各位病理學及獸醫病理學界之同仁大家好：

中華民國比較病理學會第 65 次研討會將於 104 年 12 月 20 日（日）於衛生福利部臺中醫院舉行。本次會議由衛生福利部臺中醫院主辦，本學會協辦。本次研討會題目為：**冠狀病毒及其他疾病**。敬請各會員惠予提供病理診斷病例，並請踴躍報名參加（病例診斷格式，如附件）。

重要日期：

12 月 11 日（五）以前：

1)請欲提供病例之同仁將報名表（Registration Form）以及相關病例文件（Case History & Case Result sheets）以電子郵件寄回 cscptaiwan@gmail.com。並請所欲提供參考之組織切片寄達中興大學進行數位切片掃描及上網，掃描後再寄回歸還提供者：

收件人：廖俊旺 教授

地址：國立中興大學獸醫病理生物學研究所 (40227 台中市南區興大路 145 號 動物疾病診斷中心 4 樓 406 室)

2) 請其他與會人員將報名表於 12 月 15 日(二)前寄回 cscptaiwan@gmail.com 或於http://goo.gl/forms/qutLrdzo2m完成線上報名。非會員請於當日繳交講義與餐飲費，學生 100/人，非學生 500/人。本次有提供病例報告人員，如非會員，亦不需講義與餐飲費。

開會日期：104 年 12 月 20 日（日）

開會地點：衛生福利部臺中醫院 (賴銘淙 理事 403 台中市西區三民路一段 199 號)

祝　　研　安

秘書長：朱旆億

理事長：廖俊旺

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中華民國 104 年 11 月 4 日

**Call for Papers and Registration**

***65th Meetings of Comparative Pathology*** *hosted by the Chinese Society of Comparative Pathology (CSCP) and the* Taichung Hospital.

You are invited to submit a case for presentation at the 65th Meeting of Comparative Pathology. This meeting is a forum for continuing education and professional development attracting human and veterinary pathologists from hospitals, academia, government, industry and diagnostic laboratories including pathology residents and graduate students.

Each presenter will submit 1 microscope slides along with single copies of a one-page case history sheet and a one-page case result sheet. Brief (15 to 20 minutes) Powerpoint presentations of an interesting diagnostic pathology case (diseases related to corona virus or its related diseases which include classic diseases, reportable diseases, and cases with uncertain diagnosis or new information regarding pathophysiology) will be given at the meeting. Prior to the meeting, all presenters will receive a set of slides for review along with the case histories. For diagnostic cases with limited materials, such as cytology or gross cases, digital photos may be substituted for the microscope slides.

**Meeting Date:** December 20, 2015 (Sunday)
Host: Taichung Hospital, Ministry of Health and Welfare (衛生福利部臺中醫院)
Location: 199, sec.1, San-Min Rd., Taichung 40343, Taiwan, R.O.C.

**Contact:**
Secretary General: Dr. P.Y. Chu (朱旆億 秘書長)
Managing Director: Dr. J. W. Liao (廖俊旺 理事長)
Phone: 04-22840894 # 406
Fax: 04-22852186
Email: cscptaiwan@gmail.com

**Registration:**
Presenters: Deadline is December 11, 2015. Complete the registration form attached and email to crjeng@ntu.edu.tw. Please include your presentation title or diagnosis at the bottom of the form.

Attendees: Deadline is December 15, 2015, if not making a case presentation. Complete the registration form and return by email to Dr. Liao.

**Case Materials:** Submission deadline of case materials is December 11, 2015, for 1 microscope slide, and single copies of a one-page case history sheet and a one-page case result sheet. Format for case history and case results can be found below.

Please submit microscope slides to:
廖俊旺 教授
國立中興大學獸醫病理生物學研究所
40227 台中市南區興大路 145 號動物疾病診斷中心 4 樓 406 室

Please submit case history and result sheets to:
e-mail: cscptaiwan@gmail.com

**Registration Form**
**65th Meeting of Comparative Pathology**
**December 20, 2015 (Sunday)**

| |
|---|
| Full Name: |
| Title: |
| Institution: |
| Address: |
| Telephone: |
| E-mail: |

For presenters:

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| Presentation title or diagnosis: |
| Signalment: |

P.S. Please submit your registration form by email to cscptaiwan@gmail.com. Registration deadline is December 11, 2015 for presenters, and December 15, 2015 for attendees.

**Case Number: 443**
**Slide no.: S2013-12259A**
**Slide view: http://www.ivp.nchu.edu.tw/slide_view.php?id=925**

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## CASE HISTORY

**Signalment:** A 72 year-old male

**Clinical History:**

A 72-year-old male presented with ataxia (unsteady gait), urinary incontinence, and amnesia for about 3 weeks.

He had a past history of (1) hypertension (2) gout (3) hollow organ perforation status post operation (4) end-stage renal disease (ESRD) receiving renal trans- plantation 16 years ago (1997/08/14) with stable renal function after transplantation (serum creatinine 2.0~2.5 mg/dl) and under regular follow-up at 高榮 with current immunesuppressant use including Prednisolone 5 mg QD + Tacrolimus 5 mg QD + Mycophenolate 500 mg QD (5) COPD.

This time, ataxia, urinary incontinence, and amnesia for about 3 weeks were noted by his family. He was first sent to the 805 hospital for help, where CT scan was arranged and cerebrovascular accident (CVA) was impressed. Therefore, he was then transferred to our hospital for further management. MRI study was scheduled and showed at least four lobulated nodular lesions over bilateral frontal and right temporal lobes with marked perifocal edema and rim-enhancement, favor of metastatic lesions. Brain tumor, CNS lymphoma, brain abscess, or opportunistic infection could not be ruled out; therefore, he was admitted for further examination and treatment.

On admission, the review of systems was nothing remarkable except neurological symptoms mentioned above. The significantly positive physical examination findings included respiratory rate 30/min, E4V4M6, and mild decreased muscle power of lower limbs (4 points). Significant lab findings informed leukocytosis (WBC 23760/ul) with elevated segmental form neutrophil (83%) with CRP within normal range (0.15 mg/dl), normocytic anemia (Hb 9.2 g/dl), hyperglycemia (glucose 158 mg/dl), elevated BUN/CRE (84/2.5 mg/dl), elevated uric acid level (9.4 mg/dl), decreased albumin level (2.6 g/dl), and proteinuria on urinalysis (2+).

Stereotactic brain biopsy of right frontal lobe was arranged on 9/9 for defining the etiology. The pathology report of biopsy showed necrosis of brain tissue with a few neutrophils, macrophages, and nuclear debris. Culture for biopsy tissue showed negative for bacterial, TB, and fungus growth and acid-fast stain showed not found. Therefore, we consulted infectious doctor and considered *Toxoplasma*, *Nocardia*, or other fungal infection because the patient had received long-term immune- suppressants. Sevatrim (Sulfamethoxazole 400mg/Trimethoprim 80mg, 5ml/amp) 10 ml

Q8H was prescribed for suspect toxoplasmosis since 9/16. Toxoplasma IgM and IgG were also measured and both the results showed negative.

Brain MRI was arranged again on 9/15 and revealed mild enlargement of the right frontal lesion. Whole body PET was also performed for etiology survey which showed a large focal area of decreased FDG uptake at right frontal area of cerebrum and several focal areas of increased FDG uptake at right frontal and right temporal areas of cerebrum, malignant brain metastases with marked perifocal edema was considered first. A tiny nodule in posterior segment of right upper lung was also noted, but the nature to be ascertained. Sevatrim was kept for covering suspect toxoplasmosis.

On 9/24, the patient developed sepsis and acute on chronic renal failure (Cre 2.3 → 3.7 mg/dl) complicated with hyperkalemia ($K^+$ 6.0 meq/L). He was transferred to SICU for further care. Blood culture was done and Kalimate, 50% dextrose water with regular insulin use, and calcium gluconate were given with hemodialysis for treatment of acute on chronic renal failure and hyperkalemia. Antibiotic was shifted to Clindamycin 600 mg Q6H.

Craniotomy with removal of the tumor was performed on 9/25. Post-operative recovery from anesthesia procedure was well with extubation. However, on next day, conscious disturbance (E4V2M5) with left side weakness developed. Brain CT was arranged and which showed encephalomalasia at right frontal lobe with air-fluid level at the ventricle indicating right pneumocephalus. Besides, blood culture reported growth of Gram-negative bacillus for two sets. Therefore, Cefepime 2 g Q12H and Pyrimethamin (Daraprim) ST 8# + QD 3# were added.

However, profound septic shock developed on 9/27 and blood culture reported Extended-spectrum beta-lactamase producing *Escherichia coli* (ESBL). Hydration with vasopressors (Norepinephrine and Dopamine) was given and Cefepime was shifted to Meropenem 1 g Q12H. However, the condition progressed fast; DDT was arranged at night on 09/28.

**Laboratory result (Clinical Pathology)**

**Gross Finding:**

1. Stereotactic biopsy on 9/9

Nothing remarkable (several small tissue fragments, < 1 cm; grossly, they are grayish and soft.)

2. Craniotomy with removal of the tumor on 9/25

Nothing remarkable (several small tissue fragments, < 0.5 cm; grossly, they are pale and soft.)

**Case Number: 443**

**CASE RESULT**

**Histopathologic Finding:**

1. Stereotactic biopsy on 9/9: necrosis (Frozen section: necrosis)

(1) Necrosis of brain tissue with a few neutrophils, macrophages and nuclear debris.

(2) Focal perivascular inflammatory cells infiltration

(3) Fibrinoid change of blood vessels

There is no evident diffuse infiltration of atypical large lymphocytes. The histological picture may be compatible with toxoplasmosis and differential diagnosis may include other etiologies causing brain abscess in immune-compromised patient.

2. Craniotomy with removal of the tumor on 9/25

(1) Mostly necrotic tissue.

(2) A few purulent exudate and inflammatory cells cuffing vessels in peripheral areas.

(3) No evident viral cytopathic nuclear change.

(4) Foamy macrophages are not numerous.

Please note that if toxoplasmosis is suspected, it is usually present in peripheral area rather than necrotic center. Immunohistochemical stain shows *Toxoplasma* Ab (+).

**Diagnosis:**

1. Brain toxoplasmosis
2. Septic shock with infection by ESBL

**Discussion:**

Immunosuppression due to therapy after transplantation or associated with HIV infection increases the susceptibility to various central nervous system (CNS) infections. It maybe also modify the presentation, diagnosis, and treatment. Immunosuppressive therapy reduces cell-mediated immunity to prevent transplant rejection and graft-versus-host disease (GVHD), but it concomitantly increases the risk of infection due to fungi, viruses (especially herpes viruses), bacteria, and parasites. CNS infection occurs in 5%–10% of transplant recipients and most often manifests as brain abscess, encephalitis, or meningitis [2, 3]. The risk of CNS infection varies with the type of organ transplanted. *Aspergillus fumigatus, Listeria monocytogenes, and Cryptococcus neoformans* are the most common causes of post-transplantation CNS infections. But immunosuppression also increases the risk of acquiring parasitic CNS infections and can increase the severity of these infections (Table 1).

The susceptibility to CNS infection after transplantation changes over time [4, 5]. During the initial month after transplantation, CNS infection is most often due to common bacterial pathogens or opportunistic pathogens present in the environment or host (ex: *Aspergillus* species and

*Mycobacterium tuberculosis*). Immunosuppres- sion is most pronounced from month 1 to month 6 CNS infection during this period is most often due to herpesviruses, especially cytomegalovirus and Epstein-Barr virus (EBV); fungi; or atypical bacteria. Parasitic CNS infection most often occurs during this period, with *Toxoplasma gondii* being the most common infecting organism [6]. Six months after transplantation, immunosuppression therapy is reduced, and CNS infection becomes less common.

Acute and chronic manifestations of parasitic CNS infection are various and depend mainly on which CNS site is affected. Neurologic symptoms during chronic infection are frequently due to mechanical obstruction, invasion of vasculature, or enlarging-mass effect. The common symptoms caused by toxoplasmosis include headache, cognitive changes, seizure, and focal neurologic deficits (such as hemiparesis, ataxia, and facial weakness). Infection by parasites may immediately cause symptoms or may remain undetected for years. Local tissue damage produced by migrating or growing parasites can induce marked inflammatory responses, but, in patients with chronic infection or suppressed immune systems, the inflammatory response may be blunted and the clinical manifestations may be minimal [7, 8].

The evaluation of neurologic symptoms in an immunosuppressed host should be guided by (1) the type of transplantation or CD4+ cell count (2) the time since transplantation and the receipt of immunosuppressive therapy (3) the serologic status with respect to *T. gondii*, *C. neoformans*, and parasites (with evaluation directed by the travel and exposure history) (4) concomitant systemic symptoms (especially pulmonary and gastrointestinal symptoms) (5) neuroimaging findings (table 2. The neuroimaging findings of CNS infection caused by toxoplasmosis include solitary or multiple round ring-enhancing or homogeneously enhancing lesions, usually located at the hemispheric gray-white junction, in the deep white matter, or in the basal ganglia. MRI is more sensitive and may detect multiple lesions not seen on CT scan. Edema is usually present.) Eosinophilia in CSF or blood may be absent during parasitic CNS infection, especially during chronic infection [9]. Pulmonary infection usually precedes or accompanies CNS infection with *A. Fumigatus*, *C. neoformans*, *Nocardia asteroides*, *M. tuberculosis*, and endemic mycoses [5, 10].

Felines are the definitive hosts of *T. gondii* and excrete infectious oocysts in feces [11]. Humans acquire *T. gondii* infection most often by (1) ingestion of oocysts in contaminated soil or food (2) ingestion of bradyzoites in undercooked meat (3) via mother-to-fetus transmission (4) blood transfusion (5) organ transplantation [11, 12]. After ingestion of an oocyst, the parasitic organism invades the intestinal epithelium, disseminates throughout the body, encysts, and remains dormant in any nucleated cell. In the United States, 10%–40% of people have latent infection with *T. gondii*, which is determined by the presence of serum anti-toxoplasma IgG antibodies [13, 14]. In transplant recipients, toxoplasmosis occurs by reactivation of latent infection or is a primary infection if a donor organ containing encysted *T. gondii* was transplanted into a seronegative recipient [40]. Patients who are seronegative for *T. gondii* and receive allografts, especially cardiac allografts, from seropositive donors are at the highest risk of developing toxoplasmosis after transplantation [15, 16].

Clinical manifestations of CNS toxoplasmosis are similar for both transplant recipients and

HIV-infected patients and typically include headache, altered mental status, seizures, focal neurologic deficits, hemiparesis, ataxia, and facial weakness [3, 5]. Although uncommon, toxoplasmosis of the spinal cord has been reported in transplant recipients and HIV-infected patients [17, 18]. Unlike HIV-infected patients, who reveal a marked ring-enhancement pattern noted on neuroimages, transplant recipients often show a variable enhancement pattern on neuroimages, with the lesion enhancement inversely correlated with the severity of immunosuppression [19, 20].

Definitive diagnosis requires the identification of tachyzoites in biopsy samples, but identification of anti–T. gondii antibodies by ELISA is a sensitive and specific method. Although PCR assay of CSF is highly specific and sensitive in some laboratories, its sensitivity varies by laboratory and technique, and PCR assay should not be used to exclude the diagnosis of toxoplasmosis. The presence of multiple ring-enhancing lesions in the basal ganglia or cerebrum on neuroimages, especially in the presence of anti-toxoplasma IgG antibodies, is suggestive of CNS toxoplasmosis and is sufficient to start presumptive treatment for CNS toxoplasmosis.

Regardless of the host immune status, drug treatment for CNS toxoplasmosis should include pyrimethamine 25–100 mg/day for 3–4 weeks, and sulfadiazine 1.5 g QID for 3–4 weeks.

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