Competing differentials may coexistent in patient living with HIV; Guillain Barre and Burkitt lymphoma

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HISTORY

A 68 year old Ukranian man presenting with lower limb weakness, increased work of breathing and general fatigue worsening over a two week period. His background history included a new HIV diagnosis 5 months previously and he was also diagnosed with stage 4 diffuse large b-cell lymphoma (DLBCL) at that time. **CD nadir was 17(4%) cells/mm^3.**

He was commenced on bictegravir, tenofovir alafenamide, and emtricitabine and received 6 cycles of rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine and prednisolone (R-CHOP) chemotherapy. A Positron Emission Tomography (PET) CT done two weeks prior showed complete remission. His **CD4 count was 48 (38.2%) cells/mm^3** and his **HIV viral load not detected** at his routine HIV out-patient appointment two weeks prior to presentation.

On examination he had global limb weakness, worse in lower limbs with absent lower limb reflexes. Bilateral lateral rectus palsy was noted and work of breathing continued to increase with rising arterial pCO_2 requiring intubation. Clinically findings were consistent with Guillain Barre Syndrome (GBS) and ocular involvement suggested Miller-Fisher variant. Serological samples including EBV, CMV serology and autoantibodies including antiganglioside and anti-GQ1b were taken prior to the initiation of intravenous immunoglobulin.

Lumbar puncture was performed when patient presented to Emergency Department to rule out any opportunistic infection and other pathology that may contribute to the patient's presentation. **Cerebrospinal fluid examination showed 810 WCC/mm, predominantly lymphocytic (60%), raised protein (7959mg/l), low glucose (<0.1mmol/l).**

An MRI brain and whole spine was done urgently on transit from ED to the intensive care unit reported normal age related changes. ***Campylobacter jejuni* was confirmed on stool polymerase chain reaction**. **Anti-ganglioside antibodies were positive in serum.**

The initial very high protein was not consistent with GBS, and given the patients epidemiology, HIV status, persistent immunosuppression with chemotherapy, and recent remission status it was felt *mycobacterium tuberculosis*(TB) meningitis must be out ruled and treatment with rifampicin, isoniazid, ethambutol and pyrazinamide was commenced until TB diagnostics were complete. **Flow cytometry subsequently identified Burkitt's lymphoma and CSF EBV was 24,760,676 copies/ml.** Findings confirm a diagnosis of Burkitt lymphoma

He was then transferred to ICU for intubation for airway protection and for close monitoring. He was treated thoroughly with TB medication, HIV medication but showed no signs of recovery. The **decision to palliate the patient** was made, as combined pathology rendered him unfit for intrathecal chemotherapy and with no meaningful chance of recovery. As study, shows HIV-TBM co-infected individuals have a two-fold greater case fatality rate than HIV-negative patients. [4] Information was disclosed to family in a family meeting explaining the situation and family agreed for palliation. However, respecting to patients wishes, his status for **HIV was not disclosed by healthcare professionals as part of patient-doctor confidentiality**.

DISCUSSION

HIV is well-known to be connected to sexual activity (vertical transmission) or blood borne transmission (via intravenous drug use ; sharing needles, needle stick injury). With the advancement of medicine now in the modern era, antiretroviral therapy has been doing wonders for HIV patients. They now have a significantly better life expectancy with medication. [6]

Tuberculosis (TB) is the second most common cause of death due to a single infectious agent worldwide after COVID-19. Up to 15% of the cases are extrapulmonary, and if it is located in the central nervous system (CNS-TB), it presents high morbidity and mortality. [2]

It is recommended clinicians should be vigilant against the disease (TBM), and suspected patients should be treated with anti-tuberculosis drug based on rich clinical experience without waiting for confirmatory testing.[3]

The complexity of this case warranted us to go further into delving into management and treatment plan. Given the fact that the patient is very compliant to HIV medication and was doing well with medication, coming regularly to appointments, demonstrates how HIV at times can still cause reactivation of infections ie TB as in this case.

Treatment outcomes for adult tuberculous meningitis are very poor, especially for patients diagnosed in stage III or HIV co-infection. [3]

The biggest challenge however is disclosing the patient's HIV status to the family which is somewhat controversial in this context. It was patient's wish that his HIV positive status is not disclosed to family members but he managed to persuade family to get tested without exposing himself having HIV.

In Ireland, it is not mandatory to disclose HIV status to partner but there are cases that has been justified in court deemed punishable.

HIV remains to be a notifiable disease via the Health Protection Surveillance Centre (HPSC)/Department of Public Health. HIV must be notified by a medical practitioner "as soon as he becomes aware or suspects that a person on whom he is in professional attendance is suffering from or is the carrier of an infectious disease" (Infectious Diseases Regulations 1981) [1].

It is also the mandatory obligation for a clinical director of a diagnostic laboratory to initiate notification "as soon as an infectious disease is identified in that laboratory" (Infectious Diseases (Amendment) Regulations 2003. SI No. 707 of 2003). [1]

OLOL Hospital	OLOL Hospital	OLOL Hospital	LCH / Beaumont Hospital	LCH / Beaumont Hospital	Beaumont Hospital
July 2023	August 2023	Sept 2023	Oct 2023	Nov 2023	Dec 2023
• Initial presentation to ED for bradycardia and was seen by cardiology team OLOL. Symtpoms were managed and resolved. • Patient was then discharged. He then came back again for **persistent diarrhoea** and was admitted for OGD and biopsy.	• Biopsy result came back **positive for Gastric Lymphoma with PET scan confirming a stage 4 lymphoma.** He was initially treated with R-CHOP regime by haematology team. The decision to test for HIV was done. • HIV test was noted to be positive and subsequent referral was made to Infectious diseases team which then took over care of the patient • He was noted to have shingles (possibly reactivation due to immunosuppression). • He was then started on **Biktarvy** for HIV.	• Patient was well throughout stay in ward and showed steady progression of improvement whilst being on treatment. • He had placement issue as he had no permanent residence hence his social issue is being managed and looking at best option for him to come to Beaumont Hospital for appointment. • He was then stepped down to LCH to facilitate his appointments while waiting for permanent placement.	Patient was awaiting for placement and was under ID Beaumont Hospital HIV OPD follow up		• Came back to ED OLOL, presented with descending paralysis, reduced GCS and **LP was done confirming GBS/Miller-fisher variant with co-infection of TB and Burkitt's lymphoma** • Brought to ICU for close monitoring and intubated for airway protection. • Poor recovery and decision to palliate without disclosing HIV status to family.

Clinical Details: CSF for cytology and flow cytometry

Specimen Type: CSF cytology

Macro:
Specimen pot initially sent for microbiology and flow cytometry and pot retrieved on morning of 15/12/23 for histology.
Received were approximately 1 mL of opaque fluid received. A1 Pap x 1, MGG x 1.
IT issue with Winpath 15/12/23 and 18/12/23 preventing queuing of report for authorisation.

Micro:
Cellular CSF composed of a single population of abundant mononuclear single/dyscohesive cells, with large prominent nucleoli and minimal cytoplasm. There are few other cells for size comparison on the PAP stain, however the cells appear somewhat enlarged.

Conclusion: CSF showing what appears to be an atypical lymphocytic pleocytosis, favouring involvement by this patient's known lymphoma. Clinical correlation advised.

	Appearance	WCC/cmm	RCC/cmm	Clot
CSF 1	Clear and colourless	na	na	Nil
CSF 2	Clear and colourless	na	na	Nil
CSF 3	Clear and colourless	1,590	20	Nil

* Differential performed on last sample

Differential

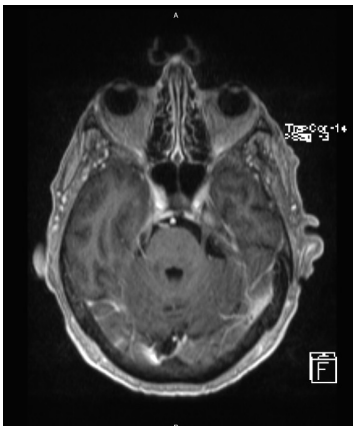
Neutrophils	0	%	Lymphocytes	70	%	Large Mono Cells	30	%

Gram Stain	Pus cells ++ No organisms seen. Provisional Gram stain report: Gram stain will be confirmed on culture.

Ranges

Leucocytes	Neonates (< 28days)	0-30 cells x 10^6/L
	Infants (1 - 12 months)	0-15 cells x 10^6/L
	Children\Adults (1 year +)	0-5 cells x 10^6/L
Erythrocytes	No RBCs should be present in normal CSF	

A WBC-RBC ratio of 1:500 to 1:1000 is regarded as not indicative of infection



MRI showed no positive findings of leptomeningeal enhancement or infection/collection despite CSF highly suggestive of TB meningitis and CSF flow cytometry highly suggestive of Burkitt's lymphoma

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