

ABSTRACT BOOK

BIAMA

British Infection Association

TRAINEES' DAY

OLD & NEW:

**INFECTIONS IN THE
IMMUNOCOMPROMISED**

Wednesday 15th May 2013

**Brunei Gallery Lecture Theatre
School of Oriental & African Studies
London**

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RSTMH promotes and advances the study, control and prevention of disease in humans and other animals in the tropics and plays a leading role in increasing awareness throughout the world of tropical medicine and international health issues.

Throughout our international network of Fellows we facilitate training, education and exchange of information between clinicians, health-related scientists, to non-governmental development organisations and students across all disciplines in the fields of tropical medicine and international health.

PROGRAMME

Session 1: Chair: Dr Paul Collini

- 09.45 Iatrogenic immunocompromise
Dr Sinisa Savic
*Consultant Immunologist,
Leeds Teaching Hospitals NHS Trust*
- 10.25 Susceptibility to mycobacterial infection as a feature of primary immunodeficiency
Dr Sophie Hambleton
*Clinical Senior Lecturer,
Paediatric Immunology and Infectious Disease,
Newcastle University*

11.05 *Coffee*

Session 2: Chair: Dr Thushan de Silva

- 11.40 Case presentations by trainees: Infections in the Immunocompromised
1. The less he spoke, the more he heard
Dr Pavithra Natarajan
Royal Liverpool University Hospital
 2. He wouldn't give a XXXX for anything else
Dr Anna Riddell
Hammersmith Hospital
 3. Holy cow, babes!!
Dr Anna-Rose Prior
St Vincent's University Hospital
 4. Breathing in the dirt
Dr Anika Singanayagam
Hammersmith Hospital
 5. An Odd Finding in British Game?
Dr Paul Morris & Dr Cariad Evans
Royal Hallamshire Hospital
 6. A Precarious Balance
Dr Michael Riste
University Hospital of North Staffordshire
- 12.50 Update on training issues
Dr Thushan de Silva

13.00 *Lunch*

- 14.00 Penicillium marneffeii and other HIV related fungal infections
Professor Nelson Lee
*Professor and Honorary Consultant, Head,
Division of Infectious Diseases Stanley Ho
Centre for Emerging Infectious Diseases,
Hong Kong*
- 14.40 Antibiotics in the critically ill
Professor Mervyn Singer
*Professor of Intensive Care Medicine,
University College London*

15.20 *Coffee*

Session 3: Chair: Dr Fiona McGill

- 15.50 Fungal infections in Bone Marrow Transplant recipients
Professor Chris Kibbler
*Professor of Medical Microbiology,
Royal Free Hospital, London*
- 16.30 Viral infections in organ transplant recipients
Dr Katherine Ward
*Consultant Virologist,
University College London*

17.10 *Meeting Close, presentations of prizes & refreshments*

Session 1: Chair - Dr Paul Collini

Title	Iatrogenic immunocompromise
Author	Dr Sinisa Savic
Address	<i>Leeds Teaching Hospitals NHS Trust</i>

Abstract

Our understanding of the complex interactions between various components, cells and chemical messengers which comprise the immune system, continues to develop at a rapid pace. We also have a greater appreciation of the role the immune system has in the pathogenesis of an increasing number of conditions, some of which were previously thought not to have an immunological basis. We have exploited these advances to develop a variety of ways of manipulating the immune responses to achieve therapeutic goals.

Many agents used for this purpose will have an immunosuppressive effect. Older agents, developed for the purpose of organ transplantation, have a wideranging effect on the immune system and affect many different aspects of the immune function. The newer biologics have more specific and targeted effects on the immune system, and have been developed with particular therapeutic uses in mind.

The aims of my talk are to provide an overview of how immunosuppressive agents have been developed over the decades, illustrate some principal modes of action and provide examples of infective complications that can be associated with their use.

Title	Susceptibility to mycobacterial infection as a feature of primary immunodeficiency
Author	Dr Sophie Hambleton
Address	<i>Newcastle University</i>

Abstract

Non-TB mycobacterial disease often indicates underlying immunocompromise. In this talk I will use real clinical cases to illustrate the varied presentations of mycobacterial disease as a manifestation of primary immunodeficiency in childhood, and show how these disorders inform our understanding of the anti-mycobacterial immune response.

Session 2: Chair - Dr Thushan de Silva

Case Presentation 1

Title	“The less he spoke, the more he heard”
Author	Dr Pavithra Natarajan
Address	<i>Royal Liverpool University Hospital</i>

Cryptic Abstract

A 69 year old man with psoriasis and rheumatoid arthritis, for which he was on etanercept, presented to the emergency department with confusion and melaena. On examination he was hypotensive with BP 75/40 and hypoxic. Investigations revealed WCC 22, with neutrophil count 18.2, CRP 7, Hb 13.1. He had a metabolic acidosis, an acute kidney injury with eGFR 22 and normal liver function tests. A CT scan showed dense bilateral lung consolidation and a section of thickened sigmoid colon, which was felt likely to be a sigmoid tumour.

He was commenced empirically on piperacillin/tazobactam and gentamicin and taken to ITU for inotropes and ventilatory support. Etanercept was stopped on admission. On the basis of a positive urinary pneumococcal antigen, the diagnosis was presumed to be pneumococcal sepsis and multi-organ failure. Blood cultures, legionella antigen, urine culture and CDT were all negative and no sputum was received. He had a one week stay on ITU.

Following step-down to HDU, he developed fresh PR bleeding. A sigmoidoscopy showed atrophic, ulcerated mucosa. On the background of a suspicion of a sigmoid tumour, a defunctioning loop transverse colostomy was performed. He was given a presumptive diagnosis of Dukes A adenocarcinoma.

Case Presentation 2

Title	He wouldn't give a XXXX for anything else
Author	Dr Anna Riddell
Address	<i>Hammersmith Hospital, London</i>

Cryptic Abstract

A 31 year old Nigerian renal transplant patient on tacrolimus (5mg bd) and prednisolone (10mg od), presented with a six day history of fevers and rigors. His renal function had deteriorated (creatinine 267µmol/L, baseline 124 µmol/L), he was anaemic, thrombocytopaenic and CRP was 95 mg/L. Initial treatment was intravenous fluids, hydrocortisone and antibiotics (tazocin, vancomycin and metronidazole).

A CT CAP demonstrated axillary and retroperitoneal nodes and splenomegaly. Blood and urine cultures, HIV, CMV PCR, EBV DNA and viral hepatitis serology were all negative. A bone marrow aspirate showed hypercellular marrow with no abnormal infiltrate. By day twelve, his inflammatory markers had settled (CRP 8 mg/L) and he was discharged on oral co-amoxiclav and metronidazole.

Two weeks later, the patient re-presented with fevers and a cough. He was hypotensive, his CRP was 169 mg/L and thrombocytopaenic. Chest x-ray was normal and multiple cultures were again negative. Antimicrobials (vancomycin, amikacin, tazocin and metronidazole) were re-instated and the dose of tacrolimus was reduced. By day three, he required inotropic support and haemodialysis. He was persistently febrile, anaemic and thrombocytopaenic, necessitating regular blood and platelet transfusions. Repeat CT CAP showed splenomegaly, axillary and retroperitoneal lymphadenopathy, ascites and bilateral pleural effusions. Bedside echocardiogram was normal.

Case Presentation 3

Title	Holy cow, babes!!
Author	Dr Anna-Rose Prior
Address	<i>St Vincent's University Hospital</i>

Cryptic Abstract

88 year old man from Cork, Ireland.

Background: previous adenocarcinoma, splenectomy.

Day prior to hospital presentation: was out gardening and helping with cattle on farm. Reported getting insect bites.

Presented to hospital with dark urine but feeling generally unwell.

Rapidly progressing clinical course - within 24 hours required intensive care admission - haemolysis and multi organ failure,

Cardiac arrest 2 days post admission - deceased.

Case Presentation 4

Title	Breathing in the dirt
Author	Anika Singanayagam
Address	<i>Hammersmith Hospital, London</i>

Cryptic Abstract

A 33-year-old Malaysian female was under investigation by the renal physicians with pyrexia of unknown origin for 2 months. She was the recipient of a live-donor renal transplant in 2010. Other medical history included an episode of CMV colitis and MGUS. She was taking tacrolimus, prednisolone and prophylactic valganciclovir. She was resident in UK for 7 years and travel history included Malaysia, USA and Europe.

Over 2 months, she was investigated for PUO. A series of tests including repeated cultures and screens for viruses, were negative. CTCAP showed no lymphadenopathy. Echocardiogram revealed no vegetations and renal biopsy showed only mild ATN. Autoimmune screen was negative.

She was admitted from clinic with SOB, cough, chest pain and lethargy. Temperature was 40°C. Bloods showed raised inflammatory markers (WCC=16, CRP=300), elevated liver enzymes, LDH >7000 and metabolic acidosis. Diffuse interstitial nodular infiltrates were seen on chest radiography.

She deteriorated rapidly and was admitted to intensive care, where she developed progressive respiratory failure and disseminated intravascular coagulation. A widespread papular rash developed over her body. She unfortunately died a week into admission.

The causative organism was subsequently grown on blood cultures. Characteristic histopathological features were identified on review of a variety of clinical specimens...

Case Presentation 5

Title	An Odd Finding in British Game?
Author	Dr Michael Riste
Address	<i>University Hospital of North Staffordshire</i>

Cryptic Abstract

26 year-old female patient of white caucasian British origin presented with jaundice at 19 weeks gestation. She had a 4 week history of fatigue, with an incidental finding of acute hepatitis (ALT 1179) by GP. No foreign travel or illness within contacts. Employed as Pharmacy dispenser. No new prescription or non-prescription medication. Examination confirmed painless jaundice, without hepatomegaly.

Progressive acute liver failure occurred over 5 days with hypoglycaemia and synthetic function derangement (INR 5.8) requiring referral for emergency liver transplantation.

Case Presentation 6

Title	A Precarious Balance
Author	Dr Rebecca Lester
Address	<i>University College Hospital London</i>

Cryptic Abstract

A 52 year old lady presented with a four week history of fever, splenomegaly and weight loss. She had a background history of orofacial granulomatosis, for which she was receiving long term treatment with azathioprine and topical steroids. Prior to presentation, she had been on holiday to southern Spain, with no other significant foreign travel. Blood tests showed pancytopenia with severe neutropenia, a ferritin of 8700ng/mL, and elevated EBV DNA PCR at 6162 copies per mL. A staging CT showed no evidence of malignancy. A bone marrow was performed which was of limited quality, but showed haemophagocytosis of neutrophils and erythroid precursors.

She was treated with prednisolone, ciclosporin and intravenous immunoglobulin, in addition to broad spectrum antibiotics for febrile neutropenia. Her symptoms, blood counts and ferritin initially responded, though treatment was complicated by a steroid induced proximal myopathy. Subsequently her fevers recurred along with profound pancytopenia, so a repeat bone marrow aspirate and trephine were performed.

Session 2: Chair - Dr Thushan de Silva

Title	Antibiotics in the critically ill
Author	Professor Mervyn Singer
Address	<i>University College London</i>

Abstract

Antibiotics are important tools in our treatment armamentarium though are certainly not the panacea they're dressed up to be. Worryingly, the propaganda surrounding antibiotics offers a rather skewed representation of the literature base. An equal-and-opposite number of studies that get little air time directly contradict the dogma that early antibiotics saves lives. Furthermore, the risk-benefit equation is woefully under-explored. While I will certainly not argue for a moratorium on antibiotic use, I will attempt to redress the knowledge base imbalance, and will offer what I believe to be a more cogent view of antibiotic prescribing.

Session 3: Chair - Dr Fiona McGill

Title	Fungal infections in Bone Marrow Transplant recipients
Author	Professor Chris Kibbler
Address	<i>Royal Free Hospital, London</i>

Abstract

The incidence of invasive fungal infections remains high in allogeneic stem cell transplant recipients (>15% in some recent studies), despite the use of antifungal prophylaxis. However, the risk differs between the different transplant groups with the autologous stem cell transplants being of relatively low risk. The commonest causative organism is *Aspergillus fumigatus*, with *Candida* species, *Pneumocystis jirovecii*, *Cryptococcus neoformans* and mucoraceous moulds making up the majority of the rest.

Presentation, diagnosis, prevention and treatment strategies will be discussed in this session, with the emphasis on new diagnostic standards and European treatment guidelines.

Case Presentation Answers

Title	“The less he spoke, the more he heard”
Author	Dr Pavithra Natarajan
Address	<i>Royal Liverpool University Hospital</i>

Full abstract with diagnosis

A 69 year old man with psoriasis and rheumatoid arthritis, for which he was on etanercept, presented to the emergency department with confusion and melaena. On examination he was hypotensive with BP 75/40 and hypoxic. Investigations revealed WCC 22, with neutrophil count 18.2, CRP 7, Hb 13.1. He had a metabolic acidosis, an acute kidney injury with eGFR 22 and normal liver function tests. A CT scan showed dense bilateral lung consolidation and a section of thickened sigmoid colon, which was felt likely to be a sigmoid tumour.

He was commenced empirically on piperacillin/tazobactam and gentamicin and taken to ITU for inotropes and ventilatory support. Etanercept was stopped on admission. On the basis of a positive urinary pneumococcal antigen, the diagnosis was presumed to be pneumococcal sepsis and multi-organ failure. Blood cultures, legionella antigen, urine culture and CDT were all negative and no sputum was received. He had a one week stay on ITU.

Following step-down to HDU, he developed fresh PR bleeding. A sigmoidoscopy showed atrophic, ulcerated mucosa. On the background of a suspicion of a sigmoid tumour, a defunctioning loop transverse colostomy was performed. He was given a presumptive diagnosis of Dukes A adenocarcinoma.

Diagnosis: CMV colitis caused by reactivation of CMV due to Etanercept therapy

Subsequent management and discussion

He had ongoing PR bleeds and pyrexia on the ward over the following week and a repeat sigmoidoscopy showed an inflamed, ulcerated mucosa. Subsequently, the histology of tissue taken during the initial sigmoidoscopy revealed marked crypt architectural distortion, goblet cell depletion, patchy acute and chronic inflammation and abundant viral inclusions, confirmed to be CMV by immunohistochemistry (and negative for HSV).

CMV PCR of blood was positive at a low level. He was CMV IgM negative and IgG positive with an avidity of 66% consistent with past infection, not recently acquired. Subsequent testing of his respiratory PCR swab from admission was negative for CMV, as was the CSF obtained from a lumbar puncture performed as part of his initial work up on ITU. His ALT peaked at 839, but eventually normalized. HIV antigen/antibody test was negative.

He improved spontaneously and therefore the decision was made not to treat him with an antiviral. Repeat sigmoidoscopy and biopsy showed mild changes felt to be in keeping with resolving infectious colitis and histology was negative for CMV, confirming the resolution of CMV infection, presumably as a consequence of stopping the etanercept.

Learning points

- Severe CMV infections can occur during treatment with anti-TNF agents.
- CMV infection often improves spontaneously on withdrawal of immunosuppressants and does not always warrant treatment.
- An association between colitis and biological agents has recently been described. Etanercept itself can cause colitis, apparently as a form of immune-mediated inflammatory bowel disease.

References

1. Freeman HJ et al. Colitis associated with biological agents. *World Journal of Gastroenterology* 2012 Apr 28;18(16):1871-4
2. S. Domm et al. The impact of treatment with tumour necrosis factor- α antagonists on the course of chronic viral infections: a review of the literature. *British Journal of Dermatology* 2008 Dec;159(6):1217-1228

Title	He wouldn't give a XXXX for anything else
Author	Dr Anna Riddell
Address	<i>Hammersmith Hospital, London</i>

Full abstract with diagnosis

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Diagnosis: HHV8 related Castleman disease in an HIV negative renal transplant patient

Subsequent management and discussion

Further progress:

Five weeks after first presentation, HHV8 DNA PCR: 354 million copies. Histopathology from lymph node biopsy confirmed HHV8 positive plasmoblasts consistent with multicentric Castleman disease.

Commenced on 4 cycles etoposide and rituximab. He became persistently neutropaenic post-second cycle with fever recrudescence and was subsequently started on meropenem, vancomycin and GCSF. After the 3rd cycle, he improved clinically and was no longer dialysis dependent. After the 4th cycle he was discharged.

Discussion

HHV8 related neoplastic disease is rare in non-HIV patients but has been described in solid organ transplant patients. There are three main types of disease recognised in transplant recipients: Kaposi's sarcoma, multicentric Castleman disease and primary effusion lymphoma. HHV8 related disease can be secondary to reactivation of latent HHV8 due to immunosuppression or can represent de novo infection in allograft recipients from HHV8 positive donors.

There is worldwide variation of HHV8 seropositivity, with some regions reaching a population seroprevalence greater than 50%. Distribution of classical Kaposi's sarcoma reflects this.

Due to the rarity of HHV8 related disease, there is no gold standard treatment in post-transplant patients. Limited evidence exists for decreasing immunosuppression, switching tacrolimus to sirolimus (which may offer additional antineoplastic action), CHOP chemotherapy, rituximab and tocilizumab.

Learning points

- HHV8 can rarely cause neoplastic disease in non-HIV immunosuppressed patients. It should be part of the differential diagnosis in immunosuppressed patients with lymphadenopathy, splenomegaly and fevers.
- Treatment is controversial but may be effective and may be advanced by introduction of immune modulators and newer immunosuppressive regimes. Serological testing of both transplant recipients and donors from endemic regions could be key in reducing HHV8 related disease.

Useful references

1. Riva, G et al. How I treat HHV8/KSHV-related diseases in posttransplant patients. *Blood* 2012; 120: 4150-4159.
2. Bower, M. How I treat HIV-associated multicentric Castleman disease. *Blood* 2010; 116: 4415 - 4421.
3. Regamey, N et al. Transmission of human herpesvirus 8 infection from renal transplant donors to recipients. *N Engl J Med* 1998; 339: 1358-1363.
4. Stallone, G et al. Sirolimus for Kaposi's sarcoma in renal-transplant recipients. *N Engl J Med* 2005; 352 (13): 1317-23.
5. Nishimoto, N et al. Humanized anti-interleukin-6 receptor antibody treatment of multicentric Castleman disease. *Blood* 2005; 106(8):2627-2632.

Title	Holy cow, babes!!
Author	Dr Anna-Rose Prior
Address	<i>St Vincent's University Hospital</i>

Full abstract with diagnosis

88 year old man from Cork, Ireland.

Background: previous adenocarcinoma, splenectomy.

Day prior to hospital presentation: was out gardening and helping with cattle on farm. Reported getting insect bites.

Presented to hospital with dark urine but feeling generally unwell.

Rapidly progressing clinical course - within 24 hours required intensive care admission - haemolysis and multi organ failure,

Cardiac arrest 2 days post admission - deceased.

Diagnosis: Babesiosis (*B. divergens* infection)

Subsequent management and discussion

Discussion regarding transmission and epidemiology and clinical characteristics and management of infection.

- Supportive and antimicrobial management
- Important clinical differences between different species (*B. microti* -v- *B. divergens*)

Impact in immunocompromised patients, particularly asplenic individuals.

Rare disease with few cases reports of *B. divergens* (*B. microti* is more common).

It is of note that many reported cases relate to infection acquired in west of Ireland. It is also an important bovine pathogen.

Associated with other tick-borne diseases.

Learning points

- Significance of this pathogen in splenectomised individuals and importance of awareness of clinical condition, particular if in areas where other tick-borne pathogens are endemic (e.g Lyme disease).
- Although this disease is rare, the vector is widespread and host risk factors common, therefore it is possible that disease is under-recognised.

Useful references

1. Homer M, et al. Babesiosis. *Clin Micro Rev.* 2000. 13:451-469.
2. Vannier E, Krause P. Update on babesiosis. *Interdis Perspec Infect Dis.* 2009.
3. Clarke CS, et al. Babesiosis: under-reporting or case-clustering? *Postgrad Med Jour* . 1989;65:591-593.
4. Fitzpatrick J, et al. Further details of third recorded cases of redwater (babesiosis) in man. *Brit Med Jour.* 1969;4:770-772.
5. Garnham P, et al. Human babesiosis in Ireland: further observations of this infection. *Brit Med Jour.* 1969;4:768-770.
6. Gray JS, et al. Prevalence of clinical babesiosis in an area in North Co Meath, Ireland. *Vet Rec.* 1983 Dec 3:113(23):537-9.
7. Taylor SM. Prevalence of clinical babesiosis in cattle in Northern Ireland. *Vet Rec* 1983 Mar 12;112(11):247-50.

Title	Breathing in the dirt
Author	Anika Singanayagam
Address	<i>Hammersmith Hospital, London</i>

Full abstract with diagnosis

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She deteriorated rapidly and was admitted to intensive care, where she developed progressive respiratory failure and disseminated intravascular coagulation. A widespread papular rash developed over her body. She unfortunately died a week into admission.

The causative organism was subsequently grown on blood cultures. Characteristic histopathological features were identified on review of a variety of clinical specimens...

Diagnosis: Progressive disseminated histoplasmosis (*Histoplasma capsulatum*)

Subsequent management and discussion

Histoplasma capsulatum is a soil-borne thermally dimorphic fungus, exhibiting a mycelial phase at ambient temperature and transformation into a yeast form at 37 degrees. It is endemic to certain areas of the USA. Immunosuppressed patients are at risk of progressive disseminated disease because of defective cellular immunity. *Histoplasma capsulatum* can be acquired exogenously (inhalation of mycelial filaments), through re-activation of quiescent disease, and via donor graft transmission. Presentation is often occult in transplant recipients. Radiographic changes can mimic those of miliary tuberculosis.

The estimated incidence is low in renal allograft recipients, even in endemic areas (<0.5%). Diagnosis is often delayed, due to difficulty in culturing the organism. Direct microscopy of clinical specimens with fungal staining reveals characteristic small oval budding yeast cells (2-4microns) in the cytoplasm of macrophages, surrounded by a clear zone giving the appearance of a capsule.

In this patient, *Histoplasma capsulatum* was grown from blood cultures. Features consistent with histoplasmosis were seen on isolates from broncho-alveolar lavage, skin biopsy, bone marrow, and peripheral blood smear. The patient was treated with Amphotericin B as recommended by IDSA guidelines, but unfortunately her high burden of disease and immunosuppressed state meant the histoplasmosis infection was fatal.

Learning points

With increasing numbers of immunocompromised hosts resulting from organ transplantation, HIV infection or pharmacotherapy, and a patient population with wider ethnic and travel backgrounds, histoplasmosis is a re-emergent infectious disease we must be aware of in the UK. The diagnosis of histoplasmosis requires a high index of suspicion, recognition of the common presenting features, and familiarity with diagnostic tests. A combination of *Histoplasma* serology, urine antigen assay, direct microscopy, histopathological findings and fungal culture will aid in confirming the diagnosis.

Useful references

Clinical Practice Guidelines for the Management of Patients with Histoplasmosis: 2007 Update by the Infectious Diseases Society of America

Title	An Odd Finding in British Game?
Author	Paul Morris & Cariad Evans
Address	<i>Royal Hallamshire Hospital</i>

Full abstract with diagnosis

26 year-old female patient of white caucasian British origin presented with jaundice at 19 weeks gestation. She had a 4 week history of fatigue, with an incidental finding of acute hepatitis (ALT 1179) by GP. No foreign travel or illness within contacts. Employed as Pharmacy dispenser. No new prescription or non-prescription medication. Examination confirmed painless jaundice, without hepatomegaly.

Progressive acute liver failure occurred over 5 days with hypoglycaemia and synthetic function derangement (INR 5.8) requiring referral for emergency liver transplantation.

Diagnosis: Acute Hepatitis E viral infection in pregnancy causing severe liver injury.

Subsequent management and discussion

A routine NILS revealed acute infection with Hepatitis E (positive IgM). Confirmed as genotype 1, with a viral load of 2.6×10^6 copies/ml. This represents the first described occurrence of acute liver failure during pregnancy with autochthonous genotype 1 Hepatitis E, in the UK.

There is a lack of evidence for the use of Ribavirin in acute hepatitis E and in pregnancy. Intravenous immunoglobulin was deemed not to be beneficial due to low Hepatitis E seroprevalence within UK.

In men and non-pregnant women genotype 1 disease is usually self-limiting with a case fatality rate of <0.1%. Higher-rates of acute liver failure and mortality during pregnancy are reported. In pregnancy there is evidence of suppression of T-cell mediated immunity in the first 20 weeks gestation, to aid implantation of the antigenic foetus. The mechanism is related to down regulation of p65 of NFkB, resulting in a Th2 bias. Immunity is also influenced by increased circulating hormones (progesterone, oestrogen & human chorionic gonadotropin). Further research on the immunology of hepatitis E in pregnancy is required.

Learning points

- Acute Hepatitis E is increasing in incidence within the UK
- There is little evidence for use of antiviral therapy in acute Hepatitis E viral infection.
- Genotype 1 hepatitis E can be acquired in the UK with increased incidence of acute liver failure and mortality to mother and foetus.

Useful references

1. Mallet et al. "Brief Communication: Case Reports of Ribavirin Treatment for Chronic Hepatitis E" *Ann Intern Med.* 2010; 153(2):85
2. Navaneethan et al. "Hepatitis E and Pregnancy- Understanding the pathogenesis" *Liver Int* 2008 November;28(9):1190-1199
3. Gerolami et al "Treatment of severe acute hepatitis E by ribavirin". *Journal of Clinical Virology* 52 (2011) 60-62
4. Patra et al "Maternal and Fetal Outcomes in Pregnant Women with Acute Hepatitis E Virus Infection". *Annals of Internal Medicine* 2007;147:28-33

Title	A Precarious Balance
Author	Dr Michael Riste
Address	<i>University Hospital of North Staffordshire</i>

Full abstract with diagnosis

A 52 year old lady presented with a four week history of fever, splenomegaly and weight loss. She had a background history of orofacial granulomatosis, for which she was receiving long term treatment with azathioprine and topical steroids. Prior to presentation, she had been on holiday to southern Spain, with no other significant foreign travel. Blood tests showed pancytopenia with severe neutropenia, a ferritin of 8700ng/mL, and elevated EBV DNA PCR at 6162 copies per mL. A staging CT showed no evidence of malignancy. A bone marrow was performed which was of limited quality, but showed haemophagocytosis of neutrophils and erythroid precursors.

She was treated with prednisolone, ciclosporin and intravenous immunoglobulin, in addition to broad spectrum antibiotics for febrile neutropenia. Her symptoms, blood counts and ferritin initially responded, though treatment was complicated by a steroid induced proximal myopathy. Subsequently her fevers recurred along with profound pancytopenia, so a repeat bone marrow aspirate and trephine were performed.

Diagnosis: Haemophagocytic lymphohistiocytosis and visceral leishmaniasis

Subsequent management and discussion

Immunosuppressants were rapidly tapered, and the patient received standard anti-leishmanial treatment with liposomal amphotericin. This resulted in a significant improvement in blood counts and symptoms which was sustained for several weeks, though drug related fevers occurred. Unfortunately, her symptoms recurred after completing treatment and she repeated therapy.

Following successful re treatment, she developed a dyspraxia with widespread white matter lesions on MRI, and oligoclonal bands on CSF, suggestive of cerebral vasculitis related to the fall in her immunosuppression.

Learning points

The presence of both visceral leishmaniasis and the haemophagocytic syndrome in adults is exceptionally rare. Immunosuppression yields diagnostic and management challenges, and this case illustrates the importance of a thorough investigation for patients with haemophagocytosis, and to consider rarer causes in patients with immunosuppression and a history of foreign travel.

Useful references

Rajagopal S, Dutta U et al. Visceral leishmaniasis associated haemophagocytic lymphohistiocytosis - Case report and systematic review; *Journal of Infection* (2008) 56, 381-388

Speaker Biographies

Dr Sinisa Savic
Consultant Immunologist
Leeds Teaching Hospitals NHS Trust

Dr Savic is a graduate from Newcastle University School of medicine. He completed his specialist training in Leeds Teaching Hospitals NHS Trust, where he was appointed to the post of consultant clinical immunologists in 2011.

He has a specialist interest in autoinflammatory and systemic autoimmune diseases, and maintains an active research interest in these areas which were the subject of his PhD.

His other areas of clinical and research work involve primary and secondary immunodeficiencies, laboratory medicine, allergy and in particular drug allergies and recalcitrant idiopathic urticaria.

He has an active role in undergraduate medical student teaching, and has recently being appointed clinical lead for immunology within Leeds medical school.

Dr Sophie Hambleton
Clinical Senior Lecturer, Paediatric Immunology and Infectious Disease
Newcastle University

Dr Sophie Hambleton is a clinical senior lecturer and honorary consultant in paediatric immunology and infectious diseases at Newcastle University and the Great North Children's Hospital, Newcastle upon Tyne. She interspersed clinical training in her paediatric specialty (Birmingham, Oxford, Newcastle) with basic research in molecular immunology (Oxford) and herpesvirology (Columbia). Since her CCST in 2008, Dr Hambleton has worked on the cellular and molecular basis of novel primary immunodeficiencies, with a focus on susceptibility to intracellular pathogens. A former MRC clinician scientist fellow, her work is now funded by the Sir Jules Thorn Charitable Trust.

Professor Nelson Lee
Professor and Honorary Consultant
Head, Division of Infectious Diseases Stanley Ho Centre for Emerging Infectious Diseases, Hong Kong

Professor Nelson Lee is the Head of Division of Infectious Diseases in Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong (CUHK); Consultant and Chief of the clinical infectious disease service at the Prince of Wales Hospital; and the Clinical Faculty Associate of the Stanley Ho Centre for Emerging Infectious Diseases (CEID), CUHK. Professor Lee is also serving as the Chairman of the specialty board of Infectious Diseases in The Hong Kong College of Physicians, and as an expert member in various advisory boards in the Hospital Authority, Center for Health Protection and Department of Health of Hong Kong. He is leading research, professional training, and inform clinical practices related to infectious diseases in the region.

Professor Lee's major research interests include emerging infectious diseases such as Influenza, Severe Acute Respiratory Syndrome, and severe pneumonia. His studies have contributed to the understanding of the clinical manifestations, diagnosis, treatment, viral kinetics, immunopathogenesis, transmission and control of these new infections, focusing on the severely ill hospital patients. He has published over 200 research articles, book chapters and conference papers in these areas; many of these have received high citations and referenced in clinical guidelines for health professionals. He has received multiple academic awards, both regionally and internationally. Professor Lee is also serving as an associate editor or referee for more than 20 regional and international medical journals.

Professor Mervyn Singer
Professor of Intensive Care Medicine
University College London

Mervyn Singer is Professor of Intensive Care Medicine at UCL, an NIHR Senior Investigator and a Council Member of the International Sepsis Forum. He also sits on the Wellcome Technology Transfer Committee and the Health Innovation Challenge Fund Selection Panel. He has research interests in the pathophysiology and management of sepsis and multi-organ failure, severe infection, tissue oxygenation and monitoring. He is currently working with three separate companies/bodies on early diagnostics for sepsis and the causative pathogen. He also declares a verging-on-pathological loathing of protocols.

Professor Chris Kibbler
Professor of Medical Microbiology
Royal Free Hospital, London

Chris Kibbler is Professor of Medical Microbiology at University College London and Head of Service in the Department of Medical Microbiology at the Royal Free Hospital in London.

Chris has been a member of the European Organisation for Research and Treatment of Cancer-Invasive Fungal Infections Group (EORTC-IFIG) Steering Committee. He has also been Chair of the UK National Advisory Committee on Fungal Infection, Chair of the UK Clinical Mycology Network and a member of the European Conference on Infections in Leukaemia (responsible for producing the ECIL guidelines for the management of these infections).

Professor Kibbler is Past President of the British Society for Medical Mycology and Programme Director of the British Society for Medical Mycology/University College London (BSMM/UCL) MSc Programme in Medical Mycology.

His research interests include infections in the immunocompromised host and mycology, especially diagnostic, therapeutic, and pathogenic aspects of infections caused by *Candida* and *Aspergillus* species.

Chair Biographies

Dr Paul Collini

Trainee Representative, BIA

Paul Collini is an MRC clinical training fellow in the department of Infection and Immunity of the University of Sheffield. Since 2006 he has been a clinical lecturer and honorary specialist registrar in Infectious Diseases and General Internal Medicine based at the Royal Hallamshire Hospital, Sheffield. Dr Collini qualified from Edinburgh University Medical School in 1998 and trained in general medicine at St George's Hospital London. He was involved in the roll out programme for ARV in Africa, setting up and running an HIV-1 treatment clinic in Ghana from 2003-2005 while a clinical lecturer at the Kwame Nkrumah University of Science and Technology, Kumasi, Ghana. He is a fellow of the Higher Education Academy and lectures on the MPH and MBChB courses at the University of Sheffield. Dr Collini's research interest is in the innate immune response to pneumococcal infection in HIV-1, with a specific focus on the role of the macrophage.

Dr Fiona McGill

Trainee Representative, BIA

Fiona graduated from the University of Aberdeen in 2000. She moved South of the border one year later to take up an SHO rotation in Middlesbrough. After 2 and half years there she pursued her interest in Infectious Diseases and took up a clinical fellow post in Newcastle-Upon Tyne. After a year in New Zealand and the diploma in tropical medicine she moved back to Newcastle-Upon-Tyne where she started her SpR training in Infectious Diseases as a LAT. Within the year she obtained a training number in the Yorkshire and The Humber region in ID and microbiology. Since April 2011 she has been out of programme working as a Clinical Research Fellow in the Liverpool Brain Infections Group with Prof Tom Solomon and his team working on an epidemiological study on meningitis in the UK.

Dr Thushan De Silva

Trainee Representative, BIA

I have taken over as the BIA trainee professional affairs secretary, although Fiona and I may share responsibilities between the two posts over the next 2 years. Having qualified from Bristol and completed SHO jobs in Oxford and London, I moved to Sheffield to take up a post as an SpR in Infectious Diseases/Microbiology. I have recently returned to Sheffield having taken time out to complete an MRC Clinical Research Training Fellowship based at the MRC Laboratories, the Gambia, working with HIV-1 and HIV-2 infected cohorts in the Gambia and Guinea Bissau.

Trainee Membership and Trainee Representatives

The BIA actively encourages the participation of trainees within the Society, with 3 trainee members being elected to the Council every two years. Their roles are overlapping with some specific responsibilities.

Joint responsibilities

- Attend (up to) four council meetings a year, including one to coincide with the Spring Meeting of the BIA and one to take place at the Federation of Infection Societies Meeting in the winter.
- Contribute to and update the trainees' section of the BIA website.

Individual responsibilities

- Organise trainees' meetings twice a year (Spring and Autumn)
- Responsibility for training issues including the following:
 - ✦ Attend meetings of the Infectious Diseases Specialist Advisory Committee (SAC) and Joint Committee for Infectious Diseases and Tropical Medicine Training meetings (4-6 per year)
 - ✦ Update trainees on relevant matters via the trainees' e-mail list and keep the list up to date
 - ✦ Respond to any other training issues that arise

Trainee members of the BIA have the option of free membership with benefits that include trainees' meetings and the BIA newsletter.

Any individuals interested in forming part of the training sub-committee please contact Fiona McGill at fi.mcgill@googlemail.com or Thushan De Silva at thushandesilva@hotmail.com

For further information, please visit the trainees' section of the British Infection Association website at: www.britishinfection.org



AUTUMN TRAINEES' MEETING

Thursday 14th November 2013

This year's meeting will be held in Birmingham, following the Federation of Infection Societies Conference

For further information or to request a registration form please contact anne@hartleytaylor.co.uk

British Infection Association

Delegates

Dr	Madhmanee	Abeywardena	Leicester Royal Infirmary Hospital	Microbiology
Dr	Aula	Abbara	St Thomas' Hospital	Infectious diseases
Dr	Michael	Ankorn	Sheffield Teaching Hospitals NHS Trust	Infectious Diseases
Dr	Lucinda	Barrett	Oxford University Hospitals NHS Trust	Infectious Diseases
Dr	Paul	Beckett	Sheffield Teaching Hospitals NHS Trust	Microbiology
Dr	Ruaridh	Buchanan	London School of Hygiene & Tropical Medicine	
Dr	Daniel	Burns	Birmingham Heartlands Hospital / British Army	Infectious Diseases
Dr	Graeme	Calver	East Kent Hospitals Trust	Microbiology
Dr	Bilwanath	Chattopadhyay	The London Independent Hospital	Pathology
Dr	Amy	Chue	Oxford University Hospitals NHS Trust	ID & Microbiology
Dr	Tristan	Clark	Treliske Hospital	Medicine
Dr	Katherine	Clay	Birmingham Heartlands Hospital	Infectious Diseases
Dr	Joby	Cole	University of Sheffield	Infection & Immunity
Dr	Julia	Colston	Oxford University Hospitals NHS Trust	ID & Microbiology
Dr	Luis	Cotter	Darent Valley Hospital	Pathology
Dr	Lucy	Cottle	Royal Liverpool University Hospital	Tropical & Infectious Diseases
Dr	Peter	Cowling	BIA Guidelines Secretary	Microbiology
Dr	Susanna	Davis	Sheffield Teaching Hospitals NHS Trust	Medical Microbiology
Dr	Thushan	de Silva	Royal Hallamshire Hospital	ID & Tropical Medicine
Dr	Helen	Dillon	University Hospitals Leicester	Infectious Diseases
Dr	Jake	Dunning	Imperial College London	Respiratory Infection
Dr	Nicholas	Easom	UCLH	Infectious Diseases
Dr	Simon	Ellis	Royal Victoria Infirmary	Infection & Tropical Medicine
Dr	Andree	Evans	Royal Devon & Exeter Hospital	Microbiology
Dr	Hugo	Farne	King's College Hospital	Cardiology
Dr	Vanessa	Field	National Travel Health Network and Centre	
Dr	Zsolt	Filetoth	Ministry of Defence	MOD
Dr	Donall	Forde	Birmingham	Infectious Diseases
Dr	Rachel	Foster	Sheffield Teaching Hospitals NHS Trust	ID & Tropical Medicine
Dr	Stephen	Glass	King's College Hospital	Microbiology
Dr	Gauri	Godbole	North Middlesex Hospital NHS Trust	Microbiology & Virology
Dr	Ankur	Gupta-Wright	University College London Hospitals	Medicine
Dr	Charlotte	Hall	Castle Hill Hospital	Infectious Diseases
Dr	Mashaier	Hamad	University Hospital of North Staffordshire	Pathology
Dr	Sophie	Hambleton	Newcastle University	Paediatric Immunology & Infectious Diseases
Dr	Emma	Hayton	Oxford University Hospitals NHS Trust	ID & Microbiology
Dr	Angela	Houston	St Georges Hospital	Clinical Infection
Dr	Ewan	Hunter	Royal Victoria Infirmary	Infectious Diseases
Dr	Jasmin	Islam	Royal Sussex County Hospital	ID & Microbiology
Dr	Gayti	Islam	Sheffield Teaching Hospitals NHS Trust	Medical Microbiology
Dr	Joe	Jarvis	London School of Hygiene & Tropical Medicine	Clinical Research
Dr	Megan	Jenkins	Southmead Hospital	Infectious Diseases

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Delegates

Professor	Chris	Kibbler	Royal Free London NHS Foundation Trust	Medical Microbiology
Dr	Abhinav	Kumar	Kings Mill Hospital	Microbiology
Dr	Lucy	Lamb	Imperial College London	Infectious Diseases & Immunity
Dr	Susan	Larkin	Worcester Hospitals	Microbiology
Professor	Nelson	Lee	Chinese University of Hong Kong	Infectious Diseases
Dr	Paul	Lee	MHRA	VRMM
Dr	Joanne	Legg	Worthing Hospital	Microbiology
Dr	Elias	Mariolis	St James University Hospital	Infectious Diseases
Dr	Michael	Marks	University College Hospital	Hospital for Tropical Diseases
Dr	Laura	Maynard Smith	London School of Hygiene & Tropical Medicine	Infectious & Tropical Diseases
Dr	Fiona	McGill	Brain Infections UK	Liverpool Brain Infections Group
Dr	Luke	Moore	Imperial College London	Infection & Immunity
Dr	Paul	Morris	Sheffield Teaching Hospitals NHS Trust	Infectious Diseases
Dr	Richard	Morton	NHS	Medicine
Dr	Claire	Mullender	St Georges Hospital	Infectious Diseases
Dr	Pavithra	Natarajan	Royal Liverpool University Hospital	Infectious Diseases
Dr	Linda	New	Epsom & St. Helier University Hospitals NHS Trust	Microbiology
Dr	Dimitrios	Nikolakopoulos	South London Healthcare NHS Trust	Microbiology
Dr	Fotinie	Ntziora	Not disclosed	
Dr	Davies	Nwaka	Colchester Hospital	Microbiology
Dr	Shara	Palanivel	St Helier Hospital	Medical Microbiology
Dr	David	Partridge	Northern General Hospital	Microbiology
Dr	Sneha	Patel	Kingston Hospital	Microbiology
Dr	Ruth	Payne	University of Oxford	The Jenner Institute
Dr	Louise	Pealing	London School of Hygiene & Tropical Medicine	Clinical Research
Dr	Giuseppe	Pichierri	Public Health Wales/Hywel Dda Health Board	Microbiology
Dr	Gabriele	Pollara	University College Hospital	Microbiology
Dr	James	Price	Royal Sussex County Hospital	ID & Microbiology
Dr	Anna-Rose	Prior	St Vincent's University Hospital	Microbiology
Dr	Michael	Riste	University Hospital of North Staffordshire	Infectious Diseases
Dr	Jennifer	Roe	Northwick Park Hospital	Infectious Diseases
Dr	Carlene	Rowson	Sheffield Teaching Hospitals NHS Trust	ID & Microbiology
Dr	Sinisa	Savic	Leeds Teaching Hospitals NHS Trust	Clinical Immunology & Allergy
Dr	Noha	Seoudi	Barts Health NHS Trust	Oral Microbiology
Dr	Clare	Sepping	Royal Cornwall Hospital	Gastroenterology
Dr	Hema	Sharma	Imperial College London	Infection & Immunity
Dr	Robert	Shaw	Wexham Park Hospital	
Dr	Rob	Shorten	Royal Free London NHS Foundation Trust	Microbiology
Dr	Vinutha	Siddaraju	East Surrey Hospital	Microbiology
Dr	Racheol	Sierra	St Richards Hospital	Microbiology
Professor	Mervyn	Singer	University College London	Intensive Care
Dr	Anand	Sivaramakrishnan	Barts Health NHS Trust	Microbiology

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Delegates

Dr	Bala	Subramanian	Sheffield Teaching Hospitals NHS Trust	ID & Microbiology
Dr	Alida Fe	Talento	Trinity College Dublin	Clinical Microbiology
Dr	Louise	Teare	Broomfield Hospital	Microbiology
Dr	Simon	Tiberi	Hammersmith Hospital	Infectious Diseases
Dr	Michelle	Toleman	Bristol Royal Infirmary	Microbiology
Dr	James	Ussher	University of Oxford	Medicine
Dr	Floris	van den Brink	Kennemer Gasthuis Haarlem, Amsterdam	Internal Medicine/Cardiology
Dr	Katherine	Ward	University College London	Virology
Dr	Daniel	Weiland	York Hospital	Microbiology
Dr	kate	Woods	University College London	Infectious Diseases

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