

Heidenhain variant of Creutzfeldt–Jakob disease in a patient who had bovine bioprosthetic valve implantation

Jehard Hashoul, Waleed Saliba¹, Irina Bloch², Haneen Jabaly-Habib

Creutzfeldt–Jakob disease (CJD) is a rare neurodegenerative disorder characterized by rapidly progressing dementia, general neurologic deterioration, and death. When the leading symptoms are visual disturbances, it is termed as the Heidenhain variant of CJD (HvCJD). CJD was reported following prion-contaminated pericardium transplants but never after bovine bioprosthetic cardiac valve. In this case report, we describe HvCJD in a patient who had a bovine bioprosthetic cardiac valve implant. An 82-year-old-woman was referred to neuro-ophthalmology clinic for unexplained visual loss that started 1 month previously. Medical history included aortic valve replacement with bovine bioprosthetic valve. On examination, best-corrected visual acuity was 20/120 in the right eye and 20/200 in the left eye; otherwise, the eye examination was normal. Humphrey visual fields revealed complete right homonymous hemianopsia. Magnetic resonance imaging (MRI) demonstrated nonspecific white matter changes. A week later, she was hospitalized due to memory impairment; repeated MRI and total body computed tomography scan showed no significant findings. Electroencephalography recordings and extremely elevated cerebrospinal fluid tau protein were compatible with CJD. The patient died 3 weeks later; autopsy was not performed. The patient had HvCJD. Ophthalmologists being first to see these patients should be aware of this diagnosis. Contaminated bovine bioprosthetic valve might be another source for prion disease. Further research is required to establish this issue.

Key words: Bovine bioprosthetic cardiac valve, Heidenhain variant of Creutzfeldt–Jakob disease, prion, unexplained visual loss

Creutzfeldt–Jakob disease (CJD) is the most common human prion disease with an incidence of 1 case per 1 million populations per year; it is a rare neurodegenerative disease associated with severe neuronal loss, spongiform changes, and accumulation of the abnormal prion protein. About 85% of CJD cases are sporadic CJD (sCJD), 5%–15% are familial CJD, and <1% are iatrogenic CJD. Six clinical phenotypes of sCJD have been reported; the “classic CJD” phenotype includes myoclonic and Heidenhain variant (MM1 and MV1), accounts for 70% of sCJD cases, and is associated with advanced age at onset, rapidly progressive dementia with early-prominent myoclonus, and a short duration of illness (mean 3.9 months); visual signs may precede severe dementia in about 30% of cases.^[1] When sCJD presents with isolated visual symptoms which persist even without any cognitive decline for a few weeks – it is termed the Heidenhain variant.

Case Report

An 82-year-old Jewish woman, Ukrainian descendant, was referred to neuro-ophthalmology clinic for unexplained progressive visual loss over the past month with a significant deterioration in the last few days. The patient and her son denied any behavioral change or memory impairment at this point.

Department of Ophthalmology, Baruch Padeh Medical Center, Poriya, ¹Department of Internal Medicine, Emek Medical Center, ²Department of Neurology, Emek Medical Center, Afula, Israel

Correspondence to: Dr. Jehard Hashoul, P. O. Box: 3, Jish, Galilee 13872, Israel. E-mail: jehardhashoul@gmail.com

Manuscript received: 08.01.16; **Revision accepted:** 12.09.16

Medical history included hypertension and aortic valve replacement with bovine 19 mm bioprosthetic valve, performed 5 years before her current presentation.

On examination, her best-corrected visual acuity was 20/120 in the right eye and 20/200 in the left eye, pupillary reactions and eye movement were normal, and applanation tonometry was 11/11; after dilating the pupils, both eyes revealed nonsignificant cataract, normal optic disc and retina. Humphrey visual fields revealed complete right homonymous hemianopsia with bilateral macular involvement [Fig. 1]. Brain magnetic resonance imaging (MRI) demonstrated diffuse atrophic and nonspecific white matter changes along with small cystic lesions and anatomical distortion at the basal ganglia level, no cortical pathology [Fig. 2].

One week later, the patient was admitted to the hospital due to memory impairment; repeated complete blood count, chemistry and rheumatologic panel were within normal limits. Electroencephalography (EEG) revealed diffuse slowing and periodic sharp wave discharges along with triphasic wave complexes [Fig. 3]; repeated brain MRI and total body computed tomography showed no significant

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

Cite this article as: Hashoul J, Saliba W, Bloch I, Jabaly-Habib H. Heidenhain variant of Creutzfeldt–Jakob disease in a patient who had bovine bioprosthetic valve implantation. *Indian J Ophthalmol* 2016;64:767-9.

Access this article online

Website:
www.ijo.in

DOI:
10.4103/0301-4738.195003

Quick Response Code:



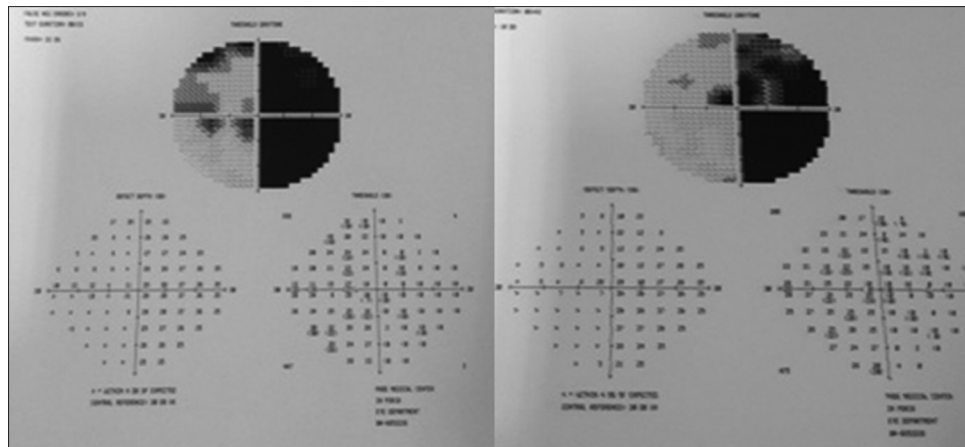


Figure 1: Automated visual fields showing right homonymous hemianopsia with bilateral macular involvement

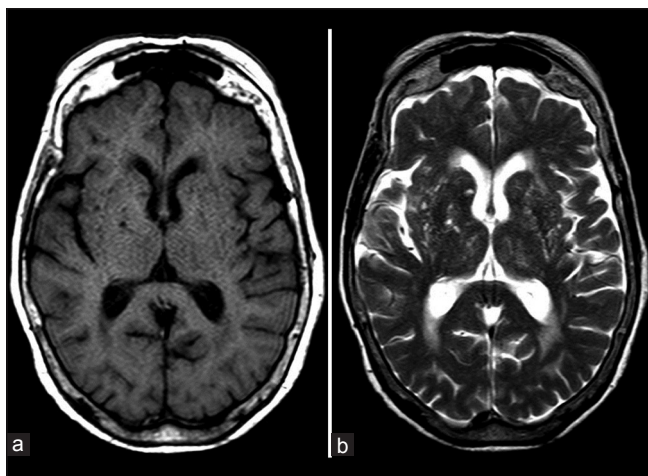


Figure 2: Axial T1 (a) and T2 (b) magnetic resonance imaging demonstrating brain atrophic changes and cystic changes (hypointense lesions in T1 and hyperintense in T2 along with anatomical distortion at the basal ganglia level)

changes compared to previous studies; cerebrospinal fluid (CSF) revealed extremely elevated tau protein >1200 pg/ml compatible with CJD.

During her hospitalization, the patient developed rapid loss of short and long memory, disorientation, incontinence, and brisk reflexes. She was discharged home according to her family request and died 3 weeks later. Unfortunately, autopsy was not performed.

Discussion

Our patient presented with progressive visual decline over 5 weeks, followed by rapidly progressive dementia and extrapyramidal tract dysfunction. The patient died 2.5 months after her presenting symptoms. According to the World Health Organization, the definite diagnosis of CJD is made by tissue diagnosis not performed in our patient.^[2] Considering the disease course, rapidly progressive dementia (<2 years), visual impairment, extrapyramidal tract dysfunction, and the EEG findings, as well as the extremely elevated tau protein, our patient had probable CJD diagnosis [Table 1].

Table 1: Diagnostic criteria for Creutzfeldt-Jakob disease

Diagnosis	Criteria
Definite	Pathologic evidence of spongiform degeneration, gliosis, neuronal loss in posterior, temporal, parietal, and occipital lobes
Probable	Rapidly progressive dementia (<2 years) Two of the following: 1. Visual impairment: Blurred vision, visual field defect, cortical blindness 2. Myoclonus 3. Pyramidal or extrapyramidal tract dysfunction 4. Akinetic mutism EEG with periodic sharp wave complexes and/or MRI: Increased cortical signal in parietooccipital region (DWI) and/or Elevation of neuronal destruction markers in CSF
Possible	Same criteria as "probable" without EEG findings, MRI, markers

EEG: Electroencephalography, MRI: Magnetic resonance imaging, DWI: Diffusion-weighted imaging, CSF: Cerebrospinal fluid

Human-to-human transmission of CJD was first reported in 1974 in a 55-year-old woman who developed symptoms 18 months after corneal transplantation from a donor who died of the disease. CJD transmission had been also reported following cadaveric dural graft transplants, radiographic embolization procedures with dura mater, liver transplants, administration of cadaveric human pituitary hormones, and by contaminated neurosurgical instruments. In 1989, a 54-year-old patient who received homograft pericardium for tympanic membrane closure 4 years earlier developed CJD.^[3]

Although the definite pathogenesis is unknown, the primary component associated with the infection of CJD is an isoform of a normal host membrane glycoprotein called cellular prion protein (Pr^{Pc}). The normal prion protein Pr^{Pc} is protease sensitive, soluble and has a high α -helix content.^[4] Pr^{Pc} can undergo conversion into a conformationally altered isoform (scrapie prion protein [Pr^{Psc}]) widely believed to be the pathogenic agent of transmissible spongiform

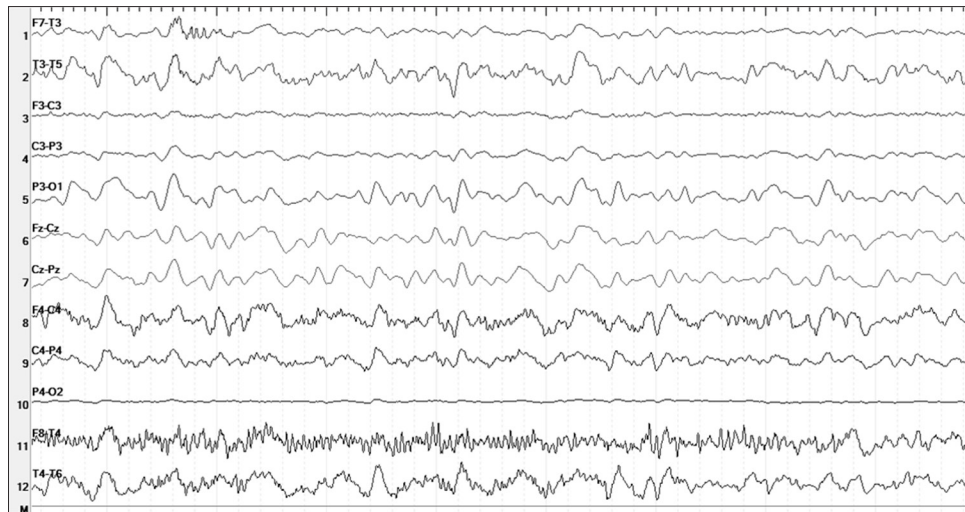


Figure 3: Electroencephalography showing general slowing with triphasic waves

encephalopathies. The PrP^{Sc} is protease-resistant, insoluble, forms of amyloid fibrils and has high β -sheet content.^[5]

The tissue-specific expression of PrP^C is crucial considering that cells expressing high levels of PrP^C bear a risk for conversion and accumulation of PrP^{Sc}. Quantitative and qualitative analysis of PrP^C revealed that widespread tissue expression pattern of PrP^C in bovine somatic tissues includes heart and myocardium;^[6] it was found also in sheep,^[7] hamster, and other nonhuman primates. Furthermore, expression of PrP^{Sc} was demonstrated in the hearts of transgenic mice as amyloid deposits that led to myocardial stiffness and cardiac disease.^[8] PrP^{Sc} has been reported in the heart tissue of one sCJD patient.^[9]

Prions exhibit an unusual resistance to conventional disinfection and sterilization methods; the procedures for sterilization of prion-contaminated medical instruments have been controversial for many years. Guidelines for sterilization that appear to be effective have been reported.^[10] We presume that all of these guidelines may dismantle any biological tissue.

According to the manufacturer, our patient bioprosthetic aortic valve leaflets were made of bovine pericardium, and no information of bovine PrP^{Sc} screening of the pericardium leaflets was available.

We are unable to offer definite proof of the transmission of CJD by the bovine pericardium-made bioprosthetic aortic valve since autopsy was not performed. Still, the interval between the valve replacement surgery and the symptoms of the disease suggests that the pericardium was the conceivable vehicle for the transmission of the patient with CJD.

Conclusion

The patient's diagnosis was probable Heidenhain variant of CJD (HvCJD), suspected to be transmitted by the bovine valve transplantation never reported before. Bovine bioprosthetic valve made of pericardium might be another source for prion disease. Although this is a rare disease, ophthalmologists should be aware of the diagnosis being first to see the HvCJD of the CJD patients. Thorough medical history and good clinical examination and

patients' follow-up may lead to the correct investigation and diagnosis. Further research is required to establish this issue.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Parchi P, Giese A, Capellari S, Brown P, Schulz-Schaeffer W, Windl O, *et al.* Classification of sporadic Creutzfeldt-Jakob disease based on molecular and phenotypic analysis of 300 subjects. *Ann Neurol* 1999;46:224-33.
2. Brown P, Brunk C, Budka H, Cervenakova L, Collie D, Green A, *et al.* World Health Organization manual for surveillance of human transmissible spongiform encephalopathies including variant Creutzfeldt-Jakob disease. Geneva, Switzerland: World Health Organization; 2003.
3. Tange RA, Troost D, Limburg M. Progressive fatal dementia (Creutzfeldt-Jakob disease) in a patient who received homograft tissue for tympanic membrane closure. *Eur Arch Otorhinolaryngol* 1990;247:199-201.
4. Glatzel M, Stoeck K, Seeger H, Lührs T, Aguzzi A. Human prion diseases: Molecular and clinical aspects. *Arch Neurol* 2005;62:545-52.
5. Prusiner SB. Prions. *Proc Natl Acad Sci U S A* 1998;95:13363-83.
6. Peralta OA, Eyestone WH. Quantitative and qualitative analysis of cellular prion protein(PrP (C)) expression in bovine somatic tissues. *Prion* 2009;3:161-70.
7. Horiuchi M, Yamazaki N, Ikeda T, Ishiguro N, Shinagawa M. A cellular form of prion protein (PrP^C) exists in many non-neuronal tissues of sheep. *J Gen Virol* 1995;76(Pt 10):2583-7.
8. Trifilo MJ, Yajima T, Gu Y, Dalton N, Peterson KL, Race RE, *et al.* Prion-induced amyloid heart disease with high blood infectivity in transgenic mice. *Science* 2006;313:94-7.
9. Ashwath ML, Dearmond SJ, Culclasure T. Prion-associated dilated cardiomyopathy. *Arch Intern Med* 2005;165:338-40.
10. Rutala WA, Weber DJ; Society for Healthcare Epidemiology of America. Guideline for disinfection and sterilization of prion-contaminated medical instruments. *Infect Control Hosp Epidemiol* 2010;31:107-17.