The perioperative management of suspected prion disease

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Introduction

Creutzfeldt-Jakob Disease (CJD) and its variants are a group transmissible spongioform encephalopathies (TSE) that lead to dementia, neurological decline and death in all infected patients. While the exact method of transmission remains a matter of debate, it is known that a prion plays a central role in the spread and progression of the disease. These infectious proteins are resistant to common disinfection procedures, and consequently have been linked to iatrogenic infection in three separate circumstances: After the use of insufficiently sterilized equipment; after the use of extracted pituitary hormones; and after the implantation of corneal and dural grafts. While some studies suggest the incidence of CJD to be as low as 1:1,000,000, a 2004 study of tonsillar tissue from asymptomatic UK patients reported between 4,000 and 30,000 carriers of the infectious protein. Due to the resistant nature of the prion protein and the devastating conseques of iatrogenic transmission among patients and healthcare workers, patients with suspected or confirmed CJD pose an interesting challenge to anesthesia providers.

We present the case of a previously healthy 46 year old African-American female admitted for acute onset of progressive neurologic decline. While her presenting labs and CSF studies were normal, her MRI was concerning for the possibility of prion disease. In order to distinguish between this and other treatable forms of encephalitis, the decision was made for brain biopsy.

We performed a review of the literature on the anesthetic management of patients with CJD. The accompanying tables summarize the recommendations on patient management based on operative staging as well as the inherent transmission risk of the surgery (Table 1; Table 2; Table 3).

Table 1: Pre-Operative Concerns

Concerns	Consensus/Rationale
1. Is suspected or confirmed prion disease an absolute contraindication to surgical intervention?	1. NO: According to WHO guidelines, patients with suspected or confirmed prion disease should not be denied surgery on this basis alone. These procedures may be necessary to improve patient well being/patient care (e.g. insertion of feeding tubes/tracheostomy) or may be completely incidental to the prion disease process.
2. Is surgical conformation (brain biopsy) needed for all cases of suspected prion disease?	2. NO: The diagnosis of most prion disease is accomplished via an intensive analysis of patient history (risk of exposure), clinical symptoms (neurologic findings and course of neurologic decline), laboratory testing (CSF Protein: Protein 14-3-3 testing), and imaging (MRI: varied findings depending on type of prion disease, most related to increased FLAIR/DWI signal in cortex or nuclei of basal ganglia). HOWEVER: Biopsy confirmation may be necessary in patients with equivocal findings to help differentiate prion disease from a treatable form of encephalopathy.
3. Planning prior to surgery: a. How is risk of transmission of prion disease evaluated?	3. a. 3 basic considerations: 1. Probability that patient has or will develop prion disease: Patients with confirmed or suspected prion disease are the highest risk and MUST be managed using specific precautions. 2. Level of infectivity of tissues: *High Risk*: Brain, Dura, Eye *Medium Risk*: Lung, Liver, CSF, Spleen *Low Risk*: Adipose, Muscle, Tears, Saliva 3. Nature or route of Exposure to tissues: *Cutaneous Exposure*: Low risk of transmission when exposed to intact skin or mucous membranes. *Trans-cutaneous Exposure*: Increased risk of transmission with non-intact skin, eye exposure, and needle sticks.
b. Who should be alerted/involved in the perioperative management of the patient?	b. Every institution should have a written protocol in place regarding perioperative management of patients with confirmed/suspected prion disease. At a minimum: 1. The infection control team should be alerted about the surgical procedure as early as possible and preferably prior to admission. 2. All staff/personnel involved in patient care should be aware of the potential infection and current hospital guidelines and appropriate training should be provided.
c. How are resources best allocated to address the complexities of perioperative management?	c. Resource allocation: 1. *Operating room*: Patients should be scheduled as the last case to give ample time for room cleaning, and lessen the chance of transmission. 2. *Equipment*: All unessential equipment should be removed from the room and not returned until the room has been terminally cleaned. 3. *Personnel*: Only properly trained and essential personnel should be involved in the surgery. As such, many institutions suggest that students and residents not be involved in the case.
4. Is there any need for patient isolation or special precautions prior to surgery?	4. NO: Patients with confirmed or suspected prion disease can be transported without additional precautions and kept in the holding area with non-infected patients. There is no evidence that prion disease can be spread through casual contact, and treating these patients differently can lead to stigmatization.

Table 2: Intra-Operative Concerns

Concerns	Consensus/Rationale
1. What precautions should be in place to protect equipment and personnel from contamination?	1. Necessary Precautions: a. *Room Precautions*: All unnecessary equipment should be removed from the room. All unnecessary equipment that cannot be removed should be covered to prevent contamination from fluid. b. *Personnel Precautions*: Those involved in the case should wear a liquid repellent operating gown, a mask with a visor (or other eye protection), and it is suggested that they double glove. Those with pre-existing cuts or abrasions should be discouraged from participating in the case.
2. Should only disposable equipment be used?	2. IDEALLY YES: It is highly recommended that only single use devices be used in these patients, especially those cases involving high risk tissues. As such anesthesiologists should use disposable laryngoscope blades/handles. In addition, shorter cases should be performed under TIVA using mask ventilation with a disposable circuit (if possible).
3. If disposable equipment cannot be used, must expensive equipment be destroyed or quarantined after the case?	3. NO: Expensive cameras and stereotactic devices may be protected with a non-permeable material to avoid the need for disposal after the case. While it was earlier suggested that ventilators should be quarantined after each of these cases and then only used on patients with confirmed disease, it is now suggested that a HEPA filter between the patient and the ventilator is all that is required.
4. How should infectious material/specimens be treated?	4. All specimens for evaluation should be placed in impervious containers and sealed in a plastic bag labeled as biohazard. All additional material should be collected and bagged for incineration.
5. How should accidental exposure be treated?	5. Ideally, protective barriers should prevent splashes to the eye, mouth as well as protect any non-intact skin areas. However if exposure occurs it is necessary to irrigate the area with copious amounts of water. In addition the exposed person should report the incident to the Occupational Health Department and file an incident report as soon as possible.

Table 3: Post-Operative Concerns

Concerns	Consensus/Rationale
1. Is patient isolation needed in the post-operative period?	1. NO: Special precautions are not needed for these patients during the post-operative period.
2. How is the room cleaned after a suspected prion case?	2. Sodium hypochlorite 20,000ppm and 2M sodium hydroxide are needed for terminal cleaning. High concentrations of hypochlorite may be caustic to metals and as such they may need to be irrigated with water after cleaning. Electrical cables cannot be cleaned with hypochlorite and as such sodium hydroxide wipes may be used. However, 2M hydroxide alone will not decontaminate surfaces that have been contaminated with prion-containing fluids.
3. How are instruments/equipment handled after a suspected prion case?	3. Ideally, single use instruments will be used in high-risk cases. If non-disposable equipment is used, treatment will be based on the risk of infectivity: a. *Laryngoscope Blades*: 5% sodium hypochlorite solution for 1 hour, followed by autoclaving for 1 hour. b. *Aluminum/Zinc Instruments*: 5% sodium hypochlorite solution for 1 hour, followed by autoclaving for 1 hour. c. *Stainless Steel Instruments*: 1-2M Sodium Hydroxide for 1 hour, followed by autoclaving for 1 hour.

Case Description

The patient is a 46 year old African-American female with a PMH of bipolar disorder, HTN and DM2 who admitted for acute onset of progressive neurologic decline. She was in her normal state of heallth prior to that except for some intermittent confusion in the previous 2 weeks and a resolved diarrheal illness. Per report, she was found unresponsive and was taken to an outside hospital.

Initial workup revealed elevated CPK, elevated WBC. There was additional concern for neuroleptic malignant/serotonin syndrome as the patient had been previously treated with anti-psychotic medications. She was started on acyclovir, ceftriaxone and vancomycin. However, she showed no improvement., and was transferred to our institution for further management.

On arrival she was evaluated by the Neurology service. Of note, the patient was only found to have elevated blood sugars. Analysis of CSF revealed an elevated 14-3-3 levels. MRI of the brain revealed Increased dilation of the lateral ventricles. Hyperintensity was noted in caudate nuclei, and posterior cortex. A cortical /subcortical lesion in the right pre-frontal cortex was noted. In addition, there was Increased signal the in pes hippocampi that was more prominent on the right.

Despite aggressive medical management, the patient's neurological status did not improve. After discussion with the family, neurology and neurosurgical services, the decision was made for brain biopsy.

Brain biopsy was performed under general anesthesia without significant event. All samples taken were negative for the presence of prion disease.

Despite aggressive medical management, the patient remains a nursing home resident, with minimal improvement in neurological status.

Conclusion

CJD and its variants are a group of TSEs that lead to dementia, neurological decline and death in all infected patients. Recent reports reveal that the actual incidence may be much higher than actually expected. Given the social stigma associated with the disease, the ease of transmission and the resistance of the prion to normal decontamination procedures, it is necessary to have plan in place for compassionately and effectively dealing with patients.