Clinical and Hereditary Features of Familial Vitreous Amyloidosis in Chinese

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Abstract
Purpose: To investigate the clinical and hereditary features of a Chinese Han pedigree with familial vitreous amyloidosis.

Methods: The hereditary features of familial traits were detected by drawing genealogy, and the clinical manifestations were observed.

Results: This family with 4 generations of 32 family members had the characteristics of euchromosome dominant inheritance. The age of onset in heterozygotes was over 40 years old in male and over 55 in female. All affected individuals had curly hair. Among the 23 family members of the first 3 generations, 7 had the final diagnosis. Four of the cases treated by vitrectomy was found to have open angle glaucoma during the follow-up.

Conclusion: We reported a Chinese Han pedigree with familial vitreous amyloidosis which is a rare condition in Chinese and described the clinical and hereditary features. The genetic sequencing and animal model are undergoing.

Keywords: Vitreous amyloidosis; genealogy

Vitreous amyloidosis is a rare eye disease. Doft reported that only more than 60 eyes of less than 50 cases were found to be affected by this condition so far. No complete case series of familial vitreous amyloidosis from China have been reported. Here we report a family consisting of 4 patients in 3 generations. The follow-up period was up to over 13 years. The clinical and hereditary characteristics of familial vitreous amyloidosis are also reviewed.

Case Reports

Case 1: The proband was a 42-year-old male, presented with progressively deteriorating vision in both eyes for one year. The patient was initially diagnosed as uveitis. Systemic examination showed normal results. Visual acuity was 5/200 in both eyes. The anterior segment was normal. Dilated fundus examination revealed lots of grayish vitreous opacities of irregular shape, some of which adhered to the posterior lens capsule. The fundus appeared to be normal under indirect ophthalmoscopy. Electrophysiological examination showed normal results. B-scan ultrasonography showed vitreous opacities with posterior vitreous detachment. Vitrectomy was carried out in both eyes separately within 10 days. Visual acuity was improved to 20/20 in both eyes after the operation. Fundus fluorescein angiography was normal in both eyes. The diagnosis of vitreous amyloidosis was confirmed by iodine staining of the vitreous specimen obtained during the surgery. The patient was followed for 30 months. The first 12 months after surgery were uneventful before the patient was later found to have secondary open angle glaucoma.

Case 2: The proband’s mother, 70 years old, presented with progressive bilateral visual impairment for 4 years. Visual acuity was counting fingers at 10 cm in both eyes. There was nuclear opacity in the lens. The fundus red light reflex could be seen under indirect ophthalmoscopy. Other examination results were similar to those of the proband.

Case 3: The proband’s aunt, 66 years old, presented with bilateral progressive visual impairment for one year. Examinations showed results similar to case 2. The treatment of case 2 and 3 was the same as case 1. Their postoperative visual acuities were 20/40.
in both eyes. And they all suffered secondary glaucoma 12 months postoperatively.

Case 4: The the proband’s sister, a 54-year-old female, presented with bilateral progressive deterioration of vision for one year. Systemic physical examination and routine admission examinations showed normal results. Visual acuity was hand motion in the right and counting fingers at 10 cm in the left. Intraocular pressure was normal in both eyes. The anterior ocular segment was unremarkable. Dilated fundus examination revealed lots of grayish granular opacities in the vitreous cavity and white dots attached to the posterior lens surface (pseudopodia lentis, as showed in Figure 1). The fundus couldn’t be clearly viewed. B-scan ultrasound showed vitreous opacity with posterior detachment (Figure 2). Vitrectomy was performed in the right eye. During the operation, we could see vitreous opacities with lots of grayish granules. The fundus was normal (Figure 3). The uncorrected visual acuity was 20/40 on post-operative day 1, improved to 20/25 before discharge at 1 week after surgery. Pathological examination of the vitreous specimen from the operation showed positive amyloid-specific staining (Figure 4). During the one-month follow-up, the patient’s uncorrected visual acuity stabilized to 20/25 and there were a few grayish granules that adhered to the posterior capsule, resembling “pseudopodia lentis”. The vitreous was and the fundus appeared normal. Intraocular pressure was 16 mmHg in the right and 18 mmHg in the left. The follow-up has lasted for 10 months so far. The intraocular pressure

Figure 1 White dots attached to the posterior lens surface (pseudopodia lentis) with split-lamp

Figure 2 Vitreous opacity with posterior detachment in B scan
Translational considerations may associate with mutations in the transthyretin gene. Vitreous amyloidosis may be widespread or localized. Amyloid deposits in the vitreous cavity, the mechanism of gene mutations causing protein conformational changes that correspond to erroneous function. Understanding the above mechanisms may help establish unified animal models of vitreous amyloidosis.

2.1 Analysis of the characteristics of familial vitreous amyloidosis

Case 4 was the most recently identified patient within the third generation of this family (54 years old, II 6), her mother (70 years old, II 6), aunt (66 years old, III 8) and brother (the proband, 42 years old, III 3) were diagnosed as vitreous amyloidosis, which was confirmed by the surgery. Shared clinical manifestations among these patients included progressive bilateral visual loss and bilateral vitreous opacities. In 1998, Shi Yi-Ning reported this family's, whose mother, aunt and brother treated with vitrectomy, visual acuity of mother improved to 20/30 by postoperatively, visual acuity of brother improved to 20/20 by postoperatively, but they occurred in secondary glaucoma within 3 years postoperatively, and had passed away in following years.

Case 4 recalled her family history, mentioned that her grandmother (I 2) suffered blindness, who was died in 70-year-old, her grandfather (I 1) died early, so we couldn’t trace. b. Her elder uncle (II 1) had blindness. And her younger uncle (II 3) was not onset when he died in his early age, while his son (III 3) was onset when he grew up. Her aunt (II 8) suffered the blindness, while her next (the third) generation was not onset yet. c. Her elder brother (III 1) had blindness and died earlier, while her little sister (III 8) and little brother (III 9) hadn’t onset yet until 50 years old. Ages of the children of the fourth generation were now younger than 35 years of age, we examined them and haven’t yet found vitreous abnormalities up to now.

According to the genetic characteristics of the family, we drewed the family pedigree as follows (arrow indicates the proband) and summarized the characteristics of the family (Figure 5).

1). Within the family, especially the generation III and generation II, the incidence rate was near to 1/2, and there were no significant gender differences. It is suggested that this family agree with autosomal dominant inheritance type.

2). The average age of onset was in their fifties to

Discussion

Amyloidosis is well-known as amyloid materials deposit in various tissues of the body. Its distribution may be widespread or localized. Organs involved in systemic manifestations of amyloidosis disease in clude central neuropathy, kidneys, skin, gastrointestinal system, cardiovascular system and polyneuropathy. Localized manifestations of amyloidosis is seen in skin, larynx and eye. Vitreous amyloidosis belongs to the hereditary amyloidosis, which is extremely rare. So far there have been only seven cases reported by four case series in China. Previous study suggested that amyloidosis was associated with the transthyretin (TTR) gene, and different mutations may cause different clinical phenotypes. Vitreous amyloidosis may associate with mutations in the transthyretin gene, such as Val30Met and Ile84Ser. However, there are still lots of mechanisms remained unclear, such as the nature of amyloid deposits in the vitreous cavity, the mechanism of gene mutations...
sixties in female, while in their forties in men.

3). We couldn’t trace the family’s first generation, known that the grandmother (I 2) was died in 70-year-old without onset, the grandfather (I 1) died early. And presumed that the grandfather (I 1) may be a patient (disease gene was heterozygote), and was not onset when he was alive.

The son of II 3’s was onset when he was adult, while II 3 hadn’t be onset before dying of the disease.

5). III 3 (Case1) is the proband, III 6 is the patient who is case 4.

6). We are continuing to trace the incidence of the generation IV.

2.2 Clinical features and differential diagnosis, complications

2.2.1 Diagnosis of the clinical features of vitreous amyloidosis Age at onset of symptoms is middle-aged, visual acuity is related to the degree of vitreous opacity and advanced to hand movement in the end. The anterior ocular segment is unremarkable. The vitreous is cloudy with fine fibril opacities, during which high-density white cloudy spots, and adhered to the posterior capsule and peripheral retinal closely. Most of them do not need treatment, unless their visual acuity impacted. Vitrectomy may be an effective management. Clinical diagnosis are based on the white dots attached to the posterior lens surface (pseudopodia lentis). Surgical extract of the vitreous cavity may be sent for further pathological examination.

2.2.2 Differential diagnosis. The patient (Case 4) had been diagnosed as “vitreous haemorrhage/opacification” and prepared for in-patient surgery before. That may be the possible reason for fewer domestic literature about the vitreous amyloidosis, lack of knowledge about the disease.

Followed are the focal points for identified diagnosis of vitreous opacities clinically, a. white dots attached to the posterior lens surface (pseudopodia lentis) is diagnostic elements, b. posterior vitreous detachment adhering to optic disc, which need to identify with retinal detachment; c. fundus red reflex can be seen with indirect ophthalmoscope, ERG/VEP was normal.

It may be misdiagnosed as; a. complicated cataract, b. uveitis, c. long-standing vitreous hemorrhage, d. retinal detachment.

2.2.3 Complications The first three patients of the family occurred secondary glaucoma at different times postoperatively, which don’t agree with “better prognosis” of the Doft’s report. Some,9,10 found that vitreous amyloidosis with secondary glaucoma was due to trabecular amyloid deposition. The secondary glaucoma could occur at pre- or post-operation, and the specific mechanism needs further study. Therefore, the fourth patient had only performed vitreous surgery on her one eye, and treated with control inflammation and intraocular pressure by topical anti-glaucoma medications. Her intraocular pressure was controlled within 16 mm Hg and visual field test were normal by 10 months follow-up.

2.3 Prediction and genetic research of the family

The writer has been tracing this family vitreous amyloidosis for 13 years. There are 18 family members in our study within 4 generation involving nine person, four cases with seven eyes confirmed by surgery as vitreous amyloidosis. In addition to proband III 3, his onset age was 41 years old, the others’ age of onset were over 60 years old, involving both eyes. Age at onset of the rest of fourth-generation and the fifth generation were younger than 35 years of age at present. We are now carrying out the genetic analysis of the family, and trying to predict the case of the fourth-generation of the family who carry the disease genes without onset yet.

References


