Disseminated toxoplasmosis with bone marrow involvement in a patient with acute lymphoblastic leukaemia.

Dr Tulene S. Kendrick, Dr Collin K. Chin and Dr Jill Finlayson

1Department of Haematology, Sir Charles Gairdner Hospital and Pathwest Laboratory Medicine WA, Nedlands, Western Australia, Australia; 2Medical School, University of Western Australia, Crawley, Western Australia, Australia.
Haematological background

- 63y M with B-cell ALL, 2008

- Hyper-CVAD x 4; 2 years maintenance prednisolone, vincristine, mercaptopurine and methotrexate

- Relapsed 2016, IDA-FLAG-rituximab → remission
- Probable aspergilloma of the lung

- Declined allograft
- Oral mercaptopurine and methotrexate maintenance
- Valaciclovir prophylaxis
Presenting complaint

- Attended ED with 4 days of rigors and sweats

- 3 months flu-like illness:
  - rhinorrhoea & sinus pain
  - persistent dry cough
  - myalgia
  - diarrhoea
  - weight loss 5 kg

- Several courses of poABs for presumed LRTI
On admission

- T 39.1
- SBP 70
- HR 129
- SaO2 98% 1 L
- Septic ?source

- IvAbs:
  - ceftazime, azithromycin, vancomycin
  - meropenem

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<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Hb</td>
<td>82</td>
</tr>
<tr>
<td>WCC</td>
<td>3.9</td>
</tr>
<tr>
<td>Plts</td>
<td>20</td>
</tr>
<tr>
<td>Neut</td>
<td>3.6</td>
</tr>
<tr>
<td>Lymph</td>
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<tr>
<td>Blasts</td>
<td>0.0</td>
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<tr>
<td>CRP</td>
<td>160</td>
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</table>
Investigations

- Urine – negative
- Blood culture – negative
- Faeces PCR – negative
- CXR – clear

- CTPA
  - interstitial oedema with bilateral shallow pleural effusions

- CT abdomen
  - free fluid in perihepatic space, RIF, pelvis
  - no evidence of perforation
  - no lymphadenopathy
Progress

- Ongoing fevers for 2 days

- HDU
  - hypotension despite aggressive IVH
  - Inotropes not required

- Transfer to tertiary centre 3 days later

- PUO
- ?sepsis
- ?relapsed ALL
On arrival

- Alert, clammy, rigoring
- Haemodynamically stable
- Examination non-informative – reduced air entry

- CT chest
  - Trace of pericardial fluid and small bilateral pleural effusions.
  - Small amount of free intraperitoneal fluid in the RUQ.
  - No findings to suggest atypical pulmonary infection.

- CT sinuses – normal
Day 2

- Neurological deterioration
- Coagulopathic
- CTH - no bleed or infection
- LP delayed due to coagulopathy
- BMAT
- ID review: meropenem, ambisome, acyclovir
- ICU for low GCS, intubated

?CNS infection
?relapse

?Haemophagocytic lymphohistiocytosis
Bone marrow biopsy
## Confirmatory tests

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Specimen</th>
<th>Sample Type</th>
<th>Result</th>
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<tbody>
<tr>
<td><strong>Toxoplasma Serology:</strong></td>
<td>Specimen</td>
<td>Serum</td>
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<tr>
<td>IgG Antibody</td>
<td></td>
<td>5.0 IU/mL</td>
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<tr>
<td>IgM Antibody</td>
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<td>Positive</td>
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<tr>
<td><strong>PCR:</strong></td>
<td>Specimen</td>
<td>Bone marrow aspirate</td>
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<tr>
<td>Toxoplasma gondii DNA</td>
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<td>Detected</td>
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<tr>
<td><strong>PCR:</strong></td>
<td>Specimen</td>
<td>Whole Blood</td>
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<tr>
<td>Toxoplasma gondii DNA</td>
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<td>Detected</td>
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<td><strong>HIV Serology:</strong></td>
<td>Specimen</td>
<td>Serum</td>
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<tr>
<td>HIV-1/2 Antigen/Antibody</td>
<td></td>
<td>NOT Detected</td>
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</table>
Outcome

• Empirical toxoplasmosis Rx - sulphadiazine/pyrimethamine
• Plan for dexamethasone and etoposide for presumed HLH
• Cardiac arrest: Tamponade secondary to pericardial effusion
• Unable to be resuscitated despite percutaneous pericardiocentesis and open surgical drainage

• Death due to disseminated toxoplasmosis
Toxoplasma gondii

- Obligate intracellular protozoan parasite
- Widely prevalent in humans and animals
- Disseminated disease in immunocompromised due to latent reactivation
- Any organ affected – lung, CNS common
- Rapidly fatal if untreated

- Risk factors:
  - HIV
  - HSCT
  - Immunosuppressive therapies
Life cycle

- Felid zoonotic hosts
Cerebral toxoplasmosis in a diffuse large B cell lymphoma patient

Cerebral Toxoplasmosis After Rituximab Therapy

Rituximab is a chimeric monoclonal antibody that targets CD20 antigens on B cells. It has been approved by the US Food and Drug Administration for the treatment of B-cell non-Hodgkin lymphoma and rheumatoid arthritis that is refractory to treatment with anti–tumor necrosis factor.\(^1\) Rituximab induces B-cell depletion and influences T-cell immunity, which could consequently predispose patients to serious infectious complications.\(^2\) Herein we describe the reactivation of cerebral toxoplasmosis after rituximab therapy in a patient with cutaneous vasculitis associated with type I cryoglobulinemia.
Molecular Diagnosis of Toxoplasmosis in Immunocompromised Patients: a 3-Year Multicenter Retrospective Study

Florence Robert-Gangneux, Yvon Sterkers, Hélène Yera, Isabelle Accoceberry, Jean Menotti, Sophie Cassaing, Marie-Pierre Brenier-Pinchart, Christophe Hennequin, Laurence Delhaes, Julie Bonhomme, Isabelle Villena, Emeline Scherer, Frédéric Dalle, Feriel Touafek, Denis Filliatti, Emmanuelle Varlet-Marie, Hervé Pelloux, Patrick Bastien

Centre Hospitalier Universitaire de Rennes, Université Rennes 1, Service de Parasitologie-Mycologie, Rennes, France; Pôle Biologie Moléculaire” du Centre National de Référence de la Toxoplasmosis, and Centre Hospitalier Universitaire de Montpellier, Département de Parasitologie-Mycologie, UMR CNRS 5290, IRD 224 UM (“MIVEGEC”); Montpellier, France; Université Paris Descartes, Assistance Publique Hôpitaux de Paris, Hôpital Cochin, Service de Parasitologie-Mycologie, Paris, France; Centre


• Toxoplasma+ PCRs in immunocompromised:
  - 38% HIV+
  - 40% HSCT
  - 9% other haem malignancy (CLL, lymphoma)
  - 8% solid organ Tx

• HSCT: More likely to be asymptomatic (32%)
  - Disseminated (41%) vs cerebral (16%) toxoplasmosis
  - Lower survival (67% in symptomatic patients)
Prevention

- Avoid acute infection / Majority latent reactivation

- Screening?
  - France screens all pregnant women (84% prevalence)
  - serology relies on immunocompetence of hosts (false negatives)
  - significance of PCR+ in asymptomatic patients?
  - French study – regular PCR after allo-HSCT associated with improved survival (86 vs 50%)

- Prophylaxis with Bactrim?
  - no guidelines
Conclusion

• Toxoplasmosis probably underestimated in patients with haematological malignancies

• Consider cerebral toxoplasmosis in patients with haematological malignancies on immunosuppressive therapy who present with new neurologic deficits

• Early diagnosis and treatment is critical

• Should we be screening?

• Determine risk & need for secondary prophylaxis in individual patients
Toxoplasmosis

Thank you