Unusual association of diseases/symptoms

Iris mammillations in two female siblings with congenital adrenal hyperplasia

Mohammadreza Peyman, Ming Jew Ong, Tajunisah Iqbal, Visvaraja Subrayan

Department of Ophthalmology, UMMC, University of Malaya, Kuala Lumpur, Malaysia

Correspondence to Mohammadreza Peyman, drmpeyman@yahoo.com

Summary

Iris mammillations are dark brown, smooth, mound- or dome-shaped protuberances that are typically found on the anterior iris surface and are presumed to be congenital in origin. This congenital anomaly is usually unilateral and can be hereditary or sporadic. Lisch nodules in neurofibromatosis, tapioca melanoma of the iris, inflammatory iris granulomata and Cogan–Reese syndrome should be considered in the differential diagnosis. In this case report, the authors present a case of a bilateral iris mammillations in two siblings with congenital adrenal hyperplasia (CAH). To our knowledge, this is the first case where bilateral iris mammillations have been found to be associated with a systemic condition. Iris mammillations can be considered as one of the clinical signs in CAH in view of the pathogenesis discussed. Detailed ocular examination in CAH may reveal an increased incidence.

BACKGROUND

To our knowledge, this is the first case where bilateral iris mammillations have been found to be associated with a systemic condition. Iris mammillations can be considered as one of the clinical signs in congenital adrenal hyperplasia (CAH) in view of the pathogenesis discussed. Detailed ocular examination in CAH may reveal an increased incidence.

CASE PRESENTATION

Two female siblings were referred for eye assessment due to long-term usage of hydrocortisone. The elder sister presented to the paediatrics team at 3 years old with progressive enlargement of the clitoris, acne, muscular built, labioscrotal hyperpigmentation and an advanced bone age (7 years old). There was no history of salt-losing crisis or hypoglycaemia. A diagnosis of CAH was made. The younger sister at 15 months old, presented with clitoral enlargement but without other virilising sign. Similar investigations were performed and the diagnosis of CAH was confirmed. Both sisters were started on hydrocortisone upon diagnosis and later 9 α -fludrocortisone was added. Clitoral reduction and vaginal reconstruction surgery was performed for both sisters soon after the diagnosis.

Eye examination of both sisters showed bilateral diffuse iris mammillations (figures 1A,B and 2). There was no other intraocular hyperpigmentation. The eyes were otherwise normal. No iris mammillations were found in both parents.

INVESTIGATIONS

Markedly elevated 17-OH progesterone (353.9 nmol/l (normal value <43 nmol/l)), adrenocorticotrophic hormone (ACTH) (106 pg/ml (normal range=20–80 pg/ml)), renin (707 μ U/ml (normal range=7–76 U/ml)) and testosterone (19.9 nmol/l (normal range=0.21–3 nmol/l)). Chromosomal study was 46XX, confirming her as a female genotypically. Ultrasound abdomen showed normal uterus and ovaries with no ectopic adrenal glands. A diagnosis of CAH was made.

DIFFERENTIAL DIAGNOSIS

Lisch nodules in neurofibromatosis, tapioca melanoma of the iris, inflammatory iris granulomata and Cogan–Reese syndrome.

Figure 1 Anterior segment photo of the younger patient. (A) Right and left eye. (B) Magnified photo of iris shows tiny villiform lesions.

Figure 2 Anterior segment photo of older patients shows bilateral iris mammillations.

DISCUSSION

Iris mammillations are rarely described in the literature. This congenital anomaly is thin, pigmented, circular protuberances, which radiate regularly on iris the surface.^{1 2 3} They are usually unilateral and few bilateral cases have been reported.² The aetiology and clinical implications of iris mammillations remain unclear. They are thought to be congenital and sporadic, while familial cases have been described. The occurrence of iris mammillations is generally sporadic but autosomal recessive and dominant, polygenic or multifactorial inheritance pattern have been reported. Unilateral cases have been found in association with oculodermal melanosis, neurofibromatosis 1, phakomatosis pigmentovascularis IIb, ocular hypertension and intraocular malignancy.¹ Bilateral cases have been reported in bilateral congenital cataract, neurofibromatosis, oculodermal melanocytosis, congenital ptosis, morning glory syndrome, Axenfeld anomaly and Peter's anomaly.² Joondeph and Goldberg⁴ described the first two families in which all children, but no parent, had varying degrees of iris mammillations bilaterally without other oculocutaneous pigmentary changes. No systemic association was noted.

In our case, bilateral iris mammillations were detected in the examination. None of the family members had ocular or systemic disease. Iris mammillations are diagnosed with a biomicroscope and the differential diagnosis involves exclusion of other conditions.

Our case had no signs of ocular melanocytosis while most of reported cases had this background problem.

To our knowledge, this is the first case where bilateral iris mammillations has been found to be associated with a systemic condition. In CAH, ACTH level is elevated due to lack of negative feedback from low cortisol level.³ ACTH has been identified to be one of the key factors in

melanogenesis in cultured human melanocytes.⁵ Since iris mammillations represents aggregates of melanosomes histopathologically, it is plausible that elevated ACTH level in CAH may lead to the formation of iris mammillations.^{2 5}

In conclusion, iris mammillations can be considered as one of the clinical signs in CAH in view of the pathogenesis discussed. Detailed ocular examination in CAH may reveal an increased incidence.

Learning points

- Iris mammillations can be first manifestation of systemic disease and can be considered as one of the clinical signs in CAH
- Bilateral iris mammillations may be in association with CAH
- Bilateral iris mammillations may present in other family members which rise need of screening in other family members both ophthalmic and systemically.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Ragge NK**, Acheson J, Murphree AL. Iris mammillations: significance and associations. *Eye (Lond)* 1996;**10**(Pt 1):86–91.
2. **Ticho BH**, Rosner M, Mets MB, *et al*. Bilateral diffuse iris nodular nevi. Clinical and histopathologic characterization. *Ophthalmology* 1995;**102**:419–25.
3. **Speiser PW**, White PC. Congenital adrenal hyperplasia. *N Engl J Med* 2003;**349**:776–88.
4. **Joondeph BC**, Goldberg MF. Familial iris melanosis – a misnomer? *Br J Ophthalmol* 1989;**73**:289–93.
5. **Hunt G**, Todd C, Kyne S, *et al*. ACTH stimulates melanogenesis in cultured human melanocytes. *J Endocrinol* 1994;**140**:R1–R3.

This pdf has been created automatically from the final edited text and images.

Copyright 2010 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.

BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Peyman M, Ong MJ, Iqbal T, Subrayan V. Iris mammillations in two female siblings with congenital adrenal hyperplasia. *BMJ Case Reports* 2010; 10.1136/bcr.08.2010.3266, date of publication

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow