



Case Report

Miliary pattern in secondary central nervous system T-cell lymphoma

Sibi Rajendran, Jonathan J. Lee, Hung Ba Le, Gavin Britz

Department of Neurosurgery, Neurological Institute, Houston Methodist Hospital, Houston, Texas, United States.

E-mail: *Sibi Rajendran - srajendran2@houstonmethodist.org; Jonathan J. Lee - jjlee@houstonmethodist.org; Hung Ba Le - hble@houstonmethodist.org; Gavin Britz - gbritz@houstonmethodist.org



*Corresponding author:

Sibi Rajendran,
Department of Neurosurgery,
Neurological Institute, Houston
Methodist Hospital, Houston,
Texas, United States.

srajendran2@
houstonmethodist.org

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ABSTRACT

Background: Secondary central nervous system lymphoma may manifest in a variety of ways on imaging, but most commonly presents with leptomeningeal disease, isolated parenchymal lesions, or both. We present a case of secondary central nervous system T-cell lymphoma with miliary pattern of spread noted on imaging.

Case Description: Our patient had known systemic T-cell lymphoma involving the gastrointestinal and respiratory tracts and underwent stereotactic biopsy confirming secondary cerebral metastasis. This spread pattern is an uncommon manifestation of disease and in our experience carries a very poor prognosis.

Conclusion: We highlight the need to maintain a broad differential diagnosis that includes other metastatic disease and infectious etiologies, including toxoplasmosis and tuberculosis. High clinical suspicion and timely confirmatory testing including biopsy or cerebrospinal fluid flow cytometry are critical to treatment.

Keywords: CNS lymphoma, Miliary spread, T-cell lymphoma

INTRODUCTION

Adult T-cell leukemia/lymphoma (ATLL) is a type of non-Hodgkin's lymphoma that may manifest broadly, with multiorgan system involvement being common. Although classically linked to infection with human T-cell lymphotropic virus type 1, only about 5% of those infected may go on to develop ATLL.^[7] Cerebral or spinal cord involvement (secondary central nervous system lymphoma [SCNSL]) may develop in later stages and is both less common and more aggressive than systemic lymphoma alone. Diffuse large B-cell lymphoma, the most common B-cell lymphoma, accounts for ~40% of all lymphomas, while ALK-positive anaplastic large T-cell lymphoma (as described in this case presentation) accounts for only 0.3% of cases.^[10] CNS involvement in ATLL is estimated to occur in approximately 10% of cases, much lower than reported in B-cell lymphomas.^[6,7,11] The diagnosis of SCNSL is often made by stereotactic or open biopsy of a lesion but can sometimes also be made by flow cytometry study of cerebrospinal fluid specimen.^[8] CNS involvement in systemic lymphomas is almost universally fatal, making accurate diagnosis paramount.

On imaging studies, leptomeningeal spread is the more common presentation of SCNSL, with only one-third of these patients having parenchymal disease.^[7] In those with parenchymal

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disease, typically, there is only a single or few enhancing lesions in the superficial, periventricular region.^[3] Patients may also present with spinal spread, which can lead to back pain and/or radiculopathy.^[12] The imaging study of choice for evaluation of both brain and spinal lesions remains contrast enhanced MRI.^[2]

Here, we describe a miliary spread pattern of SCNSL in a patient with known systemic lymphoma involving the gastrointestinal and respiratory tracts. A miliary spread pattern reflects small, innumerable focal lesions. Although the spread is often used to describe the spread of tuberculosis, the miliary pattern in the CNS have been reported in metastatic progression.^[9] We emphasize the importance of recognizing this pattern, as secondary cerebral lymphoma rarely presents in this manner but should be in the differential diagnosis for clinicians when present on imaging studies.

ILLUSTRATIVE CASE

A 61-year-old male with prior history of T-cell lymphoma with 3 months of chemotherapy presented to the emergency department with obtundation, fever, chills, and diarrhea. The patient also had a history of deep venous thrombosis and pulmonary embolism and was on therapeutic anticoagulation. His known lymphoma had infiltrated the bowel, causing typhilitis of the terminal ileum and cecum, along with pulmonary involvement, leading to bilateral pleural effusions with ground-glass opacification and alveolar opacities. His chemotherapy course was complicated by respiratory failure, sepsis, and acute tubular necrosis, all of which eventually resolved.

Before admission, imaging at an outside facility showed extensive vasogenic edema in the right frontal, left parietal, bilateral temporal, and left cerebellar regions. On arrival to hospital, the patient became unresponsive, with agonal breathing and unequal pupils. With concern for underlying herniation syndrome, level of care was escalated to the neurointensive care unit. Noncontrast computed tomography of the head revealed rounded, slightly dense intra-axial lesions in the left temporal, left basal ganglia, left occipital lobe, and right temporal lobe with extensive surrounding vasogenic edema [Figure 1]. Additional lesions were seen in the superior cerebellum and brainstem with extensive edema. Given his prior medical history, lesions were suspicious for multifocal lymphoma; the other differential diagnoses included cerebral toxoplasmosis, neurocysticercosis, and multiple abscesses. There was no acute hemorrhage or midline shift.

Contrast-enhanced MRI of the neuroaxis [Figures 2 and 3] revealed lesions throughout the brain, cervical, and thoracic spine, with an enhancement of the leptomeninges most prominently seen in the thoracic spine. Notable spinal lesions

included osseous hyperdensities in the T6, T8, T12, L1, L4, and L5 vertebrae concerning for metastases, and a C7-T1 0.5 × 1.2 × 1.4 cm intradural, extramedullary lesion. Given the wide differential diagnosis, the patient was taken for a right-sided temporal craniotomy with biopsy under stereotactic navigation. Steroids were not administered before the craniotomy. Final pathology report revealed ALK-positive anaplastic large T-cell lymphoma, with tumor cells positive for CD4, CD45, and CD30. Reactive astrocytosis with cavitation and rarefaction of brain parenchyma was noted.

On postoperative day 1, the patient remained unresponsive and critically ill. Laboratory studies at this time revealed positive IgG antibody against toxoplasmosis. After infectious disease consultation, the patient was started on sulfadiazine and pyrimethamine for empiric toxoplasmosis treatment. On postoperative day 3, both pupils were 2 mm and nonreactive, and imaging showed communicating hydrocephalus. An external ventricular catheter was placed for intracranial pressure (ICP) monitoring and therapeutic ventricular drainage. Emergency precautions for ICP included head of bed elevation, blood pressure control, and deep sedation. ICPs remained elevated despite this measure, and on postoperative day 7, the patient lost all brainstem reflexes, with bilateral fixed and dilated pupils. The patient developed severe thrombocytopenia requiring multiple platelet transfusions and hemodynamic instability requiring support with norepinephrine, phenylephrine, epinephrine, and vasopressin drips. After family discussion about goals of care and poor neurological prognosis, care was withdrawn and the patient expired.

DISCUSSION

Lymphomas may present in the CNS in many forms, often meaning a broad differential diagnosis exists when initially discovered. A solitary or few lesions in the CNS without any systemic involvement would raise concern for primary CNS lymphoma, especially in the context of an immunocompromised patient. Secondary CNS lymphoma (SCNSL) often presents with leptomeningeal enhancement, but when parenchymal disease is present, usually only manifests as a solitary mass or as a few lesions. Here, we described a case of miliary SCNSL, with innumerable ring-enhancing lesions throughout the brain, cervical, thoracic, and lumbar spine.

It is important to discuss the differential diagnosis when imaging studies show the miliary pattern of lesion spread. The percent of SCNSL (of any kind) presenting with miliary spread is difficult to quantify, with even case reports being scant, making a broad differential, especially important when suspicion exists. Infectious disease, including cerebral toxoplasmosis, neurocysticercosis, and certain fungal

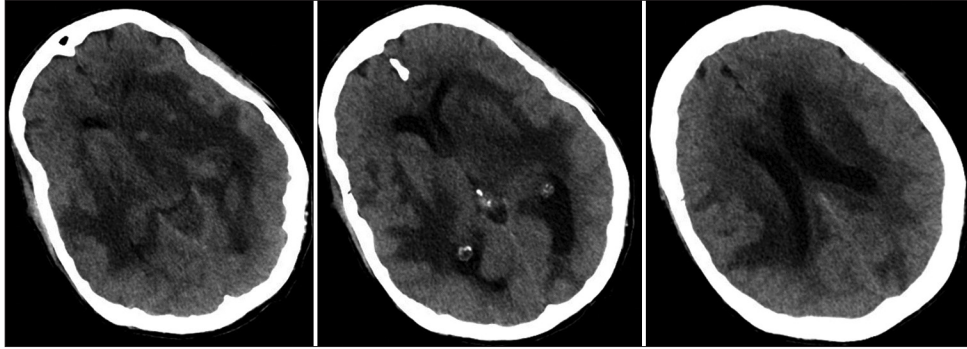


Figure 1: Axial noncontrast head CT at presentation showing extensive edema.

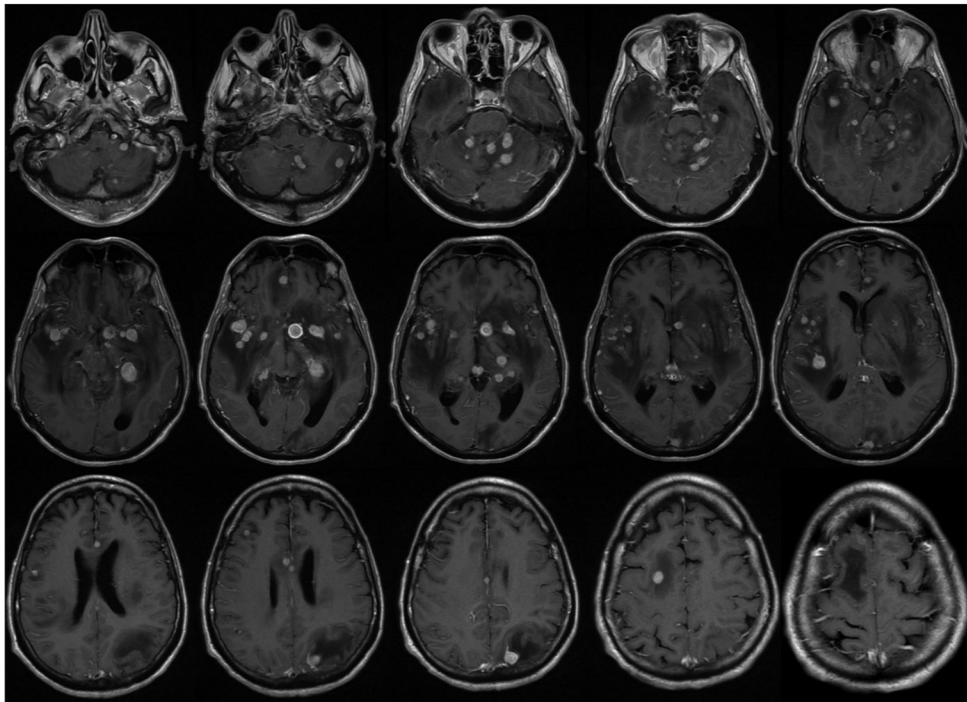


Figure 2: Axial contrast-enhanced T1 MRI brain at presentation showing extensive metastatic cerebral T-cell lymphoma.

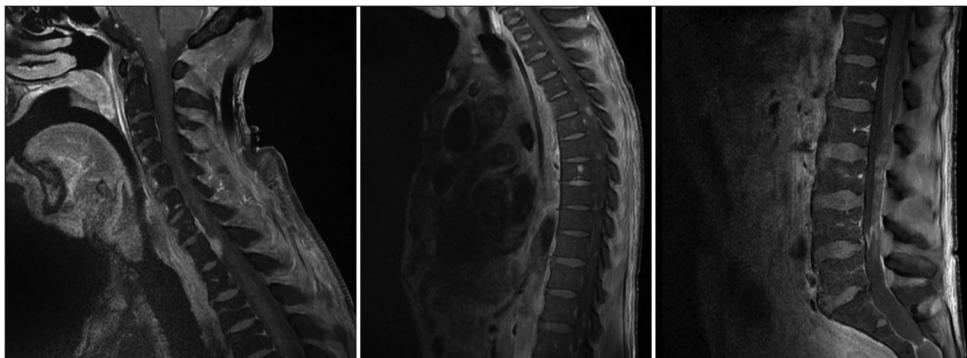


Figure 3: Sagittal contrast-enhanced T1 MRI, cervical, thoracic, and lumbar spine showing spinal cord involvement of metastatic cerebral T-cell lymphoma.

Study	History	Disease	Treatment	Survival
Zuber (1989)	60-year old man with no relevant past medical history presenting walking difficulties of recent onset	IgM kappa secreting B-cell lymphoma	n/a	Expired after 2-weeks of admission due to respiratory failure
Yagy (2020)	82-year old woman with a 1-month history cough, 10-year of type 2 diabetes, previous resection of the rectum for rectal cancer stage I, and previous treatment of metastatic liver tumor.	Follicular lymphoma and intrapulmonary small metastases	R-CHOP Therapy (rituximab 375 mg/m ² , cyclophosphamide 750 mg/m ² , liposomal doxorubicin 50 mg/m ² , vincristine sulfate 1.4 mg/m ² on day 1 and prednisone 40 mg/m ² on day 1–5 of a three-week cycle).	Complete Remission, improvement to symptoms, and abnormal radiographic findings have diminished

Figure 4: Other presentation of lymphoma with miliary pattern of spread.

diseases, may present similarly. Metastatic disease from other cancers is also on the differential diagnosis, with case reports of melanomas and lung cancers in the literature presenting with miliary cerebral spread.^[4,9]

OBSERVATIONS

Infectious disease may be a confounding variable when looking at imaging. As many patients with lymphoma are immunocompromised due to disease or treatment burden, opportunistic pathogens may lead to a convoluted clinical picture. Indeed, our patient even had positive IgG serology for toxoplasmosis and underwent empiric therapy. It is important here to realize that approximately one-third of the world's population has IgG seropositivity for toxoplasma, making further confirmatory testing for active infection crucial.^[5] In our patient with known risk factors for active toxoplasmosis infection (chemotherapy and prior lymphoma diagnosis), biopsy was especially critical to confirm SCNSL.

Finally, a point should be made on the rarity of SCNSL in general. While data are conflicting, it appears that T-cell lymphoma is in general more likely to have secondary CNS involvement, roughly twice as likely compared to B-cell lymphoma.^[6,11] However, due to sheer volume of cases of B-cell lymphoma compared to T-cell lymphoma, the vast majority of SCNSL is of B-cell lineage.^[10] There are specific examples of B-cell lymphoma with miliary pattern of spread found commonly in the literature that can be used for further studies [Figure 4].^[13,14] Chemotherapy remains the workhorse of treatment for all types of lymphoma, with specific protocols targeted to molecular profiles and lymphoma subtypes. Intrathecal delivery of these medicines is common in those with SCNSL and is even used prophylactically in those with high risk of CNS metastasis.^[1] Despite numerous advances in medical therapies, prognosis still remains dependent on subtype and spread, with SCNSL and T-cell lineage being poor prognostic indicators.

CONCLUSION

SCNSL may present with a wide array of imaging findings. We present a case of a miliary spread of adult T-cell lymphoma

in the brain, a rare imaging finding in SCNSL. Although the differential diagnosis for miliary disease is typically tuberculosis and other metastatic or infectious disease, lymphoma should be considered. Patients have a very poor prognosis with SCNSL in general, but this is especially true in those with this miliary spread pattern.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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