Usher Syndrome: Case Report

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Running Title: Usher Syndrome

Abstract:
Usher syndrome (USH) is a genetic disorder associated with a dual sensory disability (auditory and visual) called deaf blindness. We report the observation of a 20-year-old patient from a consanguineous marriage with congenital deafness with normal vestibular function and pigmentary retinopathy responsible for a bilateral decrease in visual acuity that occurred at age 9 years. This association forms type 2 of Usher syndrome. USH is inherited in an autosomal recessive pattern.

Keywords: blindness, deafness, pigmentary retinopathy

Introduction:
Usher syndrome is a disease first described by the English ophthalmologist C. H. Usher in 1914. It is associated with deafness and visual disturbances due to a dysfunction of the retina (pigment retinopathy). This syndrome is the most common cause of deafness associated with blindness. We report a case of Usher syndrome in a 20-year-old woman.

Case report:
A 20-year-old patient from a first-degree consanguineous marriage. He was affected by moderate congenital deafness, which enabled him to learn to speak. At the age of 9 years, he developed a secondary decrease in visual acuity in both eyes (initially in the right eye). Ophthalmologic examination revealed visual acuity limited to 1/10 in the right eye and 2/10 in the left eye, slit lamp examination revealed normal anterior segments in both eyes, ocular tone of 14 mmHg in the right eye and 17 mmHg in the left eye with diffuse arteriolar narrowing at the fundus, a pale optic disc, and most importantly, the presence of areas of atrophy

of the retinal pigment epithelium with whitish deposits at the periphery of the macula with sparse appearance of the vessels (Figure 1). Optical coherence tomography of the macula showed thinning of the peripheral retinal layers in both eyes (Figure 2). Subsequent autofluorescence showed a hyperautofluorescent para-foveolar ring (Figure 3). Visual field showed a global deficit of the peripheral field with preserved central vision (Figure 4). ENT examination was normal, whereas tone audiometry revealed a second-degree mean hearing loss between 50 and 70 decibels. Neurologic examination was normal and showed no cognitive impairment, no vestibular or cerebellar syndrome, and no proprioceptive ataxia. Electroretinogram (ERG) showed global extinction in both photopic and scotopic environments, confirming advanced global retinal degeneration. No treatment was suggested for this patient, but simple surveillancewith genetic counseling was suggested.

Discussion:

Usher syndrome (USH) was first described by von Graefe in 1858 and is characterized by the association of sensorineural hearing loss, retinitis pigmentosa (RP), and in some cases vestibular dysfunction. Heritability was established by Charles Usher, a British ophthalmologist [1]. The syndrome is inherited in an autosomal recessive pattern. The syndrome is the most common cause of deafblindness and accounts for more than 50% of individuals who are both deaf and blind [2, 3], approximately 18% of RP cases [4], and 5% of all cases of congenital deafness [5]. The prevalence ranges from 3.2 to 6.2/100,000 depending on the study [2,6]. The association of pigmentary retinopathy and congenital sensorineural hearing loss in the context of consanguinity suggests the diagnosis of Usher syndrome in our patient. [7]. The clinical classification of Usher syndrome established by Davenport and Omenn is still in use [8]. USH1 is the most severe form. It is characterized by severe to profound congenital sensorineural deafness, constant vestibular dysfunction (balance disorder), and retinitis pigmentosa onset before puberty [9]. Retinopathy manifests as loss of night vision and visual field loss in childhood and eventually visual acuity loss that rapidly leads to blindness. Abnormalities of the light-induced electrical response of the retina can be detected as early as 2 to 3 years of age by electroretinography, allowing early diagnosis of the disease. Later, fundus abnormalities develop, consisting of pigment deposits resembling bone needles in the midperiphery of the retina that subsequently spread inward and outward, as well as narrowing of the blood vessels. USH2 differs from USH1 primarily in having less pronounced deafness, mild hearing loss for low-pitched sounds and severe hearing loss for high-pitched sounds, with an absence of vestibular dysfunction. Loss of night vision develops around puberty (age of onset partially overlaps with USH1). The progression of visual impairment appears to have greater variability than in USH1 [10]. The presence of moderate congenital deafness with language acquisition, normal vestibular responses, and pigmentary retinopathy beginning in young adulthood suggests type 2 of this syndrome. Genetic studies of Usher syndrome conclude that it is a heterogeneous disease, with the three clinical types being subdivided into several genetic subtypes [11]. It is known that the different forms are caused by different gene mutations; to date, not all mutations are known. Recent research has focused on the identification of new genes, the function of the corresponding proteins, and the interactions between proteins, and currently 8 genes and two loci are known, corresponding to the totality of the described

cases [11, 12]. The two main genes are MYO7A and USH2A [8]. Studies have shown that all currently known Usher syndrome type 1 proteins act on the cohesion of stereo cilia located in the auditory cells of the inner ear and in the various photoreceptor structures. All forms of Usher syndrome are inherited in an autosomal recessive pattern [13]. Molecular diagnosis is now possible, guided by clinical practice, but is expensive to perform [12]. Recent neuroradiological data describe inconstant lesions such as cerebellar atrophy or, less commonly, brainstem or occipital cortex atrophy [14]. Electroretinogram (ERG) is a very useful adjunct examination for the diagnosis of early pigmentary retinopathy but has little diagnostic value in advanced cases. Ophthalmologically, remaining visual abilities should be optimized and orthoptic and low-vision consultation should be organized [15]. Complications are dominated by cataract and cystoid macular edema [16]. In cases of decreased visual acuity due to cystoid macular edema, a classic complication of this disease, acetazolamide can sometimes improve vision for a period of time [17].

Conclusion:

Usher syndrome is a clinically and genetically heterogeneous genetic disorder. An ophthalmologic examination is systematically performed before any congenital deafness to detect the association with pigmentary retinopathy, several treatments for pigmentary retinopathy have been performed, but none of them has been effective in curing the disease, and the prognosis remains grim with progression to blindness.

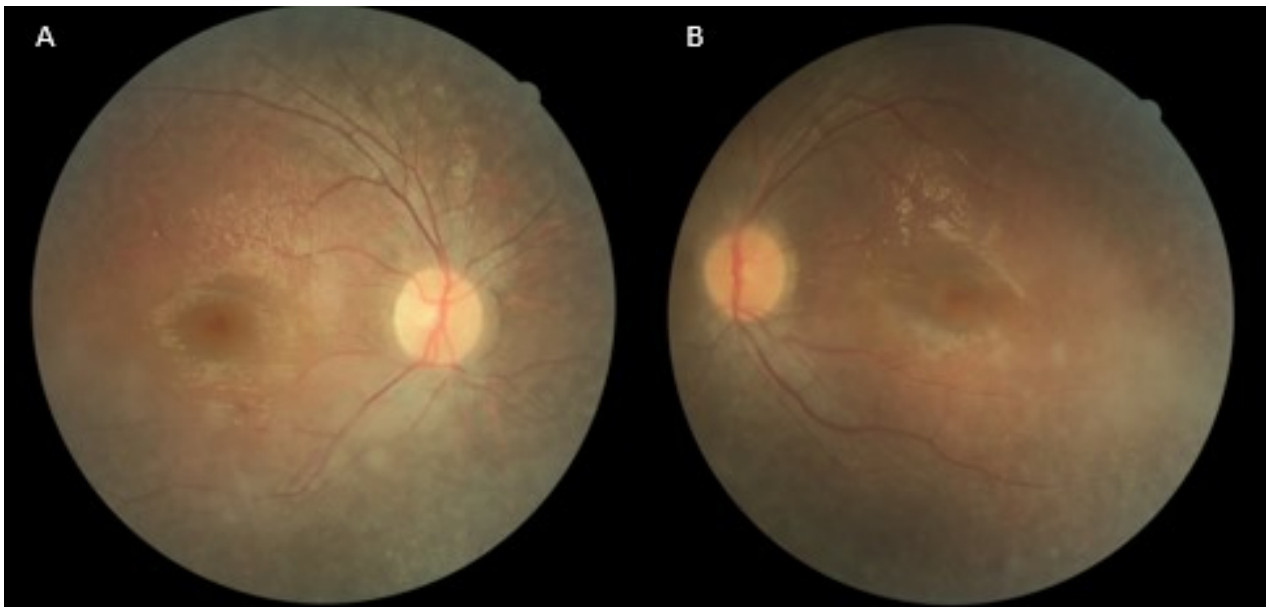

Figure 1: Retinography of both eyes with a pale optic disc, presence of areas of atrophy of the retinal pigment epithelium with whitish deposits at the periphery of the macula with sparse appearance of the vesselsA: right eye /B: left eye.

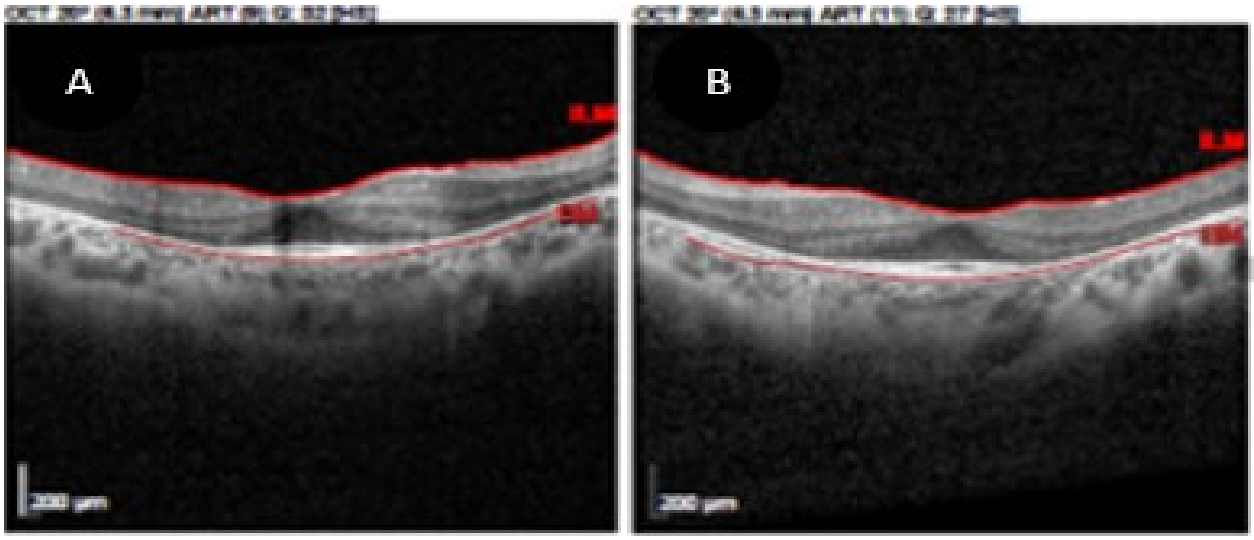

Figure 2: Optical coherence tomography of the macula showed thinning of the peripheral retinal layers in both eyes A: right eye /B: left eye.

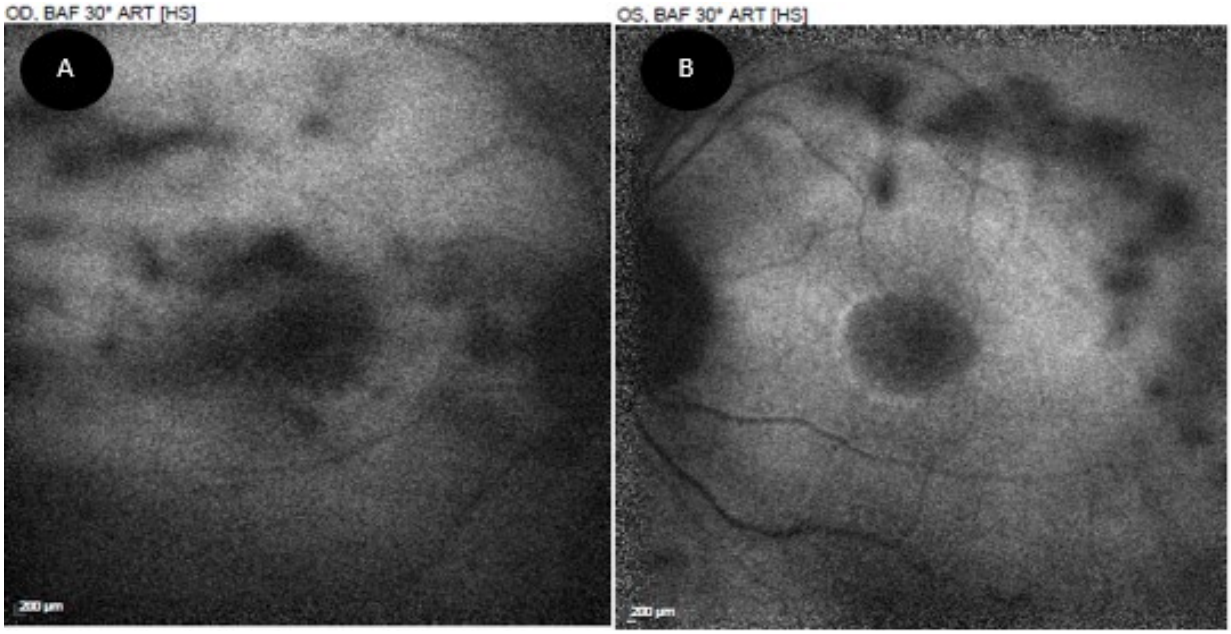

Figure 3: Autofluorescence image showed a hyperautofluorescent para-foveolar ring in both eyes A: right eye /B: left eye.

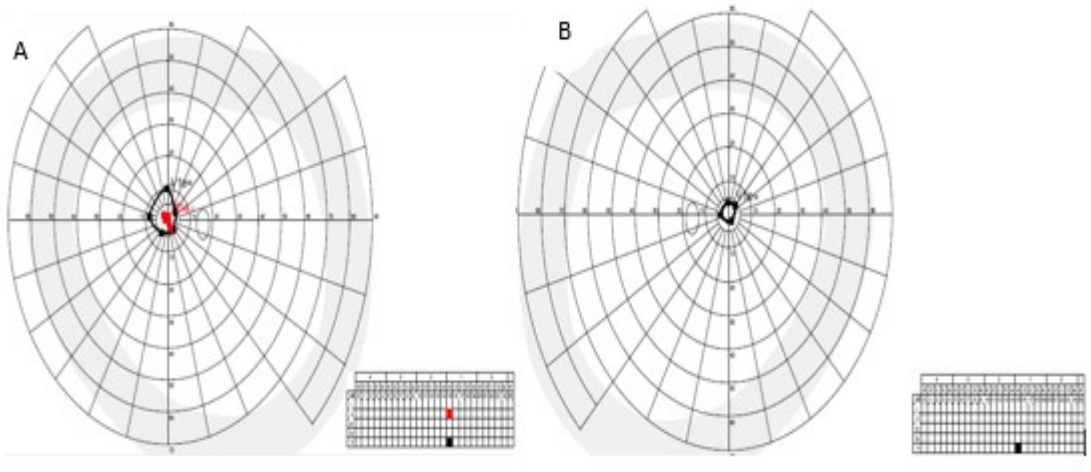

Figure 4 : Visual field showed a global deficit of the peripheral field with preserved central vision in both eyes A: right eye /B: left eye .

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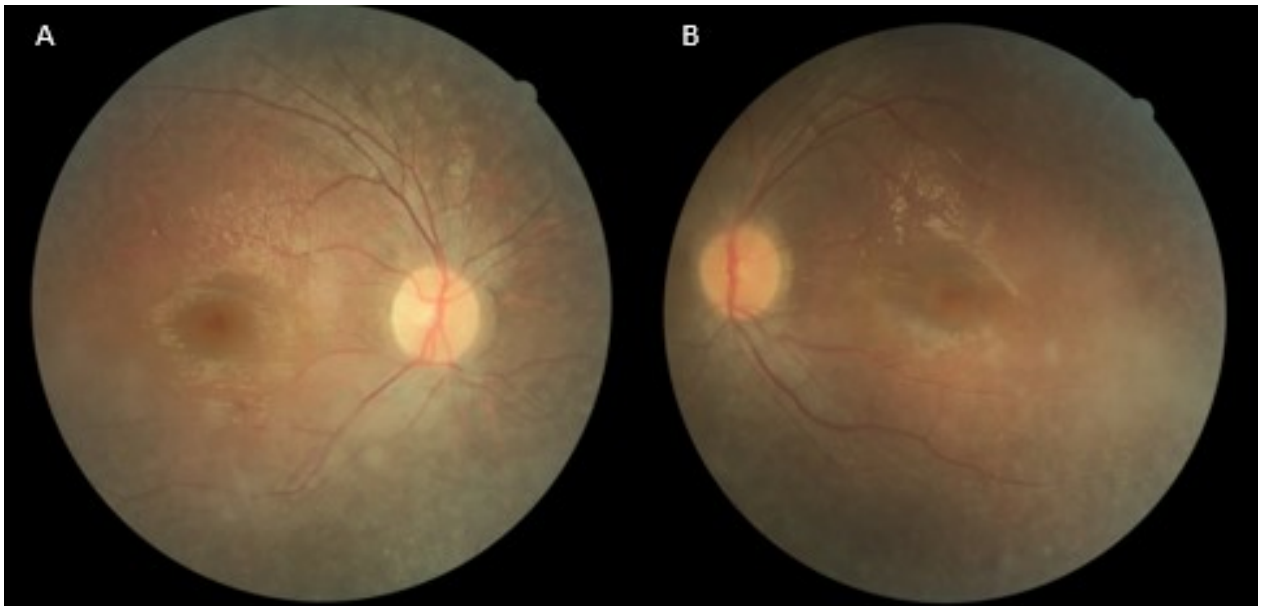

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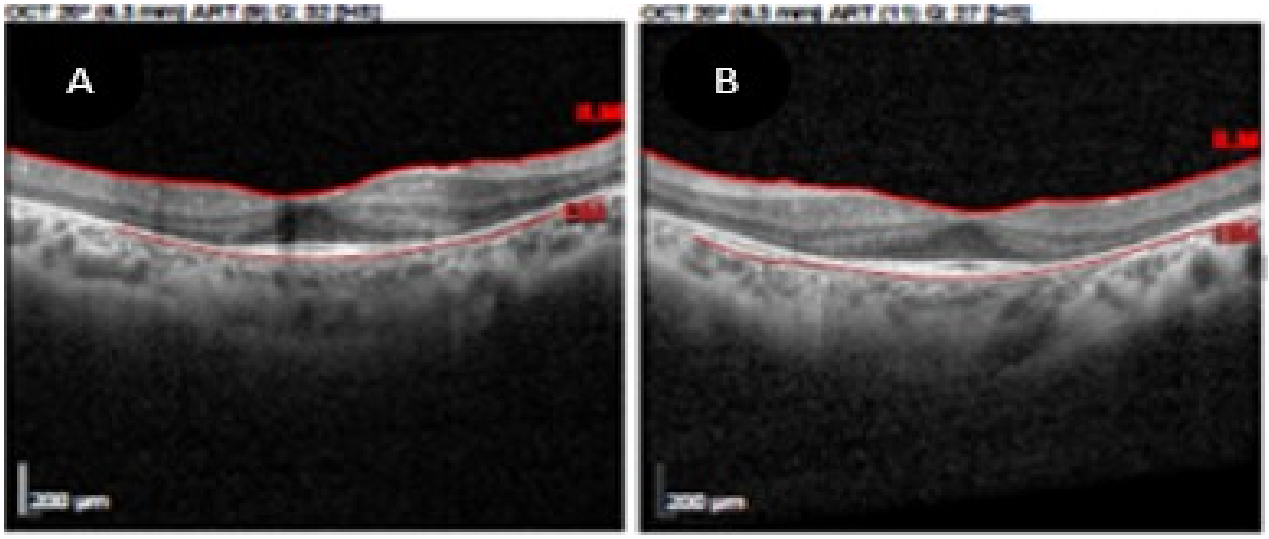

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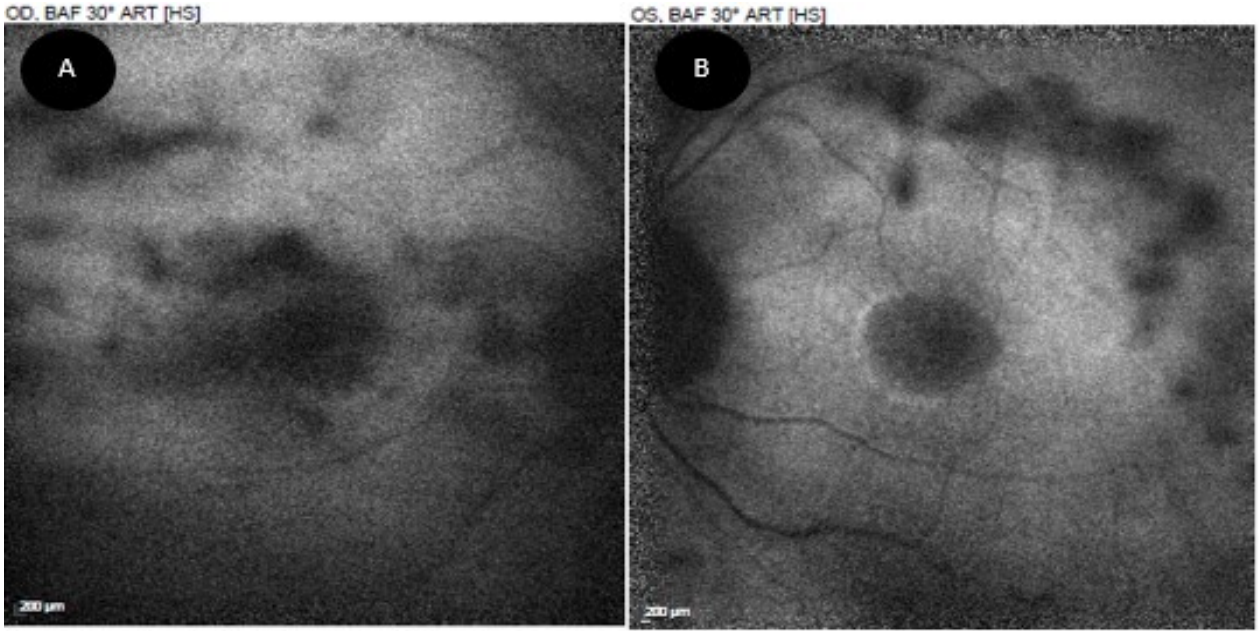

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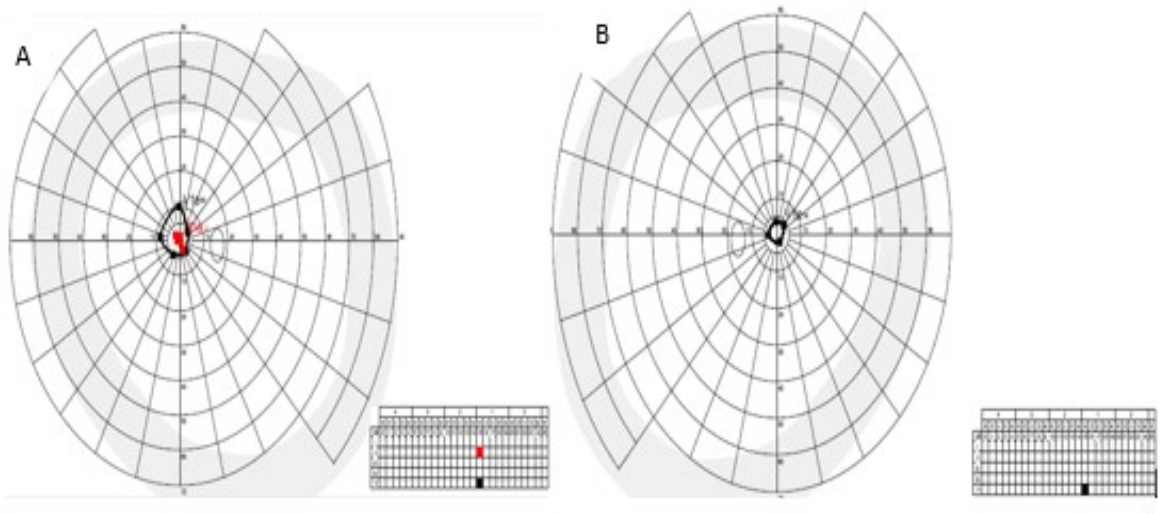

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