An autopsy case report of intravascular large B-cell lymphoma with initial neurologic presentation

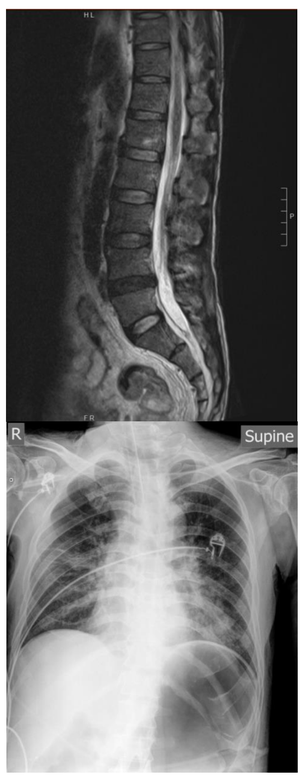
Fong Tsun, M.B.C.h.B., Tseung Kwan O Hospital

Introduction

Intravascular large B-cell lymphoma is defined as a rare type of extranodal large B-cell lymphoma characterized by the selective growth of lymphoma cells within the lumina of blood vessels, in particular capillaries, and with the exception of larger arteries and veins [1]. Here, I present an autopsy case of intravascular large B-cell lymphoma in a 60 years old Chinese male who initially presented with neurological deficit.

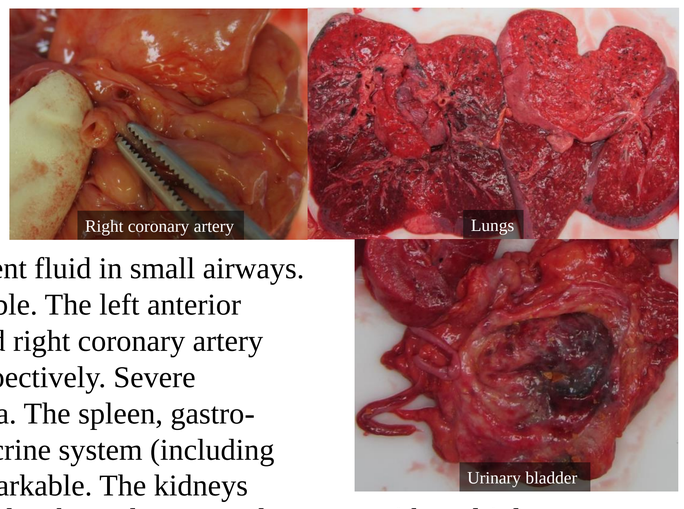
Case presentation

Clinical findings



The deceased was a 60-year-old Chinese male with a history of diabetes, hyperlipidemia, right internal capsule old infarct and tuberculosis lung abscess. He was initially admitted to the medical unit for low back pain and bilateral lower limb weakness. He developed acute retention of urine, increasing lower limb weakness, lower limb areflexia and confusion later. Initial blood tests showed mild anemia, hyponatremia, reduced thyroxine (T4) and triiodothyronine (T3) and markedly elevated lactate dehydrogenase (LDH)(1341 U/L), ferritin (10722 pmol/L), C-reactive protein (CRP)(110 mg/L) and erythrocyte sedimentation rate (ESR)(102 mm/hr). Initial neurological workups including CT brain and EEG were unremarkable. MRI spine was performed and showed nerve root enhancement at cauda equina and Guillain-Barre syndrome was suspected. MRI brain showed small old infarcts in right parietal lobe and right basal ganglia only. Lumbar puncture was performed and showed elevated protein level, white cell count (lymphocytic predominant) and normal glucose level. Nerve conduction test and electromyography showed evidence of sensory and motor axonal polyneuropathy with active denervation. Cytology study on cerebrospinal fluid was negative. Extensive microbiological, virological and metabolic investigations were unremarkable. Autoimmune antibodies and screening for multiple myeloma were all negative. The working diagnosis was Guillain-Barre syndrome with Bickerstaff encephalitis. He was treated with IVIG with partial improvement of mental status but persistent neurological deficits. Subsequently the patient developed high swinging fever with sputum culture yielding methicillin-resistant Staphylococcus aureus and patchy haziness on chest X-ray. Antibiotics were given. The patient eventually passed away two months after admission. The case was referred to the Coroner's court due to uncertain cause of death and the family of the deceased agreed for autopsy.

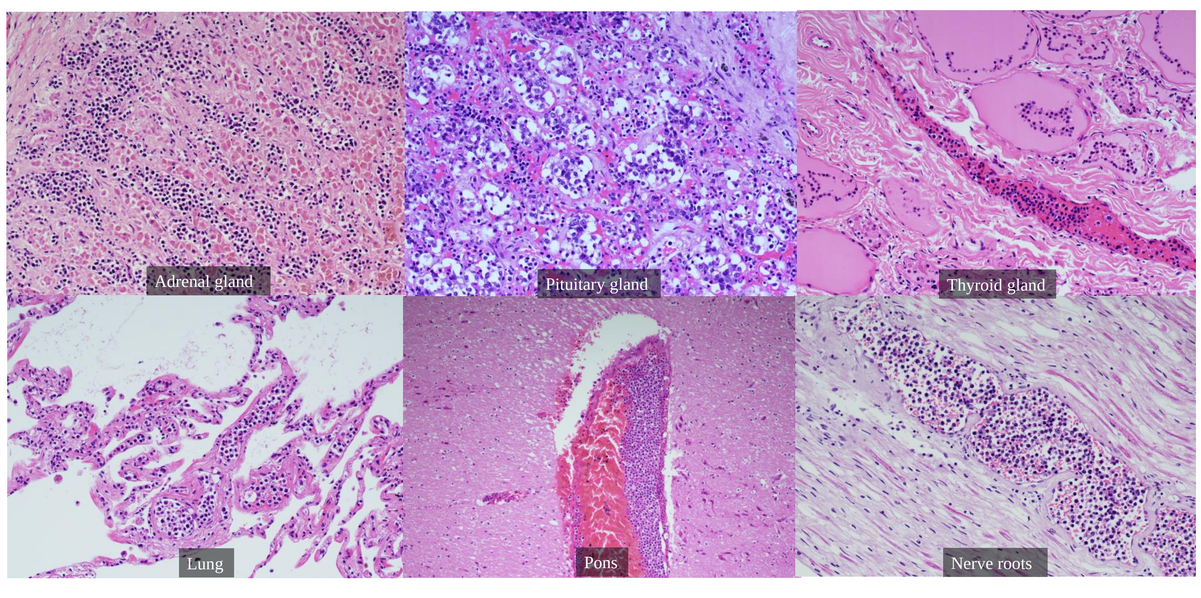
Macroscopic findings



External examination revealed generalized muscle wasting of both lower limbs and bedsores over sacrum and left ankle. Internal examination showed grossly unremarkable skull, brain, meninges, spinal cord and nerve roots. The lungs were heavy and congested with occasional purulent fluid in small airways. The pericardium and heart were unremarkable. The left anterior descending artery, left circumflex artery and right coronary artery showed 70%, 70% and 80% of stenosis respectively. Severe atheromatous changes were seen in the aorta. The spleen, gastro-intestinal, hepatopancreatobiliary and endocrine system (including adrenals, pituitary and thyroid) were unremarkable. The kidneys showed granular surfaces. The urinary bladder showed congested mucosa with multiple stones.

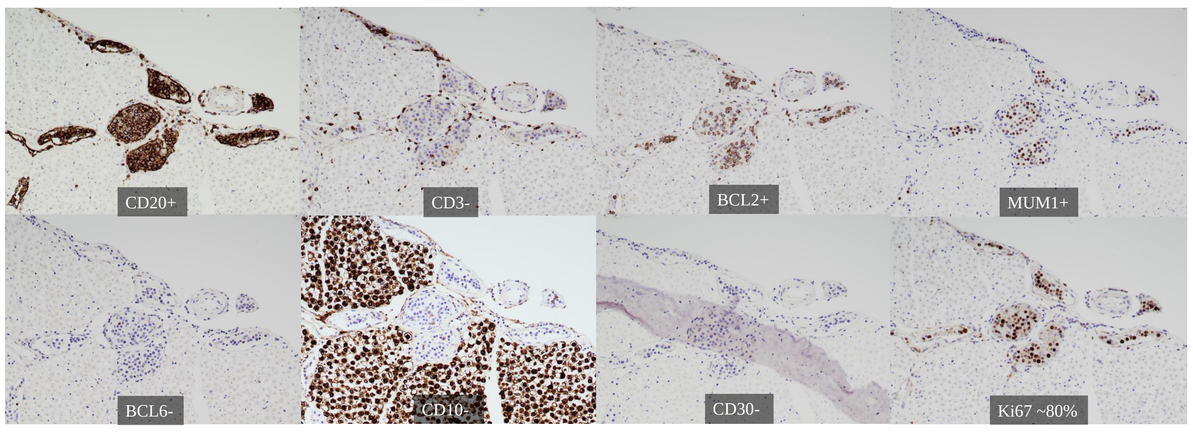
Microscopic findings

The most significant finding was the presence of large malignant lymphoid cells with irregular nuclei and occasional distinct nucleoli in the small blood vessels of cauda equina, spinal cord, brain, pituitary gland, thyroid gland, adrenal glands, lungs, epicardium, spleen, kidneys and urinary bladder.

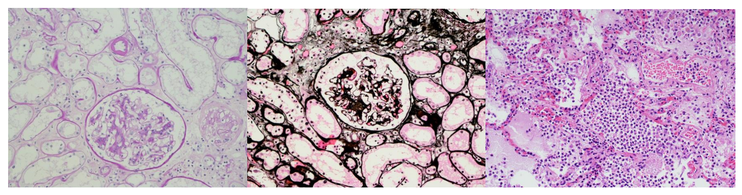


Case presentation

The large lymphoid cells were diffusely positive for CD20, BCL2, MUM1 and negative for CD3, BCL6, CD10, CD30 and ALK. No kappa or lambda light chain restriction was demonstrated. Ki67 index was about 80%.



Other significant findings include alveolar neutrophils in lungs, consistent with pneumonia and the presence of diabetic nephropathy in kidneys.



Diagnosis and follow-up

The cause of death was issued as pneumonia with intravascular large B-cell lymphoma as the underlying cause and diabetes mellitus as a contributing factor.

Discussion

Clinico-pathological correlation

In our case, there is infiltration of lymphoma cells in the brain, spinal cord and nerve roots, correlating to the various neurological deficits detected clinically including bilateral lower limb weakness, areflexia, acute urinary retention and altered mental status. Such presentation can closely mimic a demyelinating process, as shown in our case and another case report [2]. The presence of hyponatremia and reduced thyroid hormones could be related to lymphoma infiltration in adrenal glands, pituitary gland and thyroid gland. Anemia and elevated ESR, CRP, LDH and ferritin levels are all typical in the setting of intravascular lymphoma [3-5].

Literature review

Intravascular large B-cell lymphoma is a rare type of extranodal large B-cell lymphoma occurring in adults. The median age is 67 years but it can occur over a wide age range from 13 to 90 years. No significant male or female predominance is observed [6].

Two different forms of clinical presentation have been described [6]. One is the classic form, which is more commonly seen in Western countries and is characterized by frequent skin and central nervous system involvement. Haematolymphoid organ involvement is less common. The other one is haemophagocytosis-related form. It is more common in Japan and shows almost constant involvement of the haematolymphoid organs and nearly always spares the skin. B-symptoms are common in both types. An isolated cutaneous variant has been described and occurs in women only [7]. Due to the heterogeneity in presentation and lack of diagnostic algorithm, up to 53% of the cases were diagnosed during autopsy in the past [8]. But with increased recognition, more and more cases are diagnosed in vivo (>80%) [5,7]. Random skin biopsy from normal-appearing skin was shown to be very useful in the diagnosis of intravascular B-cell lymphoma with 77.8% sensitivity and 98.7% specificity [9]. The lymphoma cells are typically in the blood vessels in subcutaneous tissue but not the dermal vessels. Bone marrow biopsy is also useful in diagnosis in some cases [4].

Pathologically, the lymphoma cells are found in small blood vessels, typically capillaries and post-capillary venules. Medium-sized blood vessels and sinusoids can also be affected, but not large arteries, large veins or lymphatics [3]. The lymphoma cells are typically large with vesicular nuclei, distinct nucleoli and brisk mitosis. Occasionally irregular nuclei and smaller cell size may be encountered [3]. Haemophagocytosis may be seen. Immunohistochemically, the lymphoma cells are positive for CD20, BCL2 and often shows a non-GCB phenotype by Hans algorithm, with MUM1 positivity, CD10 and BCL6 negativity [5]. CD5 positivity is observed in a subset of cases. PD-L1 positivity is present in 44% of patients in a small case series [10]. In-situ hybridization for EBV-encoded RNA (EBER) is almost always negative [5]. Recently, a study shows that MYD88 (44%) and CD79B (26%) mutations are common in intravascular large B-cell lymphoma [11].

The prognosis of intravascular B-cell lymphoma is in general poor but has improved significantly over the years with the use of chemotherapy which is often anthracycline-based [3]. The isolated cutaneous variant has better prognosis in general [7]. The addition of rituximab to anthracycline-based chemotherapy also appears to improve the outcome of patients [12,13].

Conclusion

Intravascular large B-cell lymphoma is a rare lymphoma in adults. Diagnosis is often missed due to heterogeneous clinical presentation. High clinical suspicion is required for diagnosis. Early diagnosis is crucial as chemotherapy with rituximab therapy can significantly increase the survival.

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