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Letter to the Editor

Reassessing donor/recipient screening practices in light of iatrogenic cerebral amyloid angiopathy: Medicolegal aspects – A letter to the editor

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Dear Editor,

This brief letter serves as an addendum to our previously published article, "Iatrogenic cerebral amyloid angiopathy: two cases linked to childhood cadaveric dural transplantation for different intracranial pathologies, diagnosed using the simplified Edinburgh computed tomography criteria."[2]

The expanding literature on iatrogenic cerebral amyloid angiopathy (iCAA) raises important medicolegal and ethical concerns, especially regarding organ and tissue donor programs. Iatrogenic transmission of pathologically misfolded prion-like proteins – including amyloid-β (Aβ) – can occur through transplanted tissues, red blood cell transfusions, and contaminated surgical instruments.[3] Such risk is of particular concern in neurosurgery, where procedures like dural substitution have been performed on individuals later found to harbor prion-like pathologies. This raises important questions about the ethical and legal adequacy of tissue transplantation protocols.

Historically, our understanding of amyloid transmission was limited mainly to prion diseases such as iatrogenic Creutzfeldt–Jakob disease (iCJD), linked to cadaveric dural grafts and pituitary-derived hormones. The first cases of dura mater-associated CJD were recognized in 1987, with incubation periods of up to 30 years.[8] However, recent findings suggest that Aβ pathology may also be transmissible under certain iatrogenic conditions. This necessitates a critical reevaluation of donor screening procedures, especially as these risks are often poorly addressed in existing medicolegal frameworks of many healthcare systems.

iCAA is a rare but increasingly recognized form of CAA, typically affecting individuals under 55 years of age and presenting with cognitive decline, seizures, and/or lobar intracerebral hemorrhage (ICH).[1] It has been most commonly associated with the historical use of cadaveric dural grafts and potentially inadequately sterilized neurosurgical instruments.[3] Reports by Jensen-Kondering[5] and Pikija *et al.*[7] have shown spatial correlations between surgical sites and Aβ deposition, suggesting localized iatrogenic seeding. Jucker and Walker have further emphasized the potential prion-like behavior of Alzheimer's-type pathology.[6]

Given these insights, the current donor eligibility criteria may overlook individuals at risk of transmitting Aβ pathology. Brain-dead patients with lobar ICH are often accepted for corneal

or organ donation without detailed histories of distant neurosurgical procedures or transfusions, especially those performed before modern sterilization standards. This represents a potential but underappreciated transmission risk of Aβ pathology to recipients.

In response to concerns over iCJD, instrument-sterilization protocols were enhanced using sodium hydroxide, hypochlorous acid, alkaline detergents, and autoclaving. However, the effectiveness of these methods against Aβ remains uncertain. Standard decontamination procedures may not reliably inactivate amyloid seeds, posing a continued risk of iCAA transmission.[4-6] In low- and middle-income countries, limited access to single-use instruments further exacerbates the potential for iatrogenic transmission, raising ethical questions about global health equity.

Donor registries rarely record data on previous neurosurgery or blood transfusions decades earlier. Yet, a spontaneous lobar ICH in younger individuals should prompt a more thorough evaluation. While no formal guidelines currently mandate this, the medical community must begin asking: should we actively exclude potential donors with lobar ICH and a medical history suggesting possible exposure to amyloid-contaminated materials or instruments?

We are entering an era where "iatrogenic neurodegeneration" is no longer a theoretical construct. As iCAA joins iCJD in the group of preventable, procedure-related diseases, we call for a paradigm shift in clinical practice and regulatory frameworks. Long-term surveillance of patients exposed to potentially contaminated instruments or transplants is warranted, as is interdisciplinary collaboration between neurology, neurosurgery, infectious disease, and transplantation medicine.

In conclusion, every trustworthy and safe organ and tissue transplantation program must uphold professional standards, legal safeguards, and equitable access to care – ensuring safety for both donors and recipients across all socioeconomic contexts. Until definitive risk assessment tools are available, heightened awareness, rigorous donor screening, and transparent communication are essential.

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