

## BILATERAL ATROPHIC MACULOPATHY IN TWO SIBLINGS OF WOLFRAM SYNDROME

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### ABSTRACT

Wolfram disease is a rare genetic disease which mainly presents as diabetes mellitus and optic atrophy. Presence of maculopathy in a case of wolfram disease is rarely reported in literature. We present here two cases/siblings with age of 12 and 14 years. They had diabetes mellitus, deafness and disc palor. Ocular examination also revealed atrophic maculopathy in both siblings, supported by depressed response on ERG. Assosiation of maculopathy with wolfram syndrome is rare and worth reporting.

**Keywords:** Diabetes, Maculopathy, Wolfram syndrome.

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### INTRODUCTION

Wolfram disease is one of the rare genetic disorders. It has an autosomal recessive pattern of inheritance<sup>1</sup>. Mostly the first presenting signs are diabetes mellitus and optic atrophy<sup>2</sup>, however hearing problems, mental retardation, gonadal atrophy, renal problems, cardiac defects, low haemoglobin and platelet count and peripheral neuropathies have been reported in literature<sup>3,4</sup>. Generally the cause of death is respiratory failure and from other life threatening complications<sup>5</sup>. Wolfram disease and maculopathy is a rare combination. We present here cases of two siblings of Wolfram syndrome and atrophic maculopathy. Chau *et al*<sup>6</sup> and Dhalla *et al*<sup>7</sup> reported similar cases of maculopathy in wolfram syndrome. The association is rare and worth reporting.

### CASE REPORT

Fourteen year old boy with insulin dependent diabetes mellitus, hearing loss, and mentally handicap presented to us for visual assessment. On examination unaided vision was 6/24 and 6/36 improving to 6/21 and 6/24 with refraction in right and left eye respectively. He had IDDM hearing loss and anemia since 5 years of age. He also had progressively decreasing visual acuity.

Fundus examination revealed bilateral maculopathy. OCT confirmed blunting of foveal contour and atrophic maculopathy (fig-1). ERG was done which showed depressed photopic response in both eyes. The other sibling 12 year old girl with insulin dependent diabetes mellitus and hearing loss and anemia had unaided vision was 6/45 in both eyes improving to 6/9 and 6/15 with refraction in right and left eye respectively. He had IDDM hearing loss and anemia since 4 years of age. He also had progressively decreasing visual acuity. Intraocular pressure measures by goldman applation tonometer was 18 mmHg in right and left eye respectively. ERG was done which showed depressed photopic response in both eyes and depressed scotopic response in left eye. In both the siblings fundus examination revealed bilateral maculopathy and optic disc palor. OCT confirmed blunting of foveal contour and atrophic maculopathy (fig-2). Both had nystagmus. There was no evidence of diabetic retino-pathy in either sibling.

### DISCUSSION

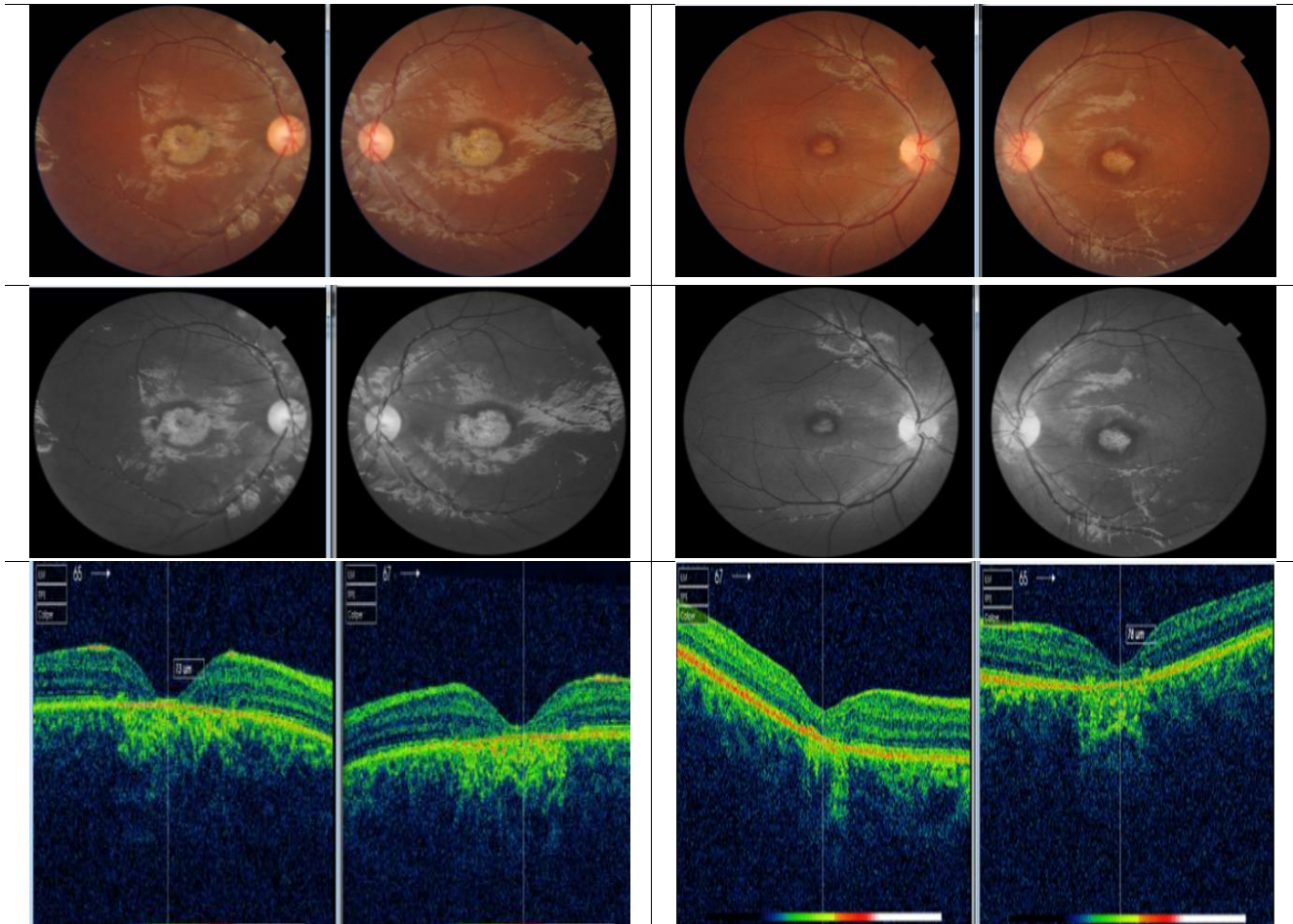
Wolfram disease is a rare inherited disorder with average onset age of 6 years. General mode of transmission is autosomal recessive but evidence about mitochondrial inheritance is also documented. Diabetes mellitus and optic atrophy are generally the initial presenting features. Studies show that about 60% of the patients of

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wolfram syndrome develop hearing loss usually by 3rd decade of life but in our case it was a bit earlier, 62% develop neurological features (like nystagmus in our case) and 25% have mental disorders. Association of pigmentary maculopathy is rather rare. Cremers *et al*<sup>8</sup> studied 91 patients of wolfram. Only 9% of the subjects had some sort of retinal pigmentary changes in

This gene encodes for a protein wolframin which is abundant in cells of nerves, muscles, pancreas, kidney, liver and ear. The deficiency/ altered protein structure in these tissues result in the peculiar disease sign and symptoms. It was found that the patients with combined presentation of wolfram and maculopathy/ pigmentary retinopathies have mitochondrial



**Figure-1: Fundus picture, red free photograph and macular cross section of first sibling.**

**Figure-2: Fundus picture, red free photograph, and macular cross section of second sibling.**

them. Types of dystrophy was however not mentioned. Similarly Gunn and Al-Till found this association in their studies<sup>9</sup>. There are three main types of disease<sup>10</sup>. WFS1, WFS2 and WFS (mitochondrial). Several genetic mutations such as 4p 16.1<sup>11,12</sup>, 4q22-q24<sup>13</sup> and mitochondrial<sup>14,15</sup> mutations have been reported in literature. Commonest type of wolfram syndrome is because of mutation in chromosome 4 (4p16).

disorders. However further genetic studies need to be done in this regard to identify exact mode of inheritance in patients with combined wolfram and pigmentary retinopathy/maculopathy. Genetic studies will not only help in correct diagnosis but will also help pick heterozygote carriers. It will help in genetic counseling before marriage in such cases.

**CONFLICT OF INTEREST**

This study has no conflict of interest to be declared by any author.

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