Intravascular Lymphoma: When Tissue is the Issue

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Introduction

- Intravascular large B-cell lymphoma (IVLBCL) is a malignancy characterized by proliferation of abnormal B-cells within blood vessels[1].
- IVLBCL has in incidence of one case per million people per year[1].
- Heterogeneous organ involvement leads to diverse clinical manifestations.

Case: A 66 year old man with leg weakness

HPI:

- A 66-year-old man was transferred to the MICU for encephalopathy and respiratory failure in the setting of worsening lower extremity weakness.
- Hospitalized 3 times in preceding 4 months for bilaterally lower extremity weakness thought to be due to transverse myelitis
- He recovered with steroid therapy with shortening duration of remission.

Objective data:

- Vitals: afebrile HR 130 BP 95/63 RR 40 SpO2 90% on HHFNC 40/40
- Exam: ill-appearing, somnolent, tachypneic, with bibasilar crackles, right upper quadrant tenderness, peripheral edema, and petechiae on his left arm.
- CT chest/abdomen/pelvis without malignancy or infection.
- Labs and brain MRI shown in Fig. 1.

Management:

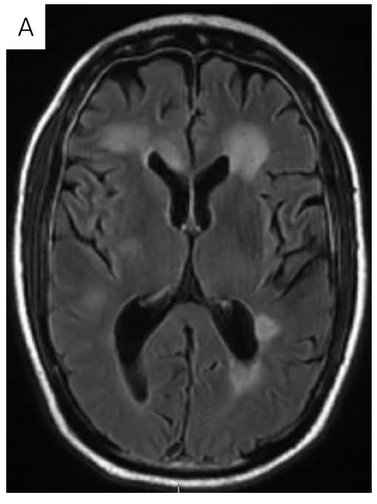
- Treated with broad spectrum antibiotics. Neurology consulted, recommended brain biopsy which was not within his goals of care.

Outcome:

- Aspiration event led to cardiac arrest in setting of DNI status.
- Found to have widely disseminated IVLBCL on autopsy (Figure 2).

Figure 1 Laboratory and imaging findings on admission to the ICU

A



B

Serum laboratory data

	12.2	
6.8		58

151	116	56
3.8	22	1.12

236

Alk Phos 102, **T bili 9.8**
AST 68, ALT 107, Albumin 2.6
LDH: 647, Lactate: 5.9

Cerebrospinal fluid analysis

Glucose 103, Protein 248, LDH 70, 2 RBC, 8 WBC (85% lymphocytes). Viral serologies & cultures negative.

(A) MRI brain with contrast showed small scattered supratentorial foci of diffusion restriction, susceptibility signal and prominent T2/FLAIR hyperintensity in the periventricular white matter, subcortical white matter and brainstem. No enhancing lesions or definitive hyperperfusion. (B) Serum and CSF laboratory data, with abnormal values highlighted in bold font.

Figure 2 Autopsy findings of IVLBCL

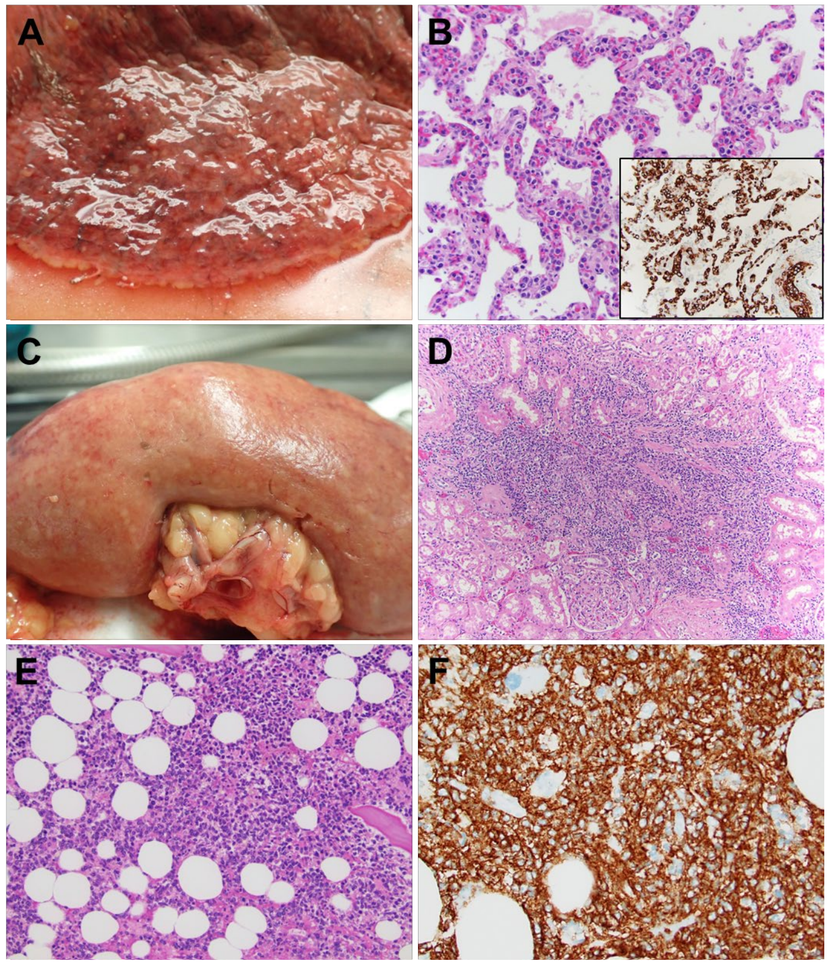
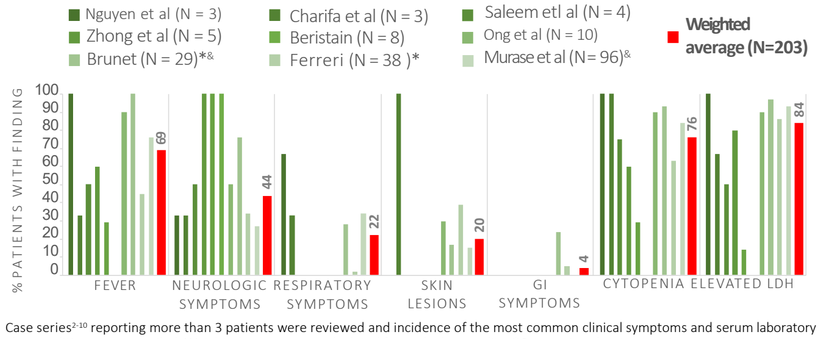


Figure 2(A) shows lung and (C) kidney with diffuse tan stippling. (B) Pulmonary capillaries filled with large, atypical lymphocytes (H&E, 20x objective), confirmed by CD20 immunohistochemical stain (insert, 20x objective). (D) Renal parenchyma with atypical lymphoid aggregates (H&E, 10x objective). (E) Hypercellular bone marrow due to lymphomatous involvement, (F) confirmed by diffuse CD20 immunoreactivity (H&E, 40x objective).

Figure 3 Varied clinical manifestations of IVLBCL



Case series[2-10] reporting more than 3 patients were reviewed and incidence of the most common clinical symptoms and serum laboratory abnormalities were compiled. Weighted average was calculated for each abnormality. *Cytopenia refers to anemia as total cytopenias not reported. & Fever refers to "B-symptoms" as fever not reported individually.

Discussion

- Clinical symptoms vary dramatically between patients, but neurological symptoms and fever are the most common manifestations (Fig 3).
- Most patients have cytopenia and elevated LDH (Fig 3).
- Because malignant cells are adherent to blood vessels, peripheral smear is almost always normal and there is no lymphadenopathy or mass.[1]
- When there is CNS involvement, CSF analysis may be normal or may show elevated protein, LDH, and/or mild leukocytosis.
- Tissue biopsy is essential for diagnosis.
- Incisional random skin biopsy offers a non-invasive means of diagnosis IVLBCL (Table 1)[11-13]

Table 1 Sensitivity and specificity of random skin biopsy

Authors	Study site	Population	Biopsy method	Sensitivity	Specificity
Matsue et al	Kameda General Hospital, Japan	111 patients with suspected IVLBCL	Incisional	79%	99%
Rozenbaum et al	Massachusetts General Hospital, USA	56 patients with suspected or known IVLBCL	Incisional or Punch	50%	100%

Conclusions

- **The clinical features of Intravascular large B-cell lymphoma vary widely among patients.**
- **The diagnosis should be considered in patients presenting with fever and neurological deficits of unknown cause, especially in the presence of cytopenias and elevated serum LDH.**
- **Random skin biopsy, specifically incisional biopsy of 3 or more sites, can offer an alternative to more invasive biopsy testing but should not be used to rule out IVLBCL.**

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