CMV PRP should be considered in patients with advanced immunosuppression presenting with ascending paraplegia, areflexia, and urinary retention with typical CSF abnormalities (polymorphonuclear pleocytosis, elevated protein concentration, and hypoglycorrhachia).

Table 1. Summary of Presenting Signs and Symptoms of the Two Cases in Comparison to the 103 Patients with CMV PRP in Anders and Goebel's Review

Sign or Symptom	Anders and Goebel [2]	Case 1	Case 2
Lower limb weakness	100%	Present	Present
Lower limb areflexia	100%	Present	Present
Urinary retention	94%	Present	Present
Paresthesia	79%	Present	Present
Sensory loss (legs)	72%	Present	Present
Fecal incontinence	67%	Absent	Absent
Lumbar pain	36%	Absent	Absent
Babinski sign	16%	Absent	Absent

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352. Towards Earlier Diagnosis of Transmissible Spongiform Encephalopathies (TSEs): A Case Series, Including One Associated With Squirrel Brain Consumption

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Session: 55. CNS Infections

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Background. TSEs present diagnostic and infection control (IC) challenges. Creutzfeldt-Jakob Disease (CJD) is the most common human TSE, occurring in 1–2/million/year in the United States, but other zoonotic factors or transmissions remain incompletely understood. Prompted by the occurrence of four suspected cases from November 2017 to April 2018, we present a case series of suspected CJD to illustrate its variable presentation and the need for more rapid identification for implementation of disease-specific disinfection, sterilization, and quarantine measures.

Methods. We defined a case as any patient with a rapidly progressive dementing or neurologic illness and laboratory tests for CJD. IC and laboratory databases, and electronic medical records were reviewed to identify possible cases from 2013 to 2018.

Results. Five patients met case definition. The average time to suspecting and confirming a diagnosis was 5.2 and 14.2 days, respectively.

Case	1	2	3	4	5
Age/sex	61 M	65 F	51 F	61 F	80 M
Cognitive symptoms	Psychosis, schizophrenia, cognitive decline	Dysphasia, depression, psychosis	Vertigo, progressive encephalopathy	Memory loss, aphasia	Aphasia, dysarthria, dysphagia
Motor symptoms	Impaired gait	Impaired gait	Bilateral ataxia	Impaired gait incontinence, abnormal muscle tone with paratonia	Unilateral weakness, jerking movements
EEG	Triphasic pattern	Abundant generalized discharges	Occasional bi-frontal sharp wave discharges	Generalized encephalopathy	NSC
MRI	Increased T2 signal in the pulvinar of the thalamus and cortex (especially frontal lobes)	NSC	NSC	NSC/small vessel infarcts	NSC/small vessel infarcts
RT-QuIC	+	+	+	–	P
14-3-3	+	+	+	–	P
T-tau	8,750	>4,000	>4,000	390	P
Epidemiology	Intake of squirrel brains	Concurrent apheresis and GYN surgery	Hotel Housekeeping	Industrial Chemist Residence in UK, intake of dog food	Janitor
CJD	V	S	S	No	P
Days to suspecting diagnosis	1	13	2	4	6
Days to confirmation	16	12	18	12	>11
Months of Illness	5	3	>2	P	P
Outcome	Dead	Dead	Alive	Alive	Alive

NSC, nonspecific changes; P, pending; S, poradic; V, variant; RT-QuIC, Realtime Quaking Induced Conversion.

Conclusion. Protean in presentation, the diagnosis of CJD can be delayed. Variant CJD and emerging zoonotic TSEs should be considered in differential diagnoses and IC measures. Improved empiric classification algorithms and tests with faster turnaround times are needed.

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353. HSV-Induced Anti-NMDAR Encephalitis

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Session: 55. CNS Infections

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Background. *N*-Methyl-D-aspartate receptor (NMDAR) is a glutamate receptor on nerve cells that controls synaptic plasticity and memory function. Anti-NMDAR encephalitis is a rare autoimmune disease causes by antibodies (Ab) against GluN1 subunit of the NMDAR. Preceding Herpes simplex virus-1 encephalitis (HSVE) is a well-recognized infectious trigger. First reported in female patients with ovarian teratoma, and more recently with germ cell tumors in males.

Methods. A 61-year-old male presented with agitation, behavioral changes, and confusion. Eight months prior, he was diagnosed with HSVE and treated with 21 days of intravenous acyclovir. Following therapy, he suffered from residual cognitive and personality changes with slow recovery until 3 months prior to admission encephalopathy again worsened. An extensive investigation was unrevealing except for a CSF lymphocytic pleocytosis, positive anti-NMDAR Ab titer 1:64 and imaging changes consistent with post-viral encephalitis. At that point, HSV-induced anti-NMDAR encephalitis was diagnosed. A PET scan did not show any occult malignancies. Two cycles of plasmapheresis were attempted over 4 months period with limited success in improving his worsening neurologic deficits.

Results. HSVE induced autoimmune encephalitis is a rare complication, primarily affecting children and young adults. Auto Ab develop 1–4 weeks after HSVE, manifesting as choreoathetosis and/or orofacial dyskinesia in children and psychiatric symptoms in young adults. CSF Ab titer is highly sensitive and specific. Proposed mechanisms include either viral reactivation or a post-infectious autoimmune process. Immunotherapy with tumor resection (if present) has been promising with less frequent need for second-line therapy in primary condition, compare with HSVE-induced condition where tumors have not been reported and resistance to first-line therapy has been observed. Progressive decline in neurologic function post HSVE prompted an evaluation for paraneoplastic conditions in our patient that ultimately revealed the diagnosis. The unique feature of this case is the age of the patient and preceding HSVE which triggered this autoimmune process.

Conclusion. Physicians should consider anti-NMDAR encephalitis in the differentials for relapsing patients post HSVE.

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354. Evidence of Aspergillosis Among Patients With Influenza-Associated Hospitalizations—United States, 2005–2017

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Background. Invasive aspergillosis primarily affects immunosuppressed persons, but it has also been observed in immunocompetent patients with severe influenza. Several case series suggest that severe influenza infection might be an under-recognized risk factor for aspergillosis. We examined the frequency of aspergillosis-related hospital discharge codes in a national surveillance database of influenza hospitalizations.

Methods. We analyzed laboratory-confirmed influenza-associated hospitalizations reported during 2005–2017 to Centers for Disease Control and Prevention (CDC)'s Influenza Hospitalization Surveillance Network (FluSurv-NET), which includes children and adults in 13 states. We obtained data on underlying conditions and clinical course through medical chart abstraction. We defined invasive aspergillosis cases as influenza hospitalizations with ≥1 of the following the International Classification of Diseases (ICD) 9th or 10th Clinical Modification discharge diagnosis codes: 117.3 (aspergillosis), 484.6 (pneumonia in aspergillosis), B44.0 (invasive pulmonary aspergillosis), B44.2 (tonsillar aspergillosis), and B44.7 (disseminated aspergillosis).

Results. Among 92,671 influenza hospitalizations, we identified 94 cases (0.1%) that had invasive aspergillosis codes. Characteristics of patients were: 60% male (56/94), 72% white race (60/83), and median age 58 years [interquartile range (IQR) 41–67].

Influenza A accounted for 80% (75/94) of cases. Seventy-nine percent (74/94) received antiviral therapy. Underlying conditions included 63% (59/94) immunocompromising condition, 51% (48/94) chronic lung disease, 22% (21/94) renal disease, and 15% (14/94) asthma. Forty-eight percent of patients (45/94) required intensive care. At the time of discharge, 60% (56/94) were diagnosed with pneumonia and 14% (13/94) died.

Conclusion. Over one-third of patients with invasive aspergillosis did not have a documented immunosuppressive condition. ICD codes are likely an imperfect way to identify invasive aspergillosis, and further studies are needed to characterize risk factors and verify diagnoses for aspergillosis among patients with severe influenza.

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355. Invasive Pulmonary Aspergillosis (IPA) Complicating Respiratory Viral Infections in Patients With Hematological Malignancies

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Background. Data regarding respiratory viral infections (RVIs) in patients with leukemia and/or stem cell transplantation (LSCT) and their predisposition to invasive pulmonary aspergillosis (IPA) are limited. To that end, we conducted a case–control study of post-RVI-IPA in LSCT patients.

Methods. We analyzed all consecutive adult patients (2006–2016) with culture-documented IPA (EORTC/MSG criteria). Cases were patients with confirmed (either by nasal wash and/or BAL PCR and/or respiratory viral culture) RVIs [respiratory syncytial virus (RSV), Influenza A/B (INFA/B), or parainfluenza virus (PIV)] followed by IPA up to 5 weeks after. Controls were patients with IPA without evidence of RVIs.

Results. We identified 54 cases (proven 1, probable 53), and 142 patients with IPA (proven 12, probable 130) as controls. The distribution of viruses were 34 PIV (52%), 18 INFA/B (27%), and 14 RSV (21%). The median days of post-RVIs-IPA infection was 8(−6–57) days. Among cases, the most common hematological malignancies were AML (34%) and CLL (26%). Most cases had prior allogeneic SCT (57%). Non-*fumigatus Aspergillus* species were the cause of IPA in 58% of cases. In univariate analysis, patients with post-RVs-IPA infection were more likely to be in complete or partial remission (43.9% vs. 22.3% $P = 0.007$), to have prior allogeneic SCT (57% vs. 31%, $P = 0.0009$) and an absolute lymphocyte count between 500 and 1,000/mm^3 at RVI diagnosis (41% vs. 27%, $P = 0.04$). In addition, coinfections within 2 weeks after viral infection (58% vs. 18%, $P = 0.0001$), especially of the lower respiratory tract (37% vs. 18%, $P = 0.004$) were more common in patients with post-RVIs-IPA. RVIs-IPA patients were less likely to have an absolute neutrophil count <100 mm^3 at IPA diagnosis (17% vs. 37%, $P = 0.005$). Need for ICU post-RVIs-IPA disease (31% vs. 26% $P = 0.5$) and 42 days crude mortality (22% vs. 27%, $P = 0.45$) were no different between cases and controls.

Conclusion. Post-RVIs-IPA occurs more frequently in patients with prior transplantation and is less associated with leukemia relapse and neutropenia. Although co-infections are common, this entity does not appear to be associated with worse outcome compared with IPA without preceding RVI.

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356. Bronchoalveolar Lavage Fluid Cytology by GMS Stain for the Diagnosis of Invasive Pulmonary Aspergillosis in Patients With Hematologic Malignancies: Analysis of 67 Episodes

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Background. The yield of direct fungal visualization by GMS (Gomori–methenamine–silver) stain in bronchoalveolar lavage (BAL) cytology has rarely been studied in the diagnosis of invasive pulmonary aspergillosis (IPA) in patients with hematological malignancies (HM).

Methods. We analysed a series of patients with proven or probable culture-documented IPA (EORTC/MSG criteria) in HM patients (1999–2015). All patients had BAL cultures that were positive for *Aspergillus* spp. and had concurrently obtained BAL cytology GMS available for analysis.

Results. We identified 67 such patients. BAL cytology based on GMS showed hyalohyphomycetes consistent with *Aspergillus* in 28/67 (41.8%) patients, whereas only in 2/67 (3.6%) direct smear Calcofluor White stain was positive. Based on BAL GMS cytology, co-infections were identified in six patients: two *Pneumocystis* and five viral infections with cytopathic changes (one had both). The yield of cytology was not different in patients with IPA caused by non-*fumigatus Aspergillus*, although patients with IPA and >1 *Aspergillus* in BAL culture had more often positive cytology GMS (100% vs. 0%, p 0.027). Cytology was also more often positive when obtained from a lesion-targeted BAL as compared with non-targeted bronchial washings (60.7% vs. 7.1%, p 0.038). Patients with IPA and cavitary lesions (32.1% vs. 5.1%, $P = 0.006$), history of SCT (64.3% vs. 33%, $P = 0.015$) or prior exposure to itraconazole (75% vs. 41%, $P = 0.007$) had positive cytology GMS results more often than did patients without these characteristics. In the multivariate analysis, only cavitary lesions were significantly associated with positive BAL GMS cytology.

Conclusion. GMS stain in cytology of BAL in patients with HM and culture-documented IPA had a sensitivity of 41.8% and was more often positive in patients with cavitary lesions. Although there were no differences in the proportion of GMS-positive cytology rates among differing *Aspergillus* spp. causing IPA, mixed *Aspergillus* spp. IPA was associated with an increase in positive cytology. BAL cytology was diagnostic for co-infections in more than 10% of patients. BAL cytology should be part of the diagnostic wok up in HM patients with suspected IPA.

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357. Aspergillus Isolates Remain Largely Susceptible to Azoles and Other Antifungals at a Large Transplant Program Using Azole Prophylaxis

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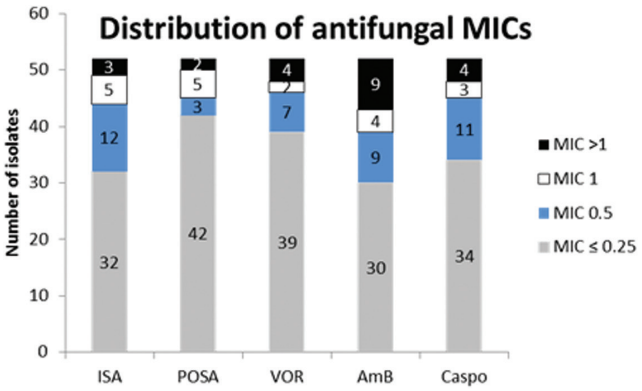
Background. The emergence of azole resistance globally among *Aspergillus* species has major clinical and agricultural implications. At our center, isavuconazole (ISA), posaconazole (POS), and voriconazole (VOR) have been used as antifungal prophylaxis in solid-organ transplant recipients. We determined susceptibility to azoles and other antifungals among *Aspergillus* isolates from our center.

Methods. Fifty-two patient isolates of *Aspergillus* species were collected from the UPMC Microbiology Laboratory between December 2016 and April 2018. Minimum inhibitory concentrations (MICs) of ISA, POS, VOR, amphotericin B (AmB), and caspofungin (CAS) were measured using EUCAST Antimicrobial Susceptibility Testing methods. *Candida parapsilosis* ATCC 22019 and *Candida krusei* ATCC 6258 were used as quality control.

Results. Seventy-one percent (37/52) of isolates were from solid-organ transplant recipients (34 lungs, two liver, and one heart). *Aspergillus* spp. were *A. fumigatus* (29), *A. terreus* (*At*, 6), *A. niger*, *A. flavus* and *Aspergillus calidoustus* (five of each species), and *A. lentulus* and *A. thermomutatus* (one of each species). Thirteen breakthrough (BT) isolates were recovered from patients on azoles: *A. calidoustus* (5), *A. niger* (4), *A. flavus* (2), *A. fumigatus* (1) and *At* (1). *A. calidoustus, A. flavus*, and *A. niger* were more likely than other species to be recovered from azole BT (75% (12/16) vs. 5% (2/36), $P = 0.06$). For all isolates, ISA, VOR, and POSA MIC$_{50}$ were 0.25 μg/mL, 0.04 μg/mL, and 0.25 μg/mL, respectively. One *A. calidoustus* and one *At* were resistant to all antifungals (azoles, AmB, and caspofungin MICs were >16 μg/mL); both were associated with azole BT. ISA, POS, and VOR MIC$_{50}$ vs. azole BT isolates (0.5, 0.125, and 0.5 μg/mL, respectively) were higher than those vs. non-BT isolates (0.25, 0.03, and 0.25 μg/mL, respectively; $P < 0.01$ for all).

Conclusion. Despite widespread use of azole prophylaxis in transplant recipients at our center, we did not observe high rates of resistance to azoles or other antifungals among *Aspergillus* isolates, although azole MICs were higher against BT isolates. Azole BT isolates were more likely to be non-*A. fumigatus* species. Clinicians should understand that antifungal resistance rates can vary by center and geographical location, and use their local epidemiology to guide decisions about the utility of specific agents in their populations.



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