et al.[11] | 60/Male | Tb, syphilis | — | BM | + | Single | NL | NL | — | — | + | II/+ | BB & BMB | IFNα2b, ST | 18 | Improved |
| 4 | Patil et al.[15] | 53/Male | — | — | — | + | Single | Punctate | C2 | — | + | — | NL/− | BB | CY, ST | 3 | Alive |
| 5 | Gaha et al.[1] | 56/Male | — | — | — | + | Single | Diffuse massive | T4-L1 | — | — | + | III/+ | BB | NL | NL | NL |
| 6 | Kim et al.[10] | 4/Female | ALL | PC for ALL | Lung, liver | — | Single | Extraaxial | T3-5 | + | — | + | II/+ | Removal | RI, ST | 72 | improved |
| 7 | Montano et al.[14] | 60/Male | — | — | LN, BM | — | Single | Extraaxial | C5-T1 | — | — | + | III/NL | Removal & BMB | CY, DX, VI, ST | 11 | Death |
| 8 | Lucantoni et al.[12] | 49/Male | — | NL | — | + | Single | Diffuse | C | — | — | + | I/− | BB | ST | 18 | Alive |
| 9 | Ishiura et al.[9] | 48/Male | Asthma, AD | — | Lung | + | Multiple | Punctate | C | — | — | + | I,II/+ | LB | RI | 18 | Improved |
| 10 | Carone et al.[6] | 29/Female | — | — | *Lung after the stage | + | NL | NL | C, T | — | + | + | NL/− | BB | CY, ST | 31 | Death |
| 11 | Patsalides et al.[16] | 53/Male | — | NL | NL | + | Multiple | Punctate | C | — | + | — | I/NL | NL | IFNα-2b | NL | NL |
| 12 | Miura et al.[13] | 28/Male | HP | PS for HP | Lung | + | Single | NL | C~T | + | — | + | I/NL | LB | CY, ST | 13 | Alive |
| 13 | Collins et al.[7] | 50/Male | — | — | Lung, S | — | Single | Extraaxial | C4-5 | + | — | + | NL/NL | LB & BMB | NL | NL | NL |
| 14 | Herderscheê et al.[5] | 19/Male | — | — | Lung | + | Single | Diffuse massive | T1-2 | + | — | + | NL/NL | LB | CY, ST | 5 | Death |
| 15 | Present case | 85/Male | HT, DM, AP | — | — | — | Single | Diffuse massive | C6 | — | — | + | III/+ | Spine biopsy | ST, radiation | 35 | Improved |

LYG, lymphomatoid granulomatosis; MRI, magnetic resonance imaging; CNS, central nervous system; EBV, Epstein-Barr virus; NL, not listed; BB, brain biopsy; CY, cyclophosphamide; ST, steroid; HIV, human immunodeficiency virus; K, kidney; LN, lymph nodule; BM, bone marrow; S, spleen; C, cervical; T, thoracic; RI, rituximab; Tb, tuberculosis; BMB, bone marrow biopsy; ALL, acute lymphocytic leukemia; PC, previous chemotherapy; DX, doxorubicin; VI, vincristine; AD, atopic dermatitis; LB, lung biopsy; IFN, interferon; HP, hypersensitivity pneumonia; PS, previous steroid; HT, hypertension; DM, diabetes mellitus; AP, angina pectoris. L, lumbar; L1, level of case 5.

*Lung lesion developed 25 months after diagnosis.

classified as a subclass of mature B cell tumors.[22] In previous reports, the pathological grade (including EBV infection) of the removed sample may not represent the complete state of the disease, and the sample from other lesions may be of different histological grade.[2,4,11,21] Since the size of the biopsy specimen of the brain and spinal cord is limited, it is undeniable that the grade and EBV infection rate may be affected by the location of the excision.

There is no standard treatment protocol for systemic LYG and isolated CNS LYG,[1,2,23] and drug treatments, such as systemic steroids, rituximab, and several chemotherapies, vary widely.[23] There are reports on the usefulness of rituximab for LYG including CNS LYG,[9,24,25] although it is not always effective.[24] Interferon-$\alpha$ was useful for low-grade LYG treatment including cases involving the CNS, and cyclophosphamide and prednisone were expected for high-grade LYG treatment. Combination immunochemotherapy including cyclophosphamide and rituximab is being attempted.[19,23] Treatment outcomes are affected by various factors, and discussing the best option for spinal LYG is beyond the scope of this study.

The prognosis of LYG varies, and the 5-year mortality rate was 60%–90%.[2,26] Although previous reports found that systemic LYG with CNS involvement had poor prognosis factors,[5,9,27] isolated CNS LYG had better prognosis than systemic LYG.[11,12] In our series, 8 of 12 patients survived, on average, 26.4 months. However, only 1 patient was followed up for >36 months and the prognosis of cases with spinal lesions cannot be mentioned from this study.

## CONCLUSIONS

We performed systematic review of the published English articles and investigated the clinical and imaging features and treatment of spinal LYG. It is rare and isolated spine-LYG is extremely rare. Thus further accumulation of cases may be necessary to better understand the characteristics of spinal LYG.

## REFERENCES

1. Gaha M, Souillard-Scemama R, Miquel C, et al. MR imaging of the brain and spinal cord in lymphomatoid granulomatosis: a case report and review of the literature. *J Neuroradiol*. 2013;40:364-367.
2. He C, Wang Y, Zhang L, et al. Isolated lymphomatoid granulomatosis of the central nervous system: a case report and literature review. *Neuropathology*. 2019;39:479-488.
3. Liebow AA, Carrington CR, Friedman PJ. Lymphomatoid granulomatosis. *Hum Pathol*. 1972;3:457-558.
4. Song JY, Pittaluga S, Dunleavy K, et al. Lymphomatoid granulomatosis—a single institute experience: pathologic findings and clinical correlations. *Am J Surg Pathol*. 2015;39:141-156.
5. Herderscheê D, Troost D, de Visser M, et al. Lymphomatoid granulomatosis: clinical and histopathological report of a patient presenting with spinal cord involvement. *J Neurol*. 1988;235:432-434.
6. Carone DA, Benedict RH, Zivadinov R, et al. Progressive cerebral disease in lymphomatoid granulomatosis causes anterograde amnesia and neuropsychiatric disorder. *J Neuroimaging*. 2006;16:163-166.
7. Collins S, Helme RD. Lymphomatoid granulomatosis presenting as a progressive cervical cord lesion. *Aust N Z J Med*. 1989;19:144-146.
8. Costiniuk CT, Karamchandani J, Bessissow A, et al. Angiocentric lymph proliferative disorder (lymphomatoid granulomatosis) in a person with newly-diagnosed HIV infection: a case report. *BMC Infect Dis*. 2018;18:210.
9. Ishiura H, Morikawa M, Hamada M, et al. Lymphomatoid granulomatosis involving central nervous system successfully treated with rituximab alone. *Arch Neurol*. 2008;65:662-665.
10. Kim I. Lymphomatoid granulomatosis with spinal involvement after childhood acute lymphoblastic leukemia. *Korean J Spine*. 2012;9:32-36.
11. Kim JY, Jung KC, Park SH, et al. Primary lymphomatoid granulomatosis in the central nervous system: a report of three cases [e-pub ahead of print]. *Neuropathology*. https://doi.org/10.1111/neup.12467, accessed April 10, 2018.
12. Lucantoni C, De Bonis P, Doglietto F, et al. Primary cerebral lymphomatoid granulomatosis: report of four cases and literature review. *J Neurooncol*. 2009;94:235-242.
13. Miura H, Shimamura H, Tsuchiya K, et al. Magnetic resonance imaging of lymphomatoid granulomatosis: punctate and linear enhancement preceding hemorrhage. *Eur Radiol*. 2003;13:2192-2195.
14. Montano N, Lucantoni C, Larocca LM, et al. Cervical extramedullary lymphomatoid granulomatosis. *J Clin Neurosci*. 2011;18:851-853.
15. Patil AK, Alexander M, Nair B, et al. Clinical, imaging and histopathological features of isolated CNS lymphomatoid granulomatosis. *Indian J Radiol Imaging*. 2015;25:56-59.
16. Patsalides AD, Atac G, Hedge U, et al. Lymphomatoid granulomatosis: abnormalities of the brain at MR imaging. *Radiology*. 2005;237:265-273.
17. Novello M, Lauriola L, Della Pepa GM, et al. ALK-positive anaplastic large cell lymphoma presenting as intradural spinal mass: first reported case and review of literature. *Neuropathology*. 2013;33:418-423.
18. Brazis PW, Menke DM, McLeish WM, et al. Angiocentric T-cell lymphoma presenting with multiple cranial nerve palsies and retrobulbar optic neuropathy. *J Neuroophthalmol*. 1995;15:152-157.
19. Fujimaki M, Kawajiri S, Ichikawa K, et al. Lymphomatoid granulomatosis with central nervous system involvement successfully treated with cyclophosphamide, high-dose Cytarabine, Dexamethasone, Etoposide, and Rituximab (CHASER therapy) followed by brain irradiation: a case study. *CNS Neurosci Ther*. 2015;21:610-612.
20. Connors W, Griffiths C, Patel J, et al. Lymphomatoid granulomatosis associated with azathioprine therapy in Crohn disease. *BMC Gastroenterol*. 2014;14:127.
21. Katzenstein AL, Doxtader E, Narendra S. Lymphomatoid granulomatosis: insights gained over 4 decades. *Am J Surg Pathol*. 2010;34:35-48.
22. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood*. 2016;127:2375-2390.
23. Melani C, Jaffe ES, Wilson WH. Pathobiology and treatment of lymphomatoid granulomatosis, a rare EBV-driven disorder. *Blood*. 2020;135:1344-1352.
24. Fernandez-Alvarez R, Gonzalez M, Fernandez A, et al. Lymphomatoid granulomatosis of central nervous system and lung driven by Epstein-Barr virus proliferation: successful treatment with rituximab-containing chemotherapy. *Mediterr J Hematol Infect Dis*. 2014;6:e2014017.
25. Quinones E, Potes LI, Silva N, et al. Lymphomatoid granulomatosis of the brain: a case report. *Surg Neurol Int*. 2016;7:S612-S616.
26. Liu H, Chen J, Yu D, et al. Lymphomatoid granulomatosis involving the central nervous system: a case report and review of the literature. *Oncol Lett*. 2014;7:1843-1846.
27. Katzenstein AL, Carrington CB, Liebow AA. Lymphomatoid granulomatosis: a clinicopathologic study of 152 cases. *Cancer*. 1979;43:360-373.

*Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.*

*Received 4 December 2020; accepted 19 April 2021*

*Citation: World Neurosurg. X (2021) 11:100106. https://doi.org/10.1016/j.wnsx.2021.100106*

*Journal homepage:* ***www.journals.elsevier.com/world-neurosurgery-x***

*Available online:* ***www.sciencedirect.com***