Autoimmune Retinopathy Caused by Anti-Paraneoplastic Antigen MA2: A Case Study

Atsuki Fukushima  Hitoshi Tabuchi
Department of Ophthalmology, Tsukazaki Hospital, Himeji, Japan

Keywords
Autoimmune retinopathy · Cancer · Paraneoplastic antigen MA2

Abstract
Autoimmune retinopathy is a cause of unexplained visual impairment and visual field impairment, which are often related with life-threatening cancers. Here, we report a case of autoimmune retinopathy positive for anti-paraneoplastic antigen MA2 (PNMA2) antibody in serum. Visual acuity and field were impaired, and OCT and ERG were performed. No abnormalities were observed in OCT, but a marked decrease in pyramidal response was observed in ERG. Paraneoplastic antigen-related antibodies in the serum were tested, and PNMA2 was positive. Systemic evaluation to search for the presence of cancer was conducted by specialists treating cancer. However, cancers were not detected, but bladder and prostate cancer were identified 3 years later, and anti-PNMA2 antibodies were again positive in the serum. Although there have been no reports on PNMA2-related retinopathy, the possibility of the paraneoplastic syndrome should be kept in mind when retinopathy of unknown cause is observed.

Introduction
Autoimmune retinopathy is a cause of unexplained visual impairment and visual field impairment. Although autoimmune retinopathy is a relatively rare disease, cancer is often present in the background and directly linked to life prognosis. Recently, cancer-related antigens are regarded as paraneoplastic ocular syndrome because they cause
various pathological conditions such as optic neuropathy in addition to retinopathy [1]. One of the cancer-related antigens is paraneoplastic antigen MA2 (PNMA2), which causes optic neuropathy.

Case Presentation

On June 14, 2017, a 74-year-old man visited our department with chief complaints of floater and haze in his left eye. The corrected visual acuity was 1.2 for both eyes. Cataract surgery was performed on the right and left on September 25, 2017. On September 29, best-corrected visual acuity was 1.5 on the right and 1.2 on the left. On October 3, he complained about the dark spot on the left. Visual acuity remained constant, and there were no issues with the central flicker frequencies. OCT revealed no abnormalities; however, ERG showed a slight drop in the pyramidal response. Blood was collected based on the disagreement between structure and function, with the possibility of paraneoplastic cerebral syndrome [2]. Anti-paraneoplastic antigen MA2 (PNMA2) antibody was strongly positive, while other tested antibodies (amphiphysin, CV2. Ri, Yo, Hu, recoverin, SX1, titin, zic 4, glutamic acid decarboxylase 65, Delta/Notch-like epidermal growth factor) were not detected. Under the evaluation by specialized doctors, detailed assessments of lung cancer, testis-related tumor, and skin cancer were performed. However, no anomaly was found. With the likelihood of a retinal circulation disorder to be avoided, blood flow velocity was measured using laser speckle flowgraphy, but there was no abnormality. In 2020, bladder cancer and prostate cancer were detected and partially resected and then given medical treatment including hormones. From 2017 to 2020, there were no changes regarding such as visual acuity and fundus findings. However, the HFA examination revealed that the sensitivity of the center of the left eye gradually decreased. On April 2021, corrected visual acuity was 1.2 on the right and 0.8 on the left. On January 2022, scotomas were detected by visual field examination (Fig. 1) and his corrected visual acuities gradually decreased to 1.0 on the right and 0.1 on the left. In February 2022, a blood sampling test for paraneoplastic antigens was performed again, and only the PNMA2 antibody was confirmed to be positive. No apparent abnormalities were found by OCT (Fig. 2). A multifocal ERG imaging (VERIS) was performed, and sensitivity...
decline was established (Fig. 3). Based on the above process, the pathology of this case may be autoimmune retinopathy involving PNMA2. Regular follow-up is planned, and if it worsens, topical or systemic administration of steroids is being considered.

**Discussion and Conclusion**

Various antigens related to cancer-related neurosis have been reported, such as amphiphysin, CV2, Ri, Yo, Hu, recoverin, SX1, titin, zic 4, glutamic acid decarboxylase 65, Delta/Notch-like epidermal growth factor, and PNMA-2. As one of the cancer-related neuroses, paraneoplastic ocular syndrome such as optic neuropathy and retinopathy has become recognized [1].

Among various cancer-related neurosis-induced antigens, there have been no reports of PNMA2-related autoimmune retinopathy. PNMA2 has been confirmed to be expressed in the retina [3]. Thus, various tumor-related antigens expressed on the retina, previously unreported as an association with cancer-related retinopathy, may trigger autoimmune retinopathy. Therefore, our report suggests that the possibility of the paraneoplastic syndrome should be kept in mind when retinopathy of an unknown cause is observed.

**Statement of Ethics**

This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

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**Fig. 2. OCT findings: horizontal section of the macula, March 2022. a Right eye. b Left eye. No apparent abnormalities were found in both eyes.**
**Conflict of Interest Statement**

The authors do not have any conflict of interest to declare.

**Funding Sources**

No funding received.

**Author Contributions**

Atsuki Fukushima and Hitoshi Tabuchi evaluated the findings of this patient and collected data. Atsuki Fukushima wrote the manuscript.

**Data Availability Statement**

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.
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