Visual disturbance in Diabetes Mellitus; don't be blind to alternatives to retinopathy

Smith TD,† Mukherjee A,† Dr S Ehtisham,‡ Tomlinson ND†
† Royal Oldham Hospital, Pennine Acute Hospitals NHS Trust ‡ Central Manchester University Hospitals NHS Foundation Trust

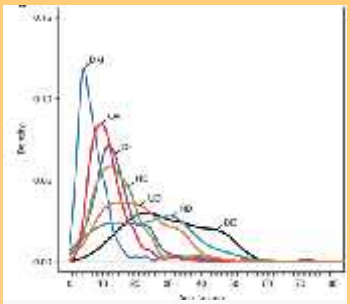
Case Summary

- Diabetes Mellitus diagnosed at 4 years old. Vision problems began at age 8
- No retinopathy. Impaired colour vision and significant bilateral optic disc pallor
- Normal neurological examination and cranial MRI
- No mitochondrial DNA deletion to suggest Leber's optic atrophy
- Parental consanguinity suggests a possible genetic aetiology
- Child is homozygous for WFS1 gene mutation (type 1 Wolfram Syndrome)

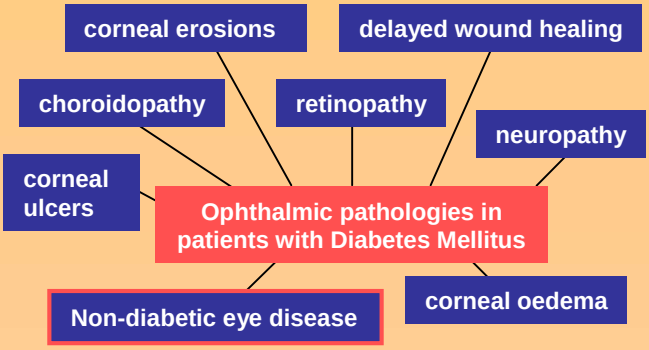
- Use of an insulin pump provides additional benefits given her vision problems
- Diabetes control had been poor, which hindered surveillance for the onset of Diabetes Insipidus
- Developed Diabetes Insipidus at 13 years old
- Hearing currently unaffected and renal ultrasound normal

- In view of the family history, when their 2 year old sibling developed Diabetes Mellitus aged 2 they were tested for the WFS1 mutation, which was present. Wolfram Syndrome was diagnosed *before* the onset of optic atrophy in this child

Optic atrophy on fundoscopy



Natural history of Wolfram Syndrome. The proportion of patients (density) for each clinical feature at onset age, measured as a nonparametric probability density distribution: DE, deceased; DI, diabetes insipidus; DM, diabetes mellitus; HD, hearing defects; ND, neurological, psychiatric, and developmental defects; OA, optic atrophy; UD, urological or renal defects



Wolfram Syndrome (type 1)[1]

- Autosomal recessive
- >90% due to mutation in WFS1 gene
- Estimated worldwide prevalence 1 in 500,000
- First presentation is usually Diabetes Mellitus
- Optic atrophy
- Diabetes Insipidus, sensorineural deafness, urinary tract pathology, hypogonadism (in males)
- Neurological and psychiatric disorders, commonly ataxia in early adulthood

Learning points

- Ophthalmic pathologies are well-recognised complications of Diabetes Mellitus
- Retinopathy screening is indicated at all ages[2]
- Alternative ophthalmic/non-ophthalmic aetiologies must be considered
- Diabetes Mellitus with optic atrophy should be investigated for Wolfram Syndrome
- Additional diagnoses cause cumulative stresses on the child and family, which can hinder disease management and treatment compliance

1. Genetics Home Reference. Wolfram syndrome [Internet]. 2012 [cited 2014 July 2015] http://ghr.nlm.nih.gov/condition/wolfram-syndrome
2. Lutty GA. Effects of diabetes on the eye. *Invest Ophthalmol Vis Sci* [Internet]. 2013;54. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864380
3. Forlenza GP, Stewart MW. Diabetic retinopathy in children. *Pediatr Endocrinol Rev* [Internet]. 2013;10(2):217-26 http://www.ncbi.nlm.nih.gov/pubmed/23539833
4. López de Heredia m, Clèries R, Nunes V. *Genetics in Medicine* [Internet] 2013;15:497–506. http://www.nature.com/gim/journal/v15/n7/full/gim2012180a.html
5. Ocular pathology photos: Primary optic atrophy: http://tedmontgomery.com/the_eye/eyephotos/index.html [website]

British Society for Paediatric Endocrinology and Diabetes

The Pennine Acute Hospitals NHS Trust

Central Manchester University Hospitals NHS Foundation Trust