A case of oculodentodigital dysplasia with incongruous eye signs and symptoms

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Introduction

- Oculodentodigital dysplasia (ODDD) is a rare genetic disorder characterised by abnormal development of the face, eyes, limbs and teeth. (1)
- It is often inherited in an autosomal dominant pattern through mutations of the GJA1 gene encoding the gap junction protein, Connexin43, found in intercellular channels of various tissues throughout the body. (1,2)
- Approximately 70% of ODDD patients will have ocular features, of which, the commonest are microphthalmia, microcornea and glaucoma. (3)
- Microcephaly, prominent columella and hypoplastic nasal alae are common craniofacial abnormalities while hypoplastic enamel, small teeth and premature teeth loss are common dental abnormalities. Digit abnormalities include syndactyly, camptodactyly and clinodactyly. (1,2)

Case report

- We report a case in the Highlands of a 35-year old woman with ODDD (carrier of GJA1 gene mutation, inherited from her mother) who was referred in 2018 for headaches, eye pain, blurred vision and photophobia.
- Her past medical history includes epilepsy, chronic pain, depression, self-harm, overactive bladder and syndactyly of the hand.
- She had characteristic facial features including a long, narrow nose with hypoplastic alae nasi, anteverted nostrils, prominent columnella and nasal bridge (Fig 1). (4)

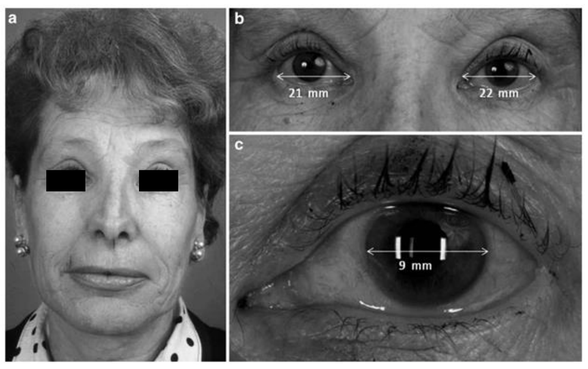

Fig 1 (a) Characteristic facial features, (b) reduced palpebral fissure length and (c) microcornea similar to that of our patient. (4)

- Her vision was 6/6 BE, no RAPD, normal IOPs, microcorneas, narrowed angles on gonioscopy and healthy optic discs.
- Visual fields were constricted bilaterally but unreliable throughout our monitoring period (Fig 2).
- Optic discs OCT showed right eye RNFL thinning compared to the left (Fig 3), but these were inconsistent with her visual field findings, possibly reflecting optic nerve changes found on her MRI (see below).
- Bilateral peripheral iridotomies were performed, resulting in slight deepening of the anterior chamber on examination.
- However, she remained symptomatic and failed to improve with Latanoprost.
- She was reviewed over 2 years with similar concerns but with no evidence of progressive optic neuropathy or glaucoma (Fig 3).
- Recent MRI (Fig 4) revealed areas of focal T2 hyperintensities in the periventricular white matter, internal capsule, corpus callosum, medulla, pons, hippocampus and cerebellum bilaterally. Focal T2 hypointensities in the thalami and globus pallidii and abnormal T2 signals within the prechiasmal optic nerves bilaterally were thought to be unchanged when compared to previous images in 2013.
- She was discharged from Ophthalmology and advised to continue with Neurology and possible Neuropsychology reviews for her symptoms.

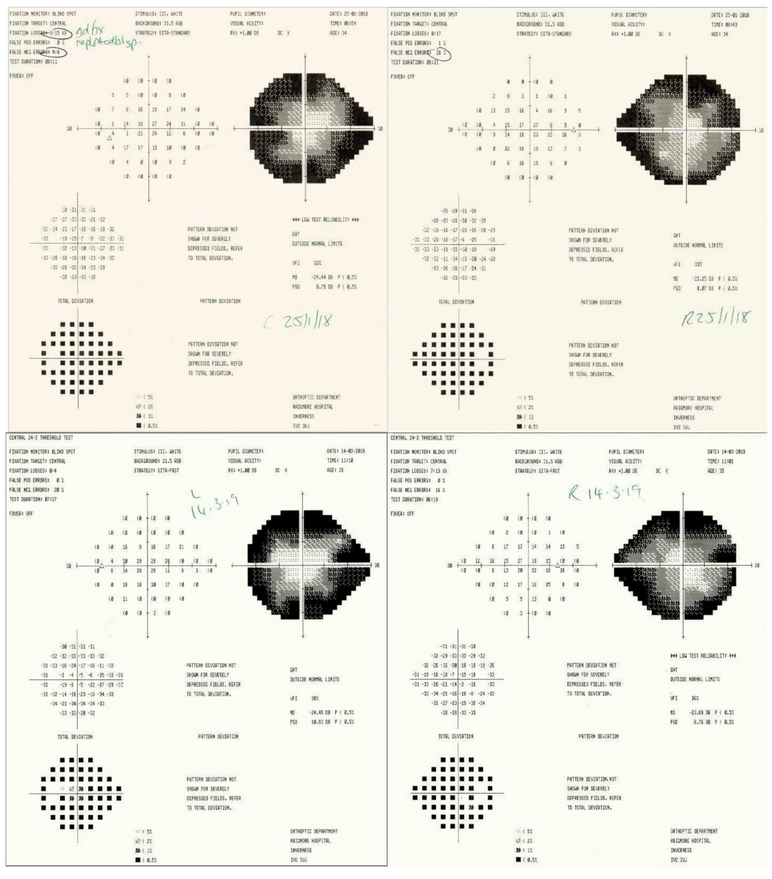

Fig 2 Humphrey perimetry visual field over a 1 year period demonstrated similar constricted visual fields bilaterally. All were unreliable.

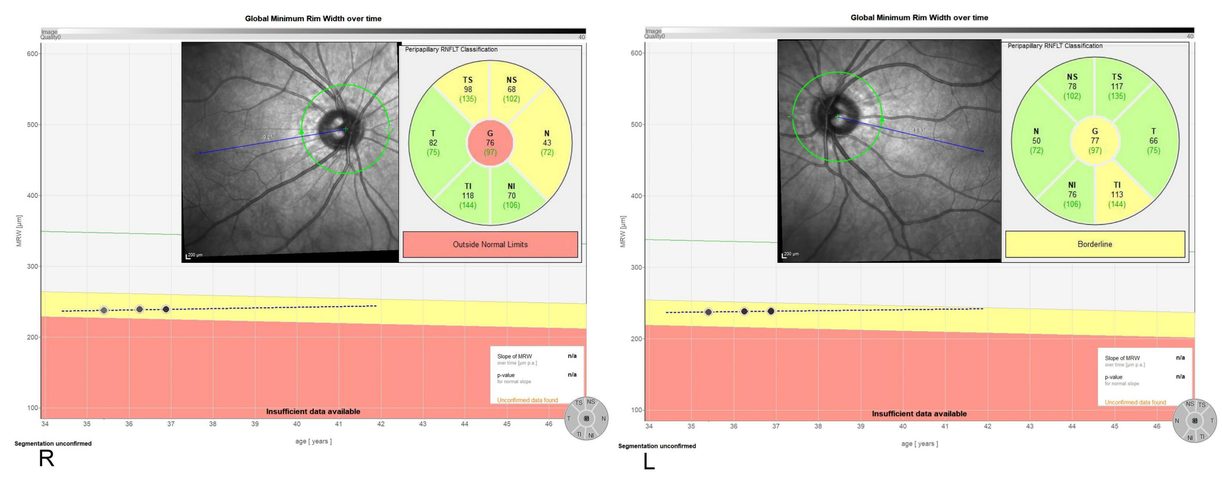

Fig 3 Progression analysis of the optic discs OCT over 3 years showing no change. Inlay shows images of the optic disc and peripapillary retinal nerve fibre layer thickness (RNFL) from her last OCT in 2020.

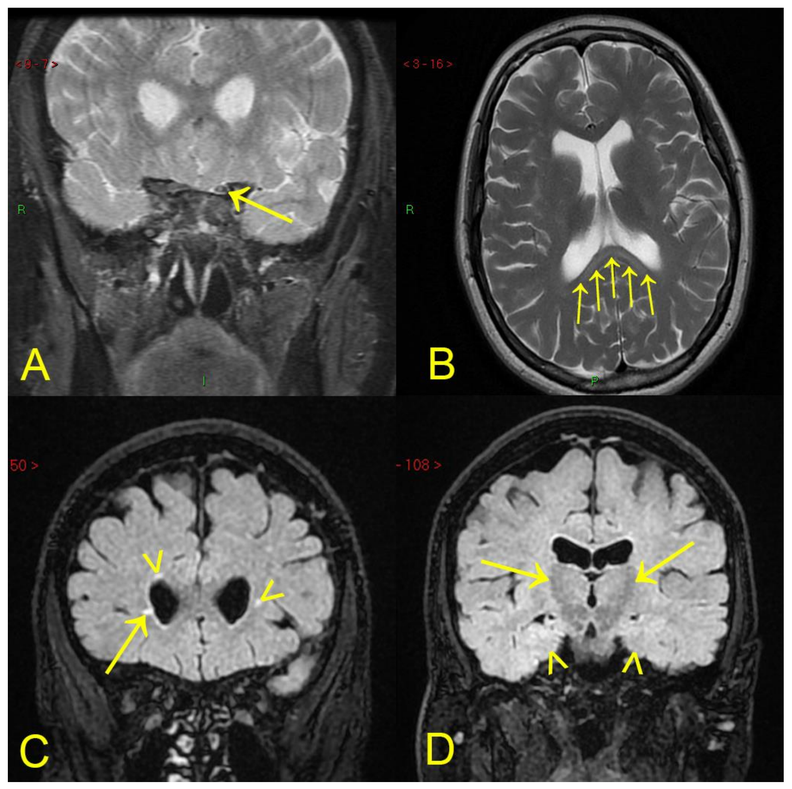

Fig 4 (A) Coronal STIR showing increased T2 signal in left pre chiasmal optic nerve (B) T2 axial showing increased T2 signal in splenium corpus callosum (C) FLAIR coronal showing white matter disease with one right periventricular T2 hyperintensity (arrow) and a few other focal T2 high signal lesions (arrowhead) (D) FLAIR coronal showing reduced T2 signal in both thalami (arrow) and increased signal in both hippocampi (arrowhead)

Discussion

- Other ocular features include short palpebral fissure, epicanthal fold, fine porous spongy iris abnormalities, cataracts and optic atrophy. (2,4)
- However, glaucoma is the main cause of visual loss in ODDD with an 8-fold increased risk compared to the general population. (4,5)
- Various mechanisms of glaucoma has been described with ODDD. (4)
  - Congenital/childhood onset glaucoma has been attributed to anterior segment dysgenesis with trabeculodysgenesis. (4) Childhood chronic angle closure glaucoma secondary to ciliary body cysts has also been described. (5)
  - In adults, a combination of anterior segment dysgenesis, microcornea, narrow drainage angles and age-related lenticular growth contribute to the development of angle closure glaucoma.(4)
- High intraocular pressures inadequately controlled on topical medication, subsequently requiring aggressive surgical intervention is often described in ODDD patients with glaucoma. (2,3)
- This case report provides a valuable aide memoire of the ocular involvement in this rare, complex condition, with MRI findings consistent with ODDD, but also describes a diagnostic dilemma with the persistent symptoms but no definite cause for them.
- We are of the conclusion that her persistent unreliable fields are due to psychosomatisation. We hope this case will generate discussion to help guide her management and whether further investigations and reviews are required.

References

1. Kumar V, Couser NL, Pandya A. Oculodentodigital Dysplasia: A Case Report and Major Review of the Eye and Ocular Adnexa Features of 295 Reported Cases. Case Rep Ophthalmol Med. 2020:1–16.
2. Anand A, Aggarwal N, Singh M, Anand AK, Rathi A. Oculodentodigital Dysplasia (ODDD) Presenting as Bilateral Advanced Glaucoma-A Case Report. Int J Anat Radiol Surg. 2018;7(3):01–4.
3. Rassi Gabriel LA, Sachdeva R, Marcotty A, Rockwood EJ, Traboulsi EI. Oculodentodigital dysplasia: New ocular findings and a novel connexin 43 mutation. Archives of Ophthalmology. 2011;129(6):781–4.
4. Musa FU, Ratajczak P, Sahu J, Pentlicky S, Fryer A, Richard G, et al. Ocular manifestations in oculodentodigital dysplasia resulting from a heterozygous missense mutation (L113P) in GJA1 (connexin 43). Eye. 2009;23(3):549–55.
5. Mosaed S, Jacobsen BH, Lin KY. Case report: Imaging and treatment of ophthalmic manifestations in oculodentodigital dysplasia Glaucoma. BMC Ophthalmol. 2016;16(1):1–4.