Of patients who eventually suffer visual loss, almost 70% will do so before the age of 30.[2] Those unaffected by the age of 50 are >95% likely to remain so, although asymptomatic carriers have been found to demonstrate significant subtle chronic changes such as peripapillary microangiopathy, retinal nerve fibre layer thickening,[3] and colour vision deficit.[4]

Metabolic or ischaemic factors are well-recognised triggers to visual loss in LHON. The precipitant of visual loss in our patient was felt to be ischaemia due to vascular disease leading to an exceptionally late clinical presentation.

This case demonstrates that there may be no upper limit to the age at which LHON should be considered in the differential diagnosis of bilateral or sequential optic neuropathy.

References

1 Newman NJ. Hereditary optic neuropathies: from the mitochondria to the optic nerve. *Am J Ophthalmol* 2005; **140**(3): 517–523.
2 Riordan-Eva P, Sanders MD, Govan GG, Sweeney MG, Da Costa J, Harding AE. The clinical features of Leber's hereditary optic neuropathy defined by the presence of a pathogenic mitochondrial DNA mutation. *Brain* 1995; **118**(Part 2): 319–337.
3 Savini G, Barboni P, Valentino ML, Montagna P, Cortelli P, De Negri AM *et al*. Retinal nerve fiber layer evaluation by optical coherence tomography in unaffected carriers with Leber's hereditary optic neuropathy mutations. *Ophthalmology* 2005; **112**(1): 127–131.
4 Quiros PA, Torres RJ, Salomao S, Berezovsky A, Carelli V, Sherman J *et al*. Colour vision defects in asymptomatic carriers of the Leber's hereditary optic neuropathy (LHON) mtDNA 11778 mutation from a large Brazilian LHON pedigree: a case-control study. *Br J Ophthalmol* 2006; **90**(2): 150–153.

JC Buchan, C Ong and TR Dabbs

Department of Ophthalmology, St James's University Hospital, Leeds, UK

Correspondence: JC Buchan, Department of Ophthalmology, St James's University Hospital, Chancellor Wing, Beckett Street, Leeds, LS9 7TF, UK
Tel: +44 (0) 113 2433144;
Fax: +44 (0) 113 2065314.
E-mail: johnbuchan@gmail.com

The authors have no proprietary or financial interest in this work

Eye (2007) **21,** 859–860; doi:10.1038/sj.eye.6702729; published online 2 February 2007

Sir,

CRMP-5-IgG in patient with paraneoplastic optic neuritis with lung adenocarcinoma

Paraneoplastic optic neuritis (PON) is an ocular manifestation of the paraneoplastic syndrome that is clinically characterized by subacute vision reduction, optic disc swelling, and neurological symptoms.[1] Previously, the diagnosis was difficult because it was based only on the clinical signs and symptoms. Recently, a distinct IgG for the 62 kDa collapsin response-mediator protein-5 (CRMP-5-IgG) was demonstrated to be a serological marker for PON.[1,2]

Case report

A 55-year-old woman noticed a subacute bilateral vision reduction and was referred to our hospital. She had a history of a lung adenocarcinoma resection at 46 years of age, but the cancer reappeared 3 years later. She also had occasional epileptic seizures beginning at 54 years of age.

On examination, her visual acuity was 20/400 in each eye. Her pupillary responses, eye movements, and anterior segments were normal. The critical fusion frequencies were markedly reduced. Funduscopic examination showed a mild swelling of both optic discs (Figure 1a). There were no inflammatory cells in the vitreous cavity. Fluorescein angiography revealed hyperfluorescence and leakage on the optic disc in accord with the swelling, but not in areas away from the disc. The arm–retina time was not delayed. Visual field examination showed a central scotoma and enlarged blind spot in both eyes (Figure 1b). Full-field cone and rod electroretinograms were within normal limits.

Cranial computed tomography (CT) and magnetic resonance imaging showed neither metastatic cancer nor white matter lesions suggestive of multiple sclerosis. Cerebrospinal fluid examination revealed a slightly elevated protein level (64 mg/dl). Laboratory findings were normal except for an elevated carcinoembryonic antigen.

Methylprednisolone pulse treatment, 500 mg/day, was given for 3 days but the visual acuity and optic disc appearance did not improve. Chest CT showed nodular lesion at the apex of the right lung.

Based on these findings, a possibility of PON was considered. We performed Western blot analysis of her serum and detected a 62 kDa band corresponding to CRMP-5-IgG (Figure 2).

Comment

Most of the previous cases of PON were associated with small-cell lung carcinoma, and a lung adenocarcinoma has been reported in only one case but without CRMP-5-IgG testing.[1,3] We are unaware of previous

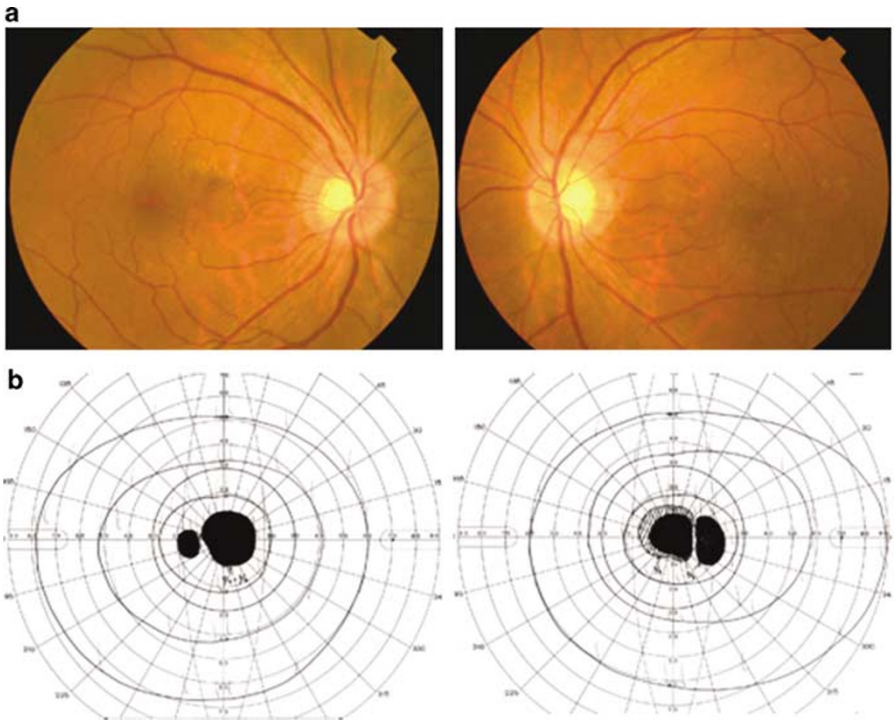

Figure 1 Fundus photographs and visual fields of patient with PON. (a) Fundus photographs showing mild swelling of both optic discs (left, right eye; right, left eye). (b) Visual fields showing bilateral central scotoma and blind spot enlargement (left, left eye; right, right eye).

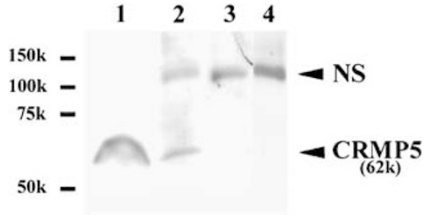

Figure 2 Western blot analysis using soluble fraction of bovine optic nerve. The primary antibodies used were lane 1, anti-human CRMP-5 (1 : 3000 dilution, CHEMICON, Temecula, CA, USA); lane 2, serum IgG from the patient (1 : 15 dilution); lane 3 and 4, sera from age-matched healthy human subjects without any retinopathy and optic neuropathy (1 : 3000 dilution). A 62 kDa protein corresponding to full-length CRMP-5 is seen only in lanes 1 and 2 (Arrowhead). HRP-labelled anti-rabbit IgG or anti-human IgG (1 : 3000 dilution; Amersham, Piscataway, NJ, USA) was used as a second antibody. NS, nonspecific.

reports of PON caused by lung adenocarcinoma that was confirmed by CRMP-5-IgG testing.

The results of autopsy examinations of a previous case of PON associated with a lung adenocarcinoma showed a destruction of the optic nerves mainly around the chiasma.[3] The optic discs in our case were swollen, but the swelling was milder than that in cases of PON associated with small-cell lung carcinoma. Therefore, further studies are required to determine if the optic disc appearance in cases of PON associated with lung adenocarcinoma is significantly different from that with small-cell lung carcinoma.

Immunosuppressive therapies are generally considered to be ineffective for PONs as in our case.[1] This is probably because CRMP-5 may play a role in maintaining dendritic plasticity in the mature central nervous system,[1] and PON results in irreversible damages such as demyelination of optic nerve and gliosis.[3–5] Therefore, the CRMP-5-IgG testing can lead to an earlier and precise diagnosis, which would then enable earlier treatments of the original tumor(s) before irreversible damage of the optic nerve.

Acknowledgements

This work was supported in part by grants-in-aid for Scientific Research from the Japanese Ministry of Education, Science, Sports, and Culture (TI and SY), The Japan Health Foundation (SY), Japanese Retinitis Pigmentosa Society (SY), and Clinical Research Foundation (SY).

References

1 Cross SA, Salomao DR, Parisi JE, Kryzer TJ, Bradley EA, Mines JA *et al*. Paraneoplastic autoimmune optic neuritis with retinitis defined by CRMP-5-IgG. *Ann Neurol* 2003; **54**: 38–50.

2 Yu Z, Kryzer TJ, Griesmann GE, Kim K, Benarroch EE, Lennon VA. CRMP-5 neuronal antoantibody: marker of lung cancer and thymoma-related autoimmunity. *Ann Neurol* 2001; **49**: 146–154.
3 Oohira A, Inoue T, Fukuda N, Uchida K-I. A case with paraneoplastic optic neuropathy presenting bitemporal hemianopsia. *Neuroophthalmology* 1991; **11**: 325–328.
4 Boghen D, Sebag M, Michaud J. Pareneoplastic optic neuritis and encephalomyelitis: report of a case. *Arch Neurol* 1988; **45**: 353–356.
5 Sheorajpanday R, Slabbynck H, Van De Sompel W, Galdermans D, Neetens I, De Deyn PP. Small cell lung carcinoma presenting as collapsin response-mediating protein (CRMP) -5 paraneoplastic optic neuropathy. *J Neuroophthalmol*. 2006; **26**: 168–172.

Y Murakami, S Yoshida, H Yoshikawa, Y Yamaji, Y Ikeda, A Ueno and T Ishibashi

Department of Ophthalmology, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan

Correspondence: S Yoshida
Tel: +81 92 642 5648;
Fax: +81 92 642 5663.
E-mail: yosida@eye.med.kyushu-u.ac.jp

Eye (2007) **21,** 860–862; doi:10.1038/sj.eye.6702730; published online 2 February 2007

Sir,

Ultrastructure of anterior lens capsule in Peters' plus syndrome

The Peters' anomaly is characterized by central corneal opacity (leukoma), thinning of the posterior aspect of the cornea, iridocorneal adhesions, and keratolenticular adhesion or cataract. The presence of lens abnormalities in Peters' anomaly is more frequently associated with systemic anomalies.[1] Peters' plus syndrome (PPS) is a rare entity that combines anterior chamber abnormality of Peters' anomaly with other systemic anomalies such as cleft lip and palate, short stature, broad hands and feet, and variable mental delay.[2] The etiology is unknown, but may involve abnormal neural crest development. Peters' anomaly has been reported to be caused by mutations in several genes such as *PAX6, PITX2, PITX3, and CYP1B1*.[2] PPS follows an autosomal-recessive pattern of inheritance,[2] but the causative gene of this syndrome remains unknown. Previous pathologic reports in Peters' anomaly revealed attenuation or absence of Descemet's membrane and corneal endothelium in the central posterior cornea, with iridocorneal adhesion or keratolenticular adhesion.[3–5] We report, herein, the ultrastructure of anterior lens capsule in a patient with PPS.

Case report

A 4-year-old boy was found to have bilateral cataract and referred to our department. Bilateral nystagmus was found. We observed a poor ambulatory activity of the patient while occluding his left eye with eye patch. Slit-lamp examination showed bilateral cataract with bulging anterior lens surface that adheres to the posterior cornea (Figure 1). Mild opacity was detected in the corneal stroma in front of the adhesion site. Microcornea and posterior synechia were also found in both eyes. Pediatric evaluation revealed short stature (<3%), low body weight (<3%), speech, and motor developmental delay. Growth hormone deficiency was also detected by stimulation test. The patient received extracapsular lens extraction in the right eye, with keratolenticular adhesion separated by viscoelastic material, and the anterior lens capsule removed by can-opening capsulectomy. Aspirated lens material was sent for virus culture and Herpes virus polymerase chain reaction (PCR), with both test results came out to be negative. Anterior lens capsule was fixed in 2% glutaraldehyde/phosphate buffer, and then washed three times in phosphate buffer. The specimen was post-fixed with 1% osmium tetraoxide. After dehydration with alcohol series, it was embedded with epoxy/resin and sectioned. The section was examined under a JEOL electron microscope (JEM 1230). We observed villus-like processes emanated from the anterior lens capsule, with two cells still attached to the process tips. These cells were presumed to be sloughed-off corneal endothelial cells, as the lens capsule adhered to the corneal endothelial side before surgical separation (Figure 2, En). Intact lens epithelial cells could be found adjacent to the lens capsule (Figure 2, Ep).

Comment

Keratolenticular adhesion is characteristic in PPS. Various pathologic results have been reported in the literature.[3–5] The lens may be adherent to the corneal stroma with absence of Descemet's membrane and lens capsule.[4] A stalk-like connection between lens and cornea has been reported as well, and the Descemet's membrane was deflected over onto the stalk.[5] The lens may be in contact or embedded in the defective posterior corneal surface, but with an intact anterior lens capsule.[4] The lens may be only opposed and not adherent to the posterior surface of the cornea, with both the anterior