Ophthalmic Surgery in Prion Diseases

Tsuyoshi Hamaguchi,*1 Moeko Noguchi-Shinohara,* Yosikazu Nakamura,‡1 Takeshi Sato,‡2 Tetsuyuki Kitamoto,§2 Hidehiro Mizusawa,¶2 and Masahito Yamada*2

Eleven (1.8%) of 597 patients underwent ophthalmic surgery within 1 month before the onset of prion disease or after the onset. All ophthalmologists reused surgical instruments that had been incompletely sterilized to eliminate infectious prion protein. Ophthalmologists should be aware of prion diseases as a possible cause of visual symptoms and use disposable instruments whenever possible.

Visual impairment occurs in 10% to 20% of patients with sporadic Creutzfeldt-Jakob disease (sCJD) during an early stage of the disease (Heidenhain variant) (1,2). Some patients with prion diseases may visit ophthalmologists with visual impairment due to prion diseases or with coexisting age-related eye diseases (3,4).

Infectious prion protein (PrPSc) was identified in the retina and optic nerve in patients with variant CJD (vCJD) and sCJD (5,6), and CJD has been transmitted by corneal transplantation (7,8). In the World Health Organization (WHO) guidelines, eyes were classified as highly infectious tissues (9).

Secondary transmission of PrPSc through ophthalmic surgery could possibly be prevented around the onset of prion diseases, although surgery that is performed long before the onset of prion diseases would not have that potential. It is important to understand the current status of ophthalmic surgery for patients with prion diseases and to clarify the clinical features of the patients with prion diseases who undergo ophthalmic surgery. Here, we describe the relevant data from CJD surveillance in Japan.

The Study

We analyzed the patients with prion diseases who had been registered by the CJD Surveillance Committee in Japan from April 1999 through March 2005. We prospectively investigated each patient with a surveillance proto-
clinical articles and those who did not was compared by Fisher exact tests, and differences in age at onset and disease duration were compared by Mann-Whitney U tests. We used $\chi^2$ tests to compare the distribution of the patients with or without dementia or visual impairment within 2 months of onset. Statistical significance was defined as $p<0.05$.

We found 597 patients with definite or probable diagnosis of prion diseases: 468 (78.4%) with sCJD; 78 (13.1%) with inherited prion diseases; 48 (8.0%) with infectious prion diseases, including 47 cases of dCJD; and 1 patient with vCJD and 3 patients with unclassified CJD.

Thirty-seven patients (6.2%) had a history of ophthalmic surgery at some time in their lives. Among them, 11 patients (1.8%) underwent ophthalmic surgery within 1 month before the obvious onset of prion disease or after the onset. Except for 1 patient with Gerstmann-Sträussler-Scheinker disease, all of these patients had sCJD. There have been no reports of the development of prion diseases in patients who underwent ophthalmic surgery after the ophthalmic surgery of patients with prion diseases.

Ten patients with sCJD underwent ophthalmic surgery within 14 months of symptom onset, and 8 of them had ophthalmic surgery within 4 months of symptom onset (Table 1). At clinical onset, 4 patients exhibited visual symptoms, 5 had dementia, and 1 patient had a gait disturbance. All patients underwent surgery for cataracts, except for 1 patient who underwent surgery for a detached retina. According to the reports on the surgical outcome by the ophthalmologists of 7 patients, visual disturbance was unchanged in 2 patients, deteriorated in 1, and improved to some extent in 4 after surgery. All ophthalmologists reused some surgical instruments and cleaned instruments by either autoclaving or the ethylene oxide gas method, which have been reported to incompletely sterilize PrPSc (9, 12).

Clinical features were compared between sCJD patients who did and did not have ophthalmic surgery (Table 2). The patients who had ophthalmic surgery had a significantly longer disease duration than those without ($p=0.0004$). Regarding early clinical symptoms within 2 months after onset, the subgroup with visual symptoms without dementia was significantly overrepresented among the patients who had ophthalmic surgery compared with those who did not have surgery ($p=0.0004$).

**Conclusions**

Our study showed that, in 1.8% of the patients with prion diseases, eye tissues were operated on within 1 month before the obvious onset of prion disease or after the onset. In addition, the sCJD patients who underwent surgery had a significantly longer duration of the disease course as well as significant overrepresentation of visual symptoms without dementia in the early phase, compared with patients who did not have ophthalmic surgery.

The prevalence of ophthalmic surgery around the time of clinical onset of prion diseases in our study is similar to that (2.0%) in a report from the United Kingdom (13). In the UK study (13), patients with Heidenhain variant cases constituted 40% of sCJD patients who had ophthalmic surgery. Early visual impairment (due to prion diseases) would prompt ophthalmologists to perform surgery.

Currently, cataract surgery is recommended to improve physical or cognitive function in elderly patients (14, 15). It should be noted that, after performing eye surgery on patients with prion disease, all ophthalmologists reused surgical instruments that were sterilized with procedures that are incomplete for the sterilization of PrPSc, although the WHO infection control guidelines for prion diseases (9) strongly recommend single-use surgical instruments (9).

---

**Table 1. Characteristics of sCJD patients and ophthalmic surgery**

| Patient no. | Sex/age, y‡ | Disease duration, mo‡ | Symptom at sCJD onset | Ophthalmic disease | Interval, mo§ | Visual symptoms after surgery | Reused instruments | Cleaning method |
|-------------|-------------|-----------------------|-----------------------|-------------------|--------------|-------------------------------|-------------------|----------------|
| 1           | M/81        | 8                     | Visual                | Cataract          | 4            | NA                            | NA                | NA Autoclave (135°C for 9 min) |
| 2           | M/81        | 15                    | Dementia              | Cataract          | 0            | Improved                       | Yes               | NA EOG |
| 3           | F/64        | 20                    | Visual                | Cataract          | 14           | Not changed                    | Yes               | NA EOG |
| 4           | F/59        | 3                     | Dementia              | Detached retina   | -1           | Improved                       | Yes               | NA EOG |
| 5           | F/57        | 10                    | Dementia              | Cataract          | 10           | NA                            | NA                | NA EOG |
| 6           | F/79        | 5                     | Dementia              | Cataract          | -1           | Improved                       | Yes               | NA EOG |
| 7           | M/74        | 16                    | Visual                | Cataract          | 3            | Improved                       | Yes               | Autoclave (132°C for 10 min), EOG |
| 8           | F/63        | 5                     | Visual                | Cataract          | 1            | Deteriorated                   | Yes               | Autoclave (121°C for 60 min) |
| 9           | M/79        | 6                     | Gait disturbance      | Cataract          | 2            | Not changed                    | Yes               | Autoclave (121°C for 60 min) |
| 10          | F/66        | 3                     | Dementia              | Cataract          | 1            | NA                            | NA                | NA |

†sCJD, sporadic Creutzfeldt-Jakob disease; visual, visual impairment; NA, not available; EOG, ethylene oxide gas.
‡Disease duration, the duration from onset to akinetic mutism state or death if the patients never displayed akinetic mutism.
§Between surgery and sCJD symptoms.
instruments for procedures involving highly infective tissues. The fact that no secondary iatrogenic cases that could be attributed to surgical procedures were found during our investigation does not diminish the need for ophthalmologists to be aware of CJD as a cause of visual symptoms (including symptoms mimicking those of cataracts) and highlight the importance of using disposable instruments whenever possible to avoid cross-contamination.

Acknowledgments

We thank Fumio Moriwaka, Yoshiyuki Kuroiwa, Masatoyo Nishizawa, Nobuyuki Sodeyama, Masatoshi Takeda, Yusei Shiga, Shigetoshi Kuroda, Shigeki Kuzuhara, Jun Tateishi, Hiroyuki Murai, and Shigeo Murayama for the CJD surveillance. The CJD Surveillance Committee belongs to the Research Group on Prion Disease and Slow Virus Infection, funded by the Ministry of Health, Labour and Welfare, Japan; the funding source had no involvement in the publication of this article.

Dr Hamaguchi is a clinical research fellow in the Department of Neurology and Neurobiology of Aging, Kanazawa University Graduate School of Medical Science, Kanazawa, Japan. His primary research interest is prion diseases.

References

1. Kropp S, Schulz-Schaeffer WJ, Finkenstaedt M, Riedemann C, Windl O, Steinhoff BJ, et al. The Heidenhain variant of Creutzfeldt-Jakob disease. Arch Neurol. 1999;56:55–61.
2. Lueck CJ, McIlwain GG, Zeidler M. Creutzfeldt-Jakob disease and the eye. II. Ophthalmic and neuro-ophthalmic features. Eye. 2000;14:291–300.
3. Cooper SA, Murray KL, Heath CA, Will RG, Knight RSG. Isolated visual symptoms at onset in sporadic Creutzfeldt-Jakob disease: the clinical phenotype of the “Heidenhain variant.” Br J Ophthalmol. 2005;89:1341–2.
4. Tullo A. Creutzfeldt-Jakob disease and eye surgery—new disease, old disease. J Cataract Refract Surg. 2003;29:629–31.
5. Head MW, Northcott V, Rennison K, Ritchie D, McCardle L, Bunn TJ, et al. Prion protein accumulation in eyes of patients with sporadic and variant Creutzfeldt-Jakob disease. Invest Ophthalmol Vis Sci. 2003;44:342–6.
6. Head MW, Peden AH, Yull HM, Ritchie DL, Bonshke RE, Tullo AB, et al. Abnormal prion protein in the retina of the most commonly occurring subtype of sporadic Creutzfeldt-Jakob disease. Br J Ophthalmol. 2005;89:1131–3.
7. Duffy P, Wolf J, Collins G, DeVoe AG, Steeten B, Cowen D. Possible person-to-person transmission of Creutzfeldt-Jakob disease. N Engl J Med. 1974;290:692–3.
8. Heckmann JG, Lang CJ, Petrukh F, Druschky A, Erb C, Brown P, et al. Transmission of Creutzfeldt-Jakob disease via a corneal transplant. J Neurol Neurosurg Psychiatry. 1997;63:388–90.
9. World Health Organization (WHO). WHO infection control guidelines for transmissible spongiform encephalopathies. Report of a WHO consultation, Geneva, Switzerland, 1999 March 23–26. Geneva: WHO; 1999. Available from http://www.who.int/csr/resources/publications/bse/WHO_CDS_CSR_APH_2000_3/en/10.
11. Masters CL, Harris JO, Gajdusek DC, Gibbs CJ Jr, Bernardi C, Asher DM. Creutzfeldt-Jakob disease: patterns of worldwide occurrence and the significance of familial and sporadic clustering. Ann Neurol. 1979;5:177–88.
11. World Health Organization (WHO). The revision of the variant Creutzfeldt-Jakob (vCJD) case definition. Report of a WHO consultation. Edinburgh, United Kingdom, 2001 17 May (WHO/CDS/CSR/EPH/2001.5). Geneva: WHO; 2001.
12. Taylor DM. Inactivation of transmissible degenerative encephalopathy agents: a review. Vet J. 2000;159:10–7.
13. S-Juan P, Ward HJ, de Silva R, Knight RS, Will RG. Ophthalmic surgery and Creutzfeldt-Jakob disease. Br J Ophthalmol. 2004;88:446–9.
14. Brenner MH, Curbow B, Javitt JC, Legro MW, Sommer A. Vision change and quality of life in the elderly. Response to cataract surgery and treatment of other chronic ocular conditions. Arch Ophthalmol. 1993;111:680–5.
15. Tamura H, Tsukamoto H, Mukai S, Shido T, Mimamada O, Ochi Y, et al. Improvement in cognitive impairment after cataract surgery in elderly patients. J Cataract Refract Surg. 2004;30:598–602.

Address for correspondence: Masahito Yamada, Department of Neurology and Neurobiology of Aging, Kanazawa University Graduate School of Medical Science, 13-1, Takara-machi, Kanazawa 920-8640, Japan; email: m-yamada@med.kanazawa-u.ac.jp

Use of trade names is for identification only and does not imply endorsement by the Public Health Service or by the U.S. Department of Health and Human Services.

All material published in Emerging Infectious Diseases is in the public domain and may be used and reprinted without special permission; proper citation, however, is required.