A case of bilateral uveitis associated with seminoma/germinoma in thymus and pineal glands, two primary lesions

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ABSTRACT

Purpose: To report a case of bilateral ocular paraneoplastic syndrome by seminoma/germinoma in thymus and pineal glands, two primary lesions.

Observations: A 18-year-old male presented at a local clinic complaining of just floaters in left eye without any other clinical signs and symptoms. The treating ophthalmologist found bilateral uveitis, and referred to our hospital. Bilateral retinal periphlebitis and optic disc swelling were shown. Vitreous opacity was found in left eye. We started ocular and systemic examinations to identify the cause of the uveitis, and also initiated oral steroid therapy. The survey using aqueous humor and blood samples showed no specific results for his uveitis. Computer tomography (CT) and magnetic resonance imaging (MRI) detected tumors in thymus and pineal glands. Five months after his first visit, the tumor in his thymus was resected, and was diagnosed as a seminoma/germinoma by pathological examination. Three months later, the tumor in the pineal gland was diagnosed as a germinoma by biopsy followed by chemotherapy and focal radiotherapy. Finally no abnormal ocular finding but slight optic disc atrophy was ascertained.

Conclusions and importance: This is a case of ocular paraneoplastic syndrome induced by seminoma/germinoma in thymus and pineal glands, two primary lesions. Systemic screening by CT and MRI enables prompt diagnosis, treatment and favorable clinical course for such pathogenesis.

1. Introduction

Germinoma is an uncommon pediatric brain tumor that is morphologically identical to its gonadal counterpart: testicular seminoma and ovarian dysegminoma, and early diagnosis and treatment are critical because the tumor is highly sensitive to chemotherapy and radiotherapy. 1

We herein report a successfully treated case of a male adolescent correctly diagnosed as having a seminoma/germinoma in thymus and pineal glands, two primary lesions during treatment for bilateral periphlebitis and optic disc swelling.

2. Case report

A 18-year-old male adolescent with no significant medical history visited a local clinic due to just floaters in his left eye. He showed no other systemic signs and symptoms. Bilateral uveitis was noted, and then he was referred to our hospital. At the initial examination, his best-corrected visual acuity (BCVA) was 1.5 for the right eye and 0.8 for the left eye. Anterior segment examination and intraocular pressures were normal. The mean critical flicker frequency (CFF) values for the right and left eyes were 31 and 33 Hz, respectively. In the fundi of his both eyes, severe segmental retinal periphlebitis from major temporal arcade to periphery and optic disc swelling were observed (Fig. 1A and B). Vitreous opacity was also detected in his left eye (Fig. 1B). Spectral
Fig. 1. Color fundus photographs of both eyes. Severe periphlebitis from major temporal arcade to periphery, optic disc swelling, and vitreous opacity were observed at the initial examination (A and B). Four months after the initial examination, the optic disc swellings and vitreous opacity partially improved by oral steroid therapy, but retinal periphlebitis deteriorated (C and D). The optic disc swellings and retinal periphlebitis considerably but not completely improved after resection of thymus seminoma despite reduced oral steroid therapy (E and F). No abnormal finding but slight optic atrophy was shown after treatment of pineal germinoma (G and H). Right eye: A, C, E, and G. Left eye: B, D, F, and H. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
Fig. 2. Vertical images of optic disc analyzed by spectral-domain optical coherence tomography. Severe optic disc swelling was observed at the initial examination (A and B). Four months after the initial examination, the optic disc swellings partially improved by oral steroid therapy for four months (C and D). The optic disc swellings well improved despite reduced oral steroid therapy after resection of thymus seminoma, but not completely (E and F). Optic disc swelling completely resolved after treatment for pineal germinoma (G and H). Right eye: A, C, E, and G. Left eye: B, D, F, and H.
domain optical coherence tomography (SD-OCT) confirmed distinct optic disc swelling (Fig. 2A and B), but showed normal foveal microstructure in both eyes (Fig. 3A and B). After treatment for pineal germinoma (G and H). Right eye: A, C, E, and G. Left eye: B, D, F, and H.

According to the clinical findings, sarcoidosis and tuberculous were mostly suspected, but a variety of tests to identify the cause of infectious and non-infectious uveitis were performed using his peripheral blood and aqueous humor for screening. The levels of serum angiotensin converting enzyme activity and serum lysozyme were normal. Tuberculosis was analyzed using an enzyme-linked immunospot assay, and was negative. The chest radiography and electrocardiography images were normal. No specific results were detected by examinations for the vasculitis using blood and aqueous humor samples.

Although the cause of his uveitis was uncertain, oral steroid therapy (prednisolone 20mg/day) was initiated and continued for four months. The optic disc swellings and vitreous opacity partially improved, but retinal periphlebitis deteriorated (Fig. 1C and D). For the right and left eyes, his BCVA were 1.2 and 1.2, but the mean CFF values were 31 and 29 Hz, respectively. SD-OCT showed partially improved optic disc

Fig. 3. Horizontal images of macula analyzed by spectral-domain optical coherence tomography. No foveal specific lesions were observed in this case. Optic disc swelling was partially observed at the initial examination (A and B). Four months after the initial examination (C and D). After resection of thymus seminoma (E and F). After treatment for pineal germinoma (G and H). Right eye: A, C, E, and G. Left eye: B, D, F, and H.

Fig. 4. A computer tomography confirmed a tumor accompanying cystic lesion in front mediastinum (arrow).
swelling, but still persisted in spite of the oral steroid therapy for four months in both eyes (Fig. 2C and D). No foveal lesions were observed (Fig. 3C and D).

During the oral steroid therapy, systemic image inspection was performed to investigate possible lesions induced by sarcoidosis, tuberculosis and other unexpected disease. A computer tomography (CT) confirmed a tumor accompanying cystic lesion in front medias tinum (Fig. 4). A brain Magnetic resonance imaging (MRI) showed a tumor on the roof of third ventricle (Fig. 5A).

Five months after his first visit, the 19 mm size tumor with his thymus (Fig. 4) was resected. The oral steroid dose was gradually decreased from 20 to 10 mg/day before the resection. The tumor showed positive Sal-like protein 4 (SALL4) and octamer-binding transcription factor 4 (Oct4) staining, but negative glypican-3 staining. The tumor was diagnosed as a seminoma/germinoma by pathological examination (Fig. 6A).

At the examination three months later, his BCVA was 1.5 for the right eye and 1.2 for the left eye. The mean CFF values for the right and left eyes were 39 and 39 Hz, respectively. The retinal periphlebitis and optic disc swellings considerably improved but not completely (Fig. 1E and F). SD-OCT confirmed well improved optic disc swelling in both eyes after the resection of thymus seminoma despite the reduced oral steroid therapy (Fig. 2E and F). No foveal lesions were observed (Fig. 3E and F).

Then a biopsy of the tumor was performed by a flexible neuro-endoscope. Since the obstruction of the aqueduct was confirmed, endoscopic thirdventriculostomy was performed (Fig. 5B). The oral steroid dose was further decreased from 10 mg/day and terminated before the biopsy. Tumor was grayish pink color with the firm surface tissue. Several pieces of the tumor sample was obtained. The diagnosis of germinoma was made based on the pathological examination (Fig. 6B and C). Chemotherapy and focal irradiation therapy followed. He received chemotherapy (bleomycin/etoposide/cisplatin; BEP). A total dose of 40 Gy was delivered to the third ventricle. Every examination revealed no signs of metastasis. Thus each seminoma/germinoma in thymus and pineal glands was regarded as primary.

Tumor markers such as alpha-fetoprotein (AFP), human chorionic gonadotropin (HCG), and lactate dehydrogenase (LDH) were always negative in sera before and after a series of treatments.

Anti-aquaporin-4 antibodies (AQP4-IgG) and anti-myelin oligodendrocyte glycoprotein antibodies (MOG-IgG) were negative in sera before a series of treatments.

At the examination six months after the brain biopsy, his BCVA was 1.5 for the right eye and 1.2 for the left eye. The mean CFF values for the right and left eyes were 40 and 39 Hz, respectively. A complete resolution of retinal periphlebitis and optic disc edema was ascertained (Fig. 1G and H). SD-OCT showed completely resolved optic disc swelling after the treatment for pineal germinoma in both eyes (Fig. 2G and H). No foveal lesions were observed (Fig. 3G and H). Both intraocular pressures were always normal throughout the treatment.

Humphrey Visual Field 30-2 SITA Fast testing (Humphrey Field Analyzer 3, Carl Zeiss Meditec, Inc.) demonstrated visual field impairment in both eyes (Fig. 7).

Anterior chamber flare has been evaluated based on the aqueous flare value measured with the Kowa FM-600 laser flare meter (Kowa Medicals, Nagoya, Japan) in photon counts per millisecond (pc/ms) (Fig. 8). The aqueous flare values transiently decreased by the initiation of oral steroid therapy, and completely decreased after resection of thymus seminoma and treatment for pineal germinoma despite the termination of oral steroid therapy.

3. Discussion

We report a case with seminoma/germinoma in thymus and pineal glands, two primary lesions who presented with bilateral periphlebitis and optic disc swelling. Although a paraneoplastic ocular involvement was reported previously in four separate case reports, the present case differs from those because of having seminoma/germinoma in thymus and pineal glands, two primary lesions.

Early diagnosis and treatment for seminoma/germinoma are critical for prognosis because the tumor is highly sensitive to therapy, and 5-year survival rates are estimated to be greater than 90%. In the present case, two distinct lesions were appropriately detected by CT and MRI images, which consequently enabled us prompt and favorable treatment for the patient.

Optic disc swelling were seen in both eyes here, but it might be a papilledema. It is uncertain because intracranial pressure was not measured in this patient. Forooghian and Uludag previously showed intracranial pressure was within normal range in cases of ocular paraneoplastic syndrome by pineal gland germinoma. It suggests that the optic nerve swelling was inflammatory and not secondary to raised intracranial pressure. In our case, since the obstruction of the aqueduct was confirmed, endoscopic thirdventriculostomy was performed. It decreased intracranial pressure. The optic disc swellings improved after resection of thymus seminoma despite the reduced oral steroid therapy. Finally optic disc swelling completely resolved after the treatment for pineal germinoma despite the terminated steroid therapy. It is unidentified, but both inflammation and intracranial pressure may have been involved in his optic disc swelling.

Consequently, only systemic image inspections such as CT and MRI examinations were able to indicate the original lesions of the ocular pathogenesis, although other blood and aqueous humor examinations all failed. It may suggest future recurrence of the tumor should be surveyed by similar systemic image inspections in the appearance of periphlebitis and optic disc swelling in the fundus.

According to the progress shown in Fig. 7, the aqueous flare value may precisely indicate the degree of his ocular inflammation including vasculitis. An increase in the aqueous flare values in the future may suggest the recurrence of the tumor.
Fig. 6. Hematoxylin and eosin staining of the thymus (A). Tumor cells with clear cytoplasm and round nuclei with prominent nucleoli proliferated in the thymus were shown. Hematoxylin and eosin staining of the pineal body (B). Most tumor cells showed severe crushed artifact due to the biopsy procedure. The crushed tumor cells were positive for SALL4 (C, arrow).
Cross reactivity between autoantibodies specific for tumor antigens with proteins in the optic nerve may be related to the bilateral optic disc edema. Previous a serum from a patient with pineal gland germi-noma demonstrated the presence of antibodies against a 35 kDa optic nerve protein. AQP4, molecular weight of 34.8 kDa protein, is known as the predominant autoimmune target in neuromyelitis optica. Anti-AQP4-IgG showed negative in this patient. Anti-MOG-IgG also showed negative.

4. Conclusions

This is a case of uveitis with periphlebitis and optic disc swelling induced by seminoma/germinoma in thymus and pineal glands, two primary lesions. Early systemic CT and MRI examination is important for prompt diagnosis and favorable treatment in such pathogenesis.

Patient consent

A written informed consent for publication was obtained from the

Fig. 7. Humphrey Visual Field 30-2 SITA Fast testing (Humphrey Field Analyzer 3, Carl Zeiss Meditec, Inc.) demonstrated visual field impairment in both eyes.

Fig. 8. Aqueous flare values analyzed by laser flare meter. The aqueous flare values transiently decreased by the initiation of oral steroid therapy, and completely decreased after resection of thymus seminoma and treatment for pineal germinoma despite the termination of oral steroid therapy. Aqueous flare values determined by the laser flare meter are reported as photon counts per millisecond (pc/ms). The daily amount of oral prednisolone is also shown.
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Authorships

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

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