Singapore Med J 1998; Vol 39(1):27-29

Case Report of Usher's Syndrome in Two Sisters – First Reported Case in Singapore

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ABSTRACT

A 28-year-old Chinese woman presented with poor night vision since childhood. Ocular examination showed pigmentary retinopathy and systemic examination revealed sensorineural hearing loss. Family history showed a similar condition in her youngest sister. Ocular and systemic examination of her sister showed similar findings. This is presented as the first case report of Usher's syndrome in Singapore. A general discussion of Usher's syndrome is also presented.

Keywords: Usher's syndrome, poor night vision, pigmentary retinopathy, sensorineural hearing loss

CASE REPORT

A 28-year-old woman (OLY) presented with a complaint of deteriorating night vision since early adolescent. Her night vision has steadily worsened since then and now she frequently stumbles over obstacles and finds difficulty walking at night. On further questioning, she also complained of poor hearing. She had previously been seen by the Ear, Nose and Throat Department when she was a child but has since been discharged.

Her family history revealed that her youngest sister, OLP, had similar symptoms. Although she had visual acuity of 6/7.5 in both eyes, she also had night blindness since her early teens. She was also seen by the Ear, Nose and Throat Department and had been found to have neurosensory deafness. Her third brother is an Air Force Pilot and had undergone extensive tests before being accepted. Her fourth brother is a tank driver in the Army and had no visual or auditory complaints. There was no history of visual or auditory complaints from her parents or her paternal/maternal relatives. Her parents' marriage is non-consanguinous.

Clinical examination showed a visual acuity of 6/9 in the right and left eyes. The anterior segments were normal in both eyes. The intra-ocular pressures were 18 mmHg in both eyes and there was no afferent pupillary defect. The main findings were in the fundi (Figs 1 & 2). There was bone-spicule pigmentation scattered throughout the mid periphery of both fundi. The optic discs were both slightly pale and the vasculature of both eyes appeared mildly attenuated.

Both systemic and neurological examinations did not show any abnormalities. Her mental status appeared normal and she did not have any speech problems. An electroretinogram was performed and she tolerated the procedure well. Under dark adapted conditions, dim flash stimuli produced flat waveforms (waves B1, B2 in Fig 3). Bright flash stimuli under dark adapted conditions produced flat waveforms (waves Dl, D2 in Fig 3). Flicker stimuli at 30 Hz produced very diminished waveforms (waves F1, F2 in Fig 3).

An audiogram was performed and it showed bilateral moderately severe sensorineural hearing loss (Fig 4).

A dark adaptation test was also performed and it showed an abnormal result with an absence of the rod phase (Fig 5).

A diagnosis of Usher's syndrome was made and the family was brought in for screening. Other than the youngest sister, the rest of the family did not turn up except for her father who was found to be normal. The two brothers claimed that they were asymptomatic and had been screened by the Air Force and the Army before employment.

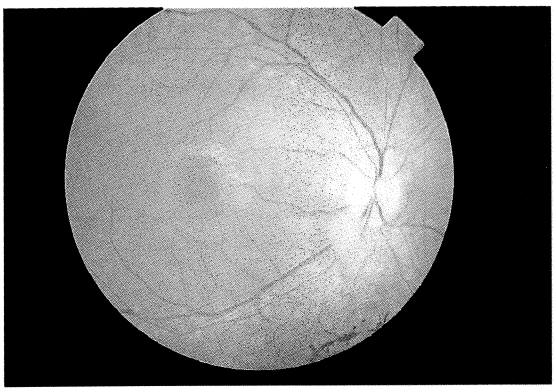

Fig 1 - (R) fundal photograph of OLY

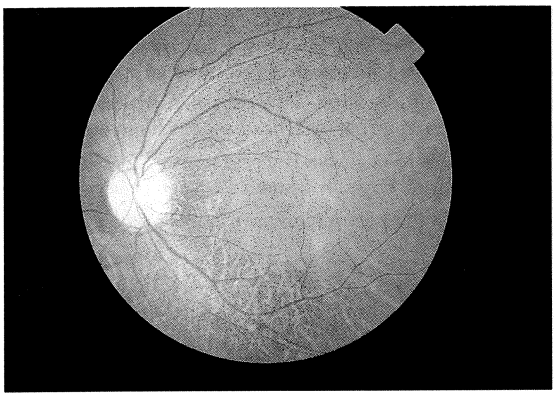

Fig 2 - (L) fundal photograph of OLY

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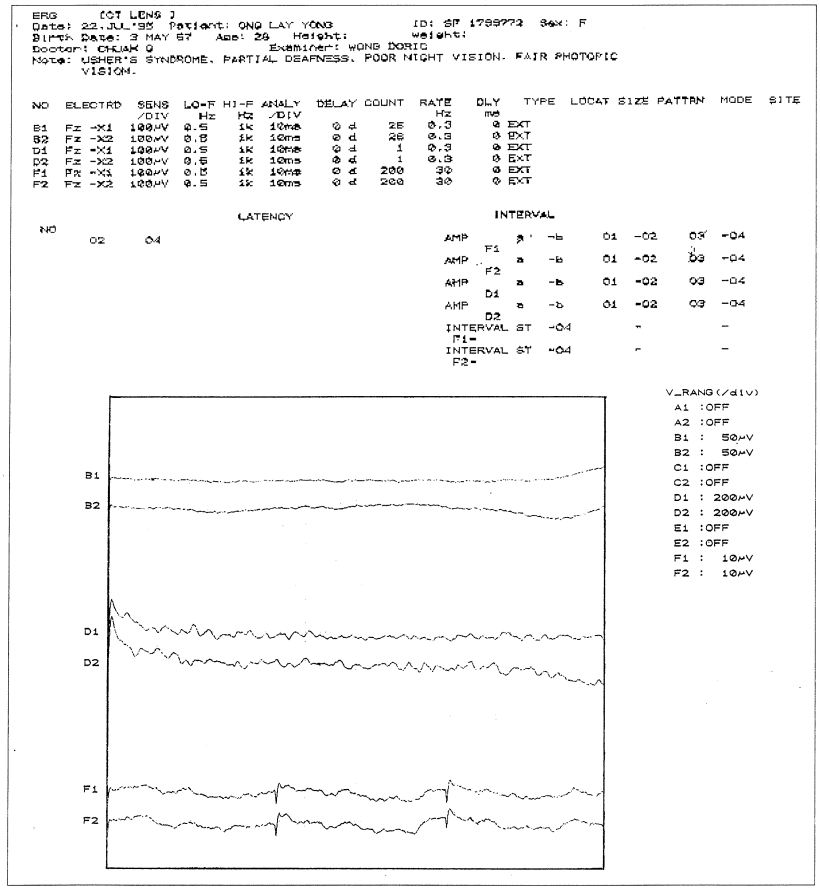

Fig 3 - Electroretinograms showing flat responses to: (B) dark adapted dim flash stimuli (D) dark adapted bright flash stimuli (F) flicker stimuli at 30 Hz

The electroretinogram is the record of an action potential produced by the retina when it is stimulated by light of adequate intensity.

It is possible to single out rod responses by stimulating the fully adapted eye with dim flash stimuli (B) and bright flash stimuli (D), and cone responses by flicker stimuli at 30 Hz (F).

The results show flat responses recorded by the patient for all 3 techniques.

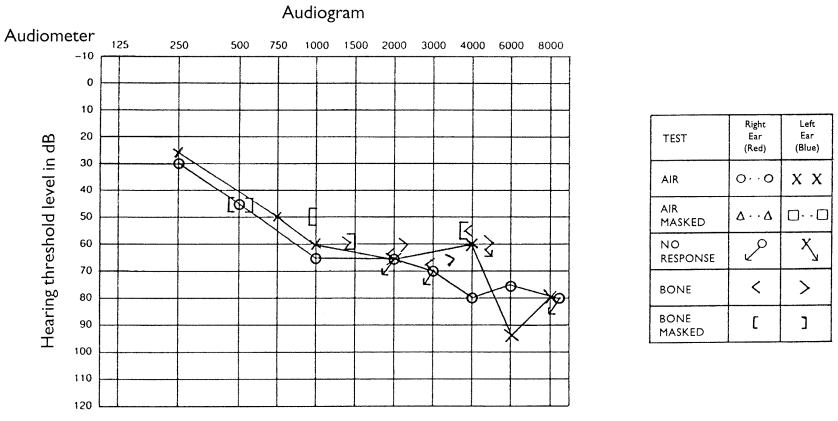

Fig 4 - Audiogram of OLY showing moderately severe bilateral sensorineural hearing loss.

The audiogram is a reflection of auditory acuity.

The threshold level at each intensity is recorded and plotted for the patient, shows moderately severe bilateral sensorineural hearing loss.

DISCUSSION

The association of retinitis pigmentosa and congenital hearing loss was first reported by Albrecht von Graefe[1]. Usher's[2] large series in 1914 added cataracts, speech disorders and mental illness to the syndrome. The associated finding of vestibular ataxia was reported by Hallgren[3, 4].

Usher's syndrome thus consists of retinitis pigmentosa and congenital sensorineural hearing loss. Cataracts, speech disorder, mental deficiency, psychosis and vestibular ataxia are various associated findings.

Although Usher's syndrome is rare, it is the most common of the various syndromes associated with retinitis pigmentosa. In the United States, the incidence is estimated to be about 3 per 100,000 population[5].

Usher's syndrome affects 3% to 6% of the deaf population and the inheritance has been found to be autosomal recessive.

Two main types have been described:

1. Usher's syndrome Type 1.
2. Usher's syndrome Type 2.

Patients with Usher's syndrome Type 1 typically have night blindness in the first or second decades of life, congenital deafness with unintelligible speech and vestibular ataxia. The electroretinogram usually shows flat response.

In Usher's syndrome Type 2, the patients suffer night blindness in the second to forth decades of life, have a partial high-tone hearing loss with intelligible speech and do not show ataxia. The retinal dystrophy is of later onset, less severe and a small electroretinogram response can usually be recorded.

The two sisters have Usher's syndrome Type 2 based on their medical history, the absence of speech abnormalities and the absence of ataxia.

In Usher's syndrome, the earliest visual symptom is night blindness. Visual acuity is excellent in the early stages. The vision may deteriorate to 6/60 or worse by the fourth decade. There is progressive peripheral visual loss with retention of central vision until late, except atypical cases with cystoid macular oedema or cataracts, usually of the posterior subcapsular type.

Psychosis often occurs as part of Usher's syndrome. The stress of the sensory deficits may contribute to the psychiatric symptoms but some authors have reported metabolic and degenerative brain diseases in Usher's syndrome that suggest a likely organic cause for the psychosis[6].

Gene linkage analysis have revealed separate loci for Usher's syndrome Type 1 and 2. Type 1 has been localised to the short and long arm of chromosome 11, whereas Type 2 is the long arm of chromosome 1[7,8].

If a child presents with profound deafness and a balance disorder manifested by late onset of walking after 15 months of age, the possibility of Usher's syndrome Type 1 should be considered. Electroretinogram testing may help to establish diagnosis. Once Usher's syndrome is diagnosed, the parents should be informed that they will have a 25% chance of having another child with this disorder. Unfortunately, no tests are available as yet to identify with certainty the carriers of Usher's syndrome.

In assessing a child with deafness and a fundal appearance resembling a retinal dystrophy, it is

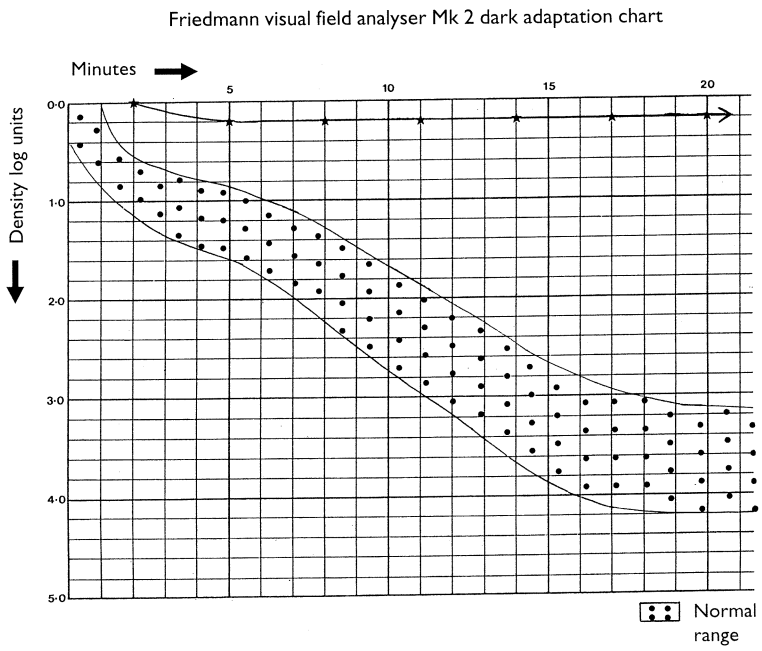

Fig 5 - Dark adaptation test of OLY showing abnormal result with absent rod phase.

The dark adaptation curve shows the change in the intensity of a stimulus necessary to just excite the retina in dim light as a function of the time the observer has been in the dark.

As is evident in the diagram, the result of the patient shows that her retinal components fail to become sufficiently stimulated with the result that the curve flattens out in contrast to that shown in normal results.

important to exclude other disorders before making a diagnosis of Usher's syndrome.

The differential diagnoses to be excluded are:

1. Congenital rubella
2. Alström's syndrome
3. Cockayne's syndrome
4. Laurence-Moon-Bardet-Biedl syndrome
5. Refsum's syndrome

Congenital rubella may cause profound deafness and a pigmentary retinopathy, although the distinguishing features are that the electroretinogram is normal and the retinal function is normal, although vision may be reduced by congenital cataracts.

Alström's syndrome is of autosomal recessive transmission and consists of infancy onset retinitis pigmentosa, diabetes mellitus of childhood onset, obesity, progressive sensorineural hearing loss with onset in late childhood, and posterior cataract formation in some patients.

Cockayne's syndrome is also of autosomal recessive transmission and consists of premature senile appearance, dwarfism, kyphosis, neural hearing loss, photosensitive dermatitis, retinitis pigmentosa, mental retardation and optic atrophy.

Laurence-Moon-Bardet-Biedl syndrome includes obesity, polydactaly, hypogonadism, mental retardation, retinitis pigmentosa and neural hearing loss.

Refsum's syndrome is characterised by autosomal recessive inheritance, hypertrophic peripheral neuropathy, retinitis pigmentosa, neural hearing loss, mild ataxia, nystagmus and increased plasma phytanic acid concentration.

CONCLUSION

In our patients (OLY and OLP), the sensorineural hearing loss and the retinitis pigmentosa in the absence of other systemic abnormalities point to a diagnosis of Usher's syndrome.

Congenital rubella can be excluded as the patients have symptoms of retinitis pigmentosa and the electroretinogram is abnormal in both our patients.

It is important to make the correct diagnosis for a child presenting with bilateral sensorineural hearing loss and pigmentary retinopathy for the following reasons:

1. Genetic counselling for the parents and patients.
   Parents must be aware that the risk of having a subsequent affected child is 25%. With regards to antenatal testing, as the loci for Usher's Type 1 and 2 are known, antenatal diagnosis should be possible but the test is at present still not available in Singapore. It is hoped that in the near future, amniocentesis with chorionic villous sampling and gene linkage analysis may be reliable enough to identify the gene loci responsible for both Usher's Type I and 2 and determine if the fetus is affected. The patients should also be warned that their offspring will have a 50% risk of being a carrier.

2. Job counselling for the patients.
   Fortunately for patients with Usher's syndrome Type 1 and 2, their central visual acuity is relatively unaffected until the third or fourth decades. The sensorineural hearing loss may also vary in severity from mild-high frequency hearing loss to profound congenital deafness. Hence, by the very nature of their disease, they are excluded from professions that require good night vision and hearing such as pilots, truck drivers, train drivers etc. They should also be warned that their visual and auditory impairment may worsen with time, though they should be reassured that the deterioration occurs gradually and not suddenly.

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