

Case Report

POEMS Syndrome in a 20-year-old Patient Diagnosed Following a Complaint of Reduced Visual Acuity

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We report a case of POEMS syndrome in a 20-year-old patient diagnosed after visiting an eye clinic with a chief complaint of reduced visual acuity. A male university student aged 20 years was referred to our department complaining of blurred vision in both eyes that had persisted for 1 month. He also noted headache, nausea, and paresthesia in the lower extremities around the same time. The visual acuity of his right and left eye was 20/40 and 20/20, respectively. Optic disc edema and serous retinal detachment were present. Brain magnetic resonance imaging showed no intracranial abnormalities, while elevated cerebrospinal fluid pressure, reduced nerve conduction velocity in both lower extremities, hepatosplenomegaly, M proteinemia, high blood VEGF levels, osteoblastic and osteolytic changes in the spine, and atypical plasma cells in bone lesions were noted. From the above findings, the patient was diagnosed with POEMS syndrome. He received high-dose dexamethasone, thalidomide, and radiotherapy on the sacral mass, followed by high-dose melphalan with autologous stem-cell support, and showed subsequent systemic and ophthalmologic improvement. Here, we report the youngest case ever of POEMS syndrome with ocular manifestation. If patients have optic disc edema in both eyes with no intracranial space-occupying lesion, POEMS syndrome should be considered in differential diagnosis, regardless of age.

Key words: POEMS syndrome, serous retinal detachment, VEGF

POEMS syndrome (also known as Crow-Fukase syndrome or Takatsuki disease) is a rare disease typically found in people aged 40 or older and associated with the underlying abnormal proliferation of monoclonal plasma cells that causes polyneuropathy and other characteristic clinical findings such as organomegaly, endocrinopathy, M proteinemia, and skin changes, the first letters of which form the name of

the syndrome [1, 2]. Since the disease has various extraocular symptoms, most POEMS-syndrome patients in the literature receive their diagnosis before visiting an ophthalmology department for potential ocular involvement. Here, we describe a case of POEMS syndrome in a 20-year-old male patient diagnosed after visiting an eye clinic with a chief complaint of reduced visual acuity.

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Case Report

The patient visited a local eye clinic after noticing blurry vision, headache, nausea, and numbness in the extremities from around early December 2011. He had optic disc edema, but brain MRI showed no intracranial space-occupying lesions. On January 10, 2012, he was referred to our ophthalmology department for further examination and treatment. The visual acuity of his right and left eye was 20/40 and 20/20, respectively. The intraocular pressure of his right and left eye was 10 and 15 mmHg, respectively. His eye position was orthophoric, pupils were equal and round, light reaction of both eyes was normal, relative afferent pupillary defect was negative, and eye movement was normal. The critical flicker fusion frequency of his right and left eye was reduced to 17 and 22 Hz, respectively. No abnormalities were noted in the anterior segment or ocular media, but swelling and an indistinct border of the optic disc were observed in the fundus of both eyes with subretinal fluid extending from the optic disc to the macula (Fig. 1A, B). Splinter hemorrhage was present in the arcade in a scattered manner. Fluorescein angiography showed hyperfluorescence along the nerve fiber layer (Fig. 1C, D). Optical coherence tomography showed serous retinal detachment in both eyes (Fig. 2A, B). Goldmann perimetry showed enlargement of Mariotte's blind spot in both eyes with no central scotoma (Fig. 3A, B). Brain magnetic resonance imaging (MRI) was performed to check for optic nerve/intracranial lesions because both eyes had optic disc edema, but no apparent abnormalities were identified. The patient was subsequently hospitalized for further examination, and we consulted other departments for general testing.

General test findings. In hematology, the white blood cell count was $6,140/\mu\text{L}$ and the C-reactive protein level was 0.14, both of which were normal and showed no evidence of inflammation, while the platelet count was elevated at $66.6 \times 10^4/\mu\text{L}$. M proteins were detected in the serum protein fraction, and immunoelectrophoresis showed monoclonal IgG λ . The serum VEGF level was increased to $5,310\text{ pg/mL}$, far above the reference value of 115. In the cerebrospinal fluid examination, the cerebrospinal fluid pressure was elevated at $420\text{ mmH}_2\text{O}$, and albuminocytologic dissociation was also observed. In the peripheral

nerve conduction study, a motor neuron-predominant decrease was noted in the amplitude and conduction velocity in both lower extremities. Whole-body computed tomography showed an osteolytic lesion greater than 3 cm in diameter in the sacrum and small scleroses in other bones, demonstrating that bone lesions were present in a scattered manner. Hepatosplenomegaly was also noted, and biopsy of bone lesions showed atypical plasma cells. We noted no lymph node enlargement suggestive of Castleman's disease, nor any endocrine abnormalities or skin manifestations.

From the above general test results, the patient was diagnosed with POEMS syndrome. After being transferred to the hematology department, he received high-dose dexamethasone therapy (40 mg/day) for 4 days starting January 20, 2012. At this point, headache and nausea were improved, and VEGF levels decreased to 873 pg/mL , but no changes in ophthalmologic findings were noted. On February 14, the patient requested to receive treatment at his parents' home (in another prefecture) and was transferred to a hospital near that location. There, he began receiving thalidomide 100 mg/day and dexamethasone 5 mg/week from February 21 and radiotherapy on the sacral mass from February 23. As of June 2012, subretinal fluid had disappeared and the visual acuity of his right and left eye was improved to 20/25 and 20/20, respectively.

Subsequently, high-dose melphalan therapy with autologous peripheral blood stem cell transplantation was performed in July, 2012 as a systemic treatment, and VEGF levels had decreased to 64.9 pg/mL as of September, 2012. He was maintaining right and left visual acuity of 20/25 and 20/20 at the latest visit in November, 2013 (Fig. 1E, F/Fig. 2C, D/Fig. 3C, D).

Discussion

POEMS syndrome was first reported by Crow in 1956. The core features of the disease are abnormal plasma cells and polyneuropathy, accompanied by major signs of organomegaly, endocrinopathy, M-protein, and skin changes [3]. In addition to the pathological findings, patients experience various conditions such as pleural effusion/ascites, osteosclerotic lesions, thrombocytosis, polycythemia, and pulmonary hypertension [1]. Ophthalmologic symptoms reported include

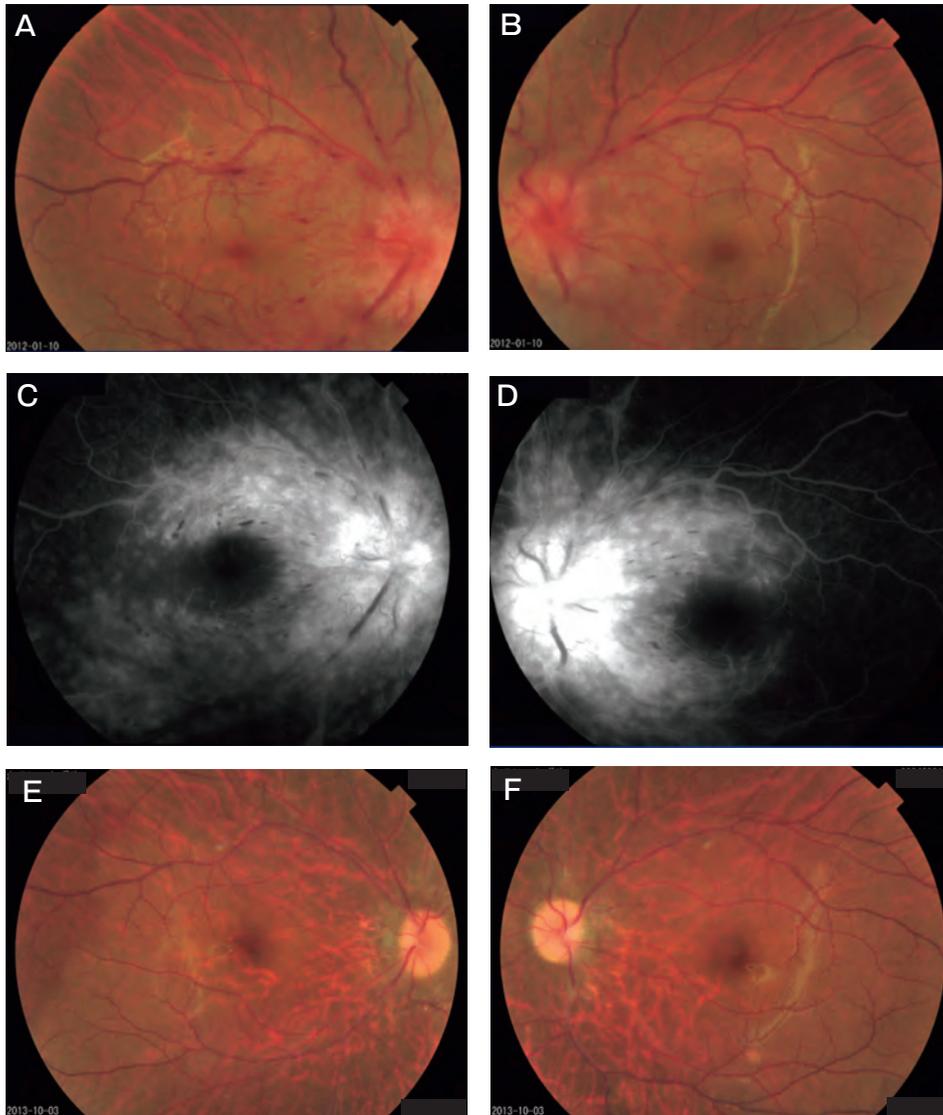


Fig. 1 A, B, Photographs of the fundus at the first visit. The optic disc of both eyes showed an indistinct border, and swelling was noted. Both eyes had serous retinal detachment from the optic nerve to macula and splinter retinal hemorrhage in a scattered manner; C, D, Fluorescein angiography at the first visit. Hyperfluorescence could be seen along the nerve fiber layer from the optic disc in both eyes; E, F, The latest (1 year 10 months after the first visit) photographs of the fundus. The optic disc of both eyes had a distinct border, and both serous retinal detachment and retinal hemorrhage had disappeared.

eye pain, reduced visual acuity, scotoma, and diplopia, with ophthalmologic findings of optic disc edema, macular edema, serous retinal detachment, abnormal visual field, eye movement disorder, strabismus, optic disc drusen, and choroidal neovascularization [4–8]. The frequency of disc edema (29%–64%) makes it somewhat less common than neurological manifestations (100%) and endocrine abnormalities (67%–

84%) [1]. Regarding cytokines considered to be involved in POEMS syndrome, high blood VEGF levels have often been reported [9, 10].

The patient reported here is considered a rare case for the following reasons: First, he was diagnosed with POEMS syndrome after visiting an eye clinic with a chief complaint of reduced visual acuity. To our knowledge, only one other patient among the 12

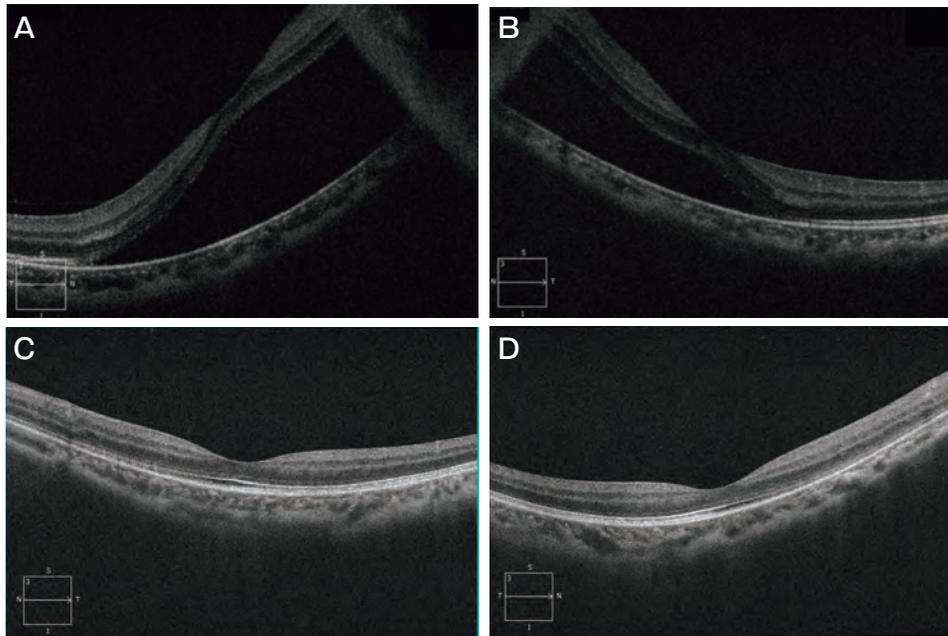


Fig. 2 A, B, OCT findings at the first visit. The macula of both eyes showed serous retinal detachment; C, D, The latest (1 year 10 months after the first visit) OCT findings. Serous retinal detachment had disappeared from both eyes.

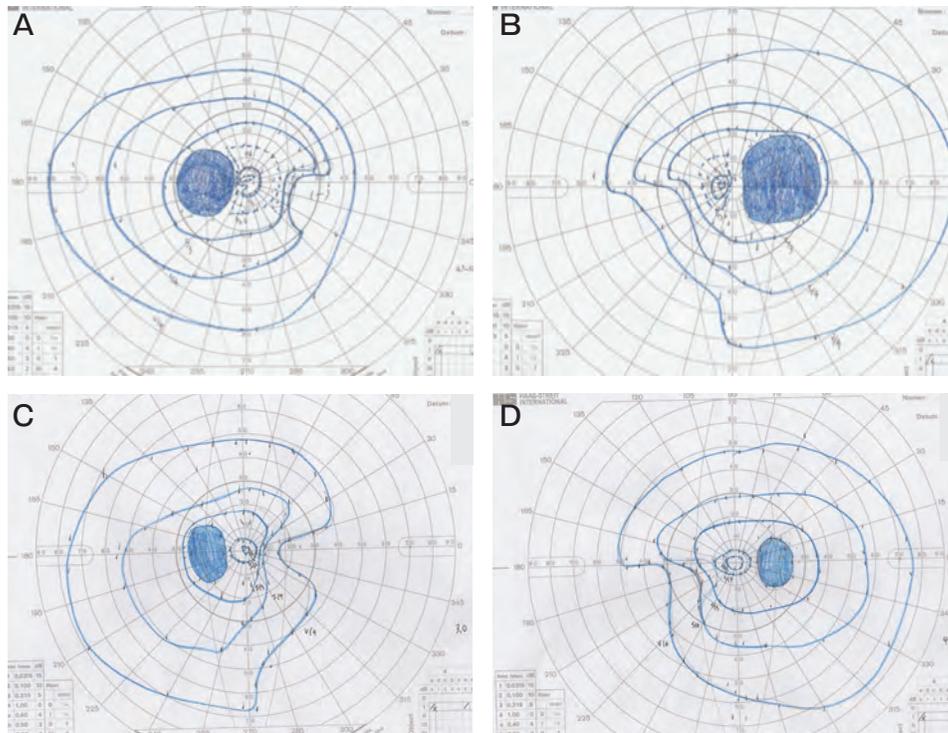


Fig. 3 A, B, Goldmann perimetry at the first visit. Both eyes showed enlargement of Mariotte's blind spot. No central scotoma was noted; C, D, The latest (1 year 10 months after the first visit) Goldmann perimetry. The enlargement of Mariotte's blind spot was reduced in both eyes.

reports in which POEMS was complicated with ocular manifestations was diagnosed upon visiting an eye clinic [11]. Most POEMS syndrome patients are diagnosed based on non-ophthalmologic systemic symptoms and referred to an eye clinic later. Patients with POEMS syndrome with a chief complaint of eye symptoms such as our present patient require further attention, with a whole-body check performed promptly in cooperation with other departments. Second, POEMS syndrome is typically found in people aged 40 to 60; thus far, the youngest case of POEMS syndrome with ophthalmologic findings was in a 25-year-old patient [11]. At 20 years of age, our patient is the youngest so far. Further, the chief symptoms of our patient were eye symptoms, which are rare in POEMS syndrome, and the patient responded to treatment and followed a relatively favorable course. The effect of age of onset on systemic symptoms, including eye symptoms, or response to treatment has not yet been examined. Studies in a larger number of patients are necessary in the future.

Current systemic treatments of POEMS syndrome include melphalan, steroid, high-dose chemotherapy with autologous peripheral blood stem cell transplantation, thalidomide, anti-VEGF, and radiotherapy [10, 11]. Our patient received thalidomide after systemic steroidal therapy, as this drug has not been approved as first-line therapy in Japan, and showed improvements of the serous retinal detachment and optic disc edema as well as systemic symptoms. Local ophthalmologic treatments of POEMS syndrome reported so far include vitrectomy with sub-tenon injection of triamcinolone acetonide or vitreous injection of triamcinolone acetonide for retinal edema and serous retinal detachment [7]. While we predicted our patient would likely show early improvement of visual acuity if serous retinal detachment was treated, such treatment was not performed because his visual acuity was not seriously reduced and his poor systemic condition might have led to serious complications, such as endophthalmitis and uncontrolled glaucoma. Further, systemic treatment should be prioritized in general, as ophthalmologic findings are only part the syndrome. Our patient had high VEGF levels before treatment, and given that VEGF levels were decreased by systemic treatment, ophthalmologic findings were improved, suggesting that VEGF might have been involved in the onset of serous retinal detachment and

optic disc edema previously reported [7]. We believe that high serum VEGF levels exacerbated vascular permeability, thereby leading to the observed disc edema and serous retinal detachment.

The mechanism of onset of optic disc edema in POEMS syndrome remains controversial, and possible mechanisms include elevated intracranial pressure, vasculitis, infiltration of the nerve, and increased VEGF levels [4, 8, 12]. Our patient had both elevated intracranial pressure and increased VEGF levels, supporting both hypotheses. Further study is thus necessary to clarify the mechanism responsible for edema in such patients.

Reference

1. Dispenzieri A: POEMS syndrome: 2011 update on diagnosis, risk-stratification, and management. *Am J Hematol* (2011) 86: 591–601.
2. Nakanishi T, Sobue I, Toyokura Y, Nishitani H, Kuroiwa Y, Satoyoshi E, Tsubaki T, Igata A and Ozaki Y: The Crow-Fukase syndrome: a study of 102 cases in Japan. *Neurology* (1984) 34: 712–720.
3. Crow RS: Peripheral Neuritis in Myelomatosis. *Br Med J* (1956) 2: 802–804.
4. Kaushik M, Pulido JS, Abreu R, Amselem L and Dispenzieri A: Ocular Findings in Patients with Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy, and Skin Changes Syndrome. *Ophthalmology* (2011) 118: 778–782.
5. Diduszyn JM, Quillen DA, Cantore WA and Gardner TW: Optic disk drusen, peripapillary choroidal neovascularization, and POEMS syndrome. *Am J Ophthalmol* (2002) 133: 275–276.
6. Okada K, Yamamoto S, Tsuyama Y and Mizunoya S: Case of POEMS syndrome associated with bilateral macular detachment resolved by autologous peripheral blood stem cell transplantation. *Jpn J Ophthalmol* (2007) 51: 237–238.
7. Imai H, Kusuhara S, Nakanishi Y, Escano MFT, Yamamoto H, Tsukahara Y and Negi A: A case of POEMS syndrome with cystoid macular edema. *Am J Ophthalmol* (2005) 139: 563–566.
8. Barnes C, Sanchez-Dalmau BF, Vela D and Alarcon S: Papilledema as an indicator of POEMS syndrome. *Arch Soc Esp Oftalmol* (2008) 83: 709–711.
9. Watanabe O, Arimura K, Kitajima I, Osame M and Maruyama I: Greatly raised vascular endothelial growth factor (VEGF) in POEMS syndrome. *Lancet* (1996) 347: 702–702.
10. Scarlato M and Previtali SC: POEMS syndrome: the matter-of-fact approach. *Cur Opin Neurol* (2011) 24: 491–496.
11. Wong VA and Wade NK: POEMS syndrome: an unusual cause of bilateral optic disk swelling. *Am J Ophthalmol* (1998) 126: 452–454.
12. Dispenzieri A and Gertz MA: Treatment options for POEMS syndrome. *Expert Opin Pharmacother* (2005) 6: 945–953.
13. Chong DY, Comer GM and Trobe JD: Optic disc edema, cystoid macular edema, and elevated vascular endothelial growth factor in a patient with POEMS syndrome. *J Neuroophthalmol* (2007) 27: 180–183.