Sinonasal mucosal melanoma has a high mortality rate, with 5 year survival between 10–50%.[6] Lacrimal sac melanoma has a similar prognosis.[7 8]

This case demonstrates the importance of thorough clinical examination (including nasal endoscopy) and imaging in patients presenting with epiphora, bloody tears, and/or epistaxis. Delay in detection and treatment may be fatal.

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References

1 **Yip CC**, Bartley GB, Haberman TM, *et al*. Involvement of the lacrimal drainage system by leukaemia or lymphoma. *Ophthal Plast Reconstr Surg* 2002;**18**:242–6.
2 **Khan MA**, Dhillon B. Epiphora due to Kaposi's sarcoma of the nasolacrimal duct. *Br J Ophthalmol* 1999;**83**:501–2.
3 **Baredes S**, Ludwin DB, Troublefield YL, *et al*. Adenocarcinoma ex-pleomorphic adenoma of the lacrimal sac and nasolacrimal duct: a case report. *Laryngoscope* 2003;**113**:940–2.
4 **Yazici B**, Setzen G, Meyer DR, *et al*. Giant cell angiofibroma of the nasolacrimal duct. *Ophthal Plast Reconstr Surg* 2001;**17**:202–6.
5 **Spira R**, Mondshine R. Demonstration of nasolacrimal duct carcinoma by computed tomography. *Ophthal Plast Reconstr Surg* 1986;**2**:159–61.
6 **Batsakis JG**, Suarez P. Mucosal melanomas: a review. *Adv Anat Pathol* 2000;**7**:167–80.
7 **Pe'er JJ**, Stefanysyn M, Hidayat AA. Nonepithelial tumours of the lacrimal sac. *Am J Ophthalmol* 1994;**118**:650–8.
8 **Stefanysyn MA**, Hidayat AA, Pe'er JJ, *et al*. Lacrimal sac tumours. *Ophthalmic Plast Reconstr Surg* 1994;**10**:169–84.
9 **Lengyel E**, Gilde K, Remenar E, *et al*. Malignant mucosal melanoma of the head and neck- a review. *Pathol Oncol Res* 2003;**9**:7–12.
10 **Owens JM**, Roberts DB, Myers JN. The role of postoperative adjuvant radiation therapy in the treatment of mucosal melanomas of the head and neck region. *Arch Otolaryngol Head Neck Surg* 2003;**129**:864–8.

Glycosylation type Ic disorder: idiopathic intracranial hypertension and retinal degeneration

We report a young woman with type Ic congenital disorder of glycosylation (CDG) with new clinical features of idiopathic intracranial hypertension, retinal degeneration, and novel mutations of ALG6. Patients with known or suspected CDG should receive a full ophthalmic examination including dilated fundus examination and electroretinography.

CDG is a rare group of autosomal recessive metabolic disorders. The two major subgroups are type I, caused by dysfunction of glycosylated protein assembly, and type II, caused by abnormal processing of glycosylated protein end products after assembly.[1] Patients with type Ic (OMIM #603147) have mental retardation, axial hypotonia, very low factor XI, and seizures; the gene defect in α1,3-glucosyltransferase (human homologue of ALG6;OMIM *604566) encodes an enzyme that catalyses the transfer of the first glucose residue to the lipid linked oligosaccharide precursor for N-linked glycosylation. The reported ophthalmic manifestations of type I CDG are summarised in table I. We report a case of type Ic congenital disorder of glycosylation with new clinical features of idiopathic intracranial hypertension, retinal degeneration and novel mutations of ALG6.

Case report

Our patient, with non-consanguineous parents, was noted at birth to have incomplete digits on her hands and feet. She had episodes of apnoea early in life and the onset of seizures at age 20 months. Delayed physical and developmental milestones were evident early. Levels of follicle stimulating hormone and luteinising hormone were low and a diagnosis of polycystic ovarian disease was made. She underwent esotropia surgery at age 4 years and at 19 years developed thrombosis of the superficial femoral vein. Coagulation factor studies revealed very low factor XI levels. Isoelectric focusing of serum transferrin was suggestive of a congenital disorder of glycosylation. Sequencing of the ALG6 gene showed a novel three base deletion (897–899 delATT) and an intronic splice site mutation (IVS7+2T>G).[2]

The patient was obese without signs of abnormal fat distribution. She blinked to light and no strabismus was identified by corneal light reflex. Further ocular examination was not feasible. On examination under anaesthesia at age 20 years, the anterior segment was normal. Dilated ophthalmoscopy showed bilateral optic nerve pallor with elevation of each nerve, diffuse retinal pigment epithelial granularity most notable in the macula, and attenuated retinal vessels (fig 1).

Electroretinography revealed prolonged implicit times on scotopic and photopic functions. Because of the elevated optic nerve heads, head magnetic resonance imaging was performed and was normal; lumbar puncture revealed an elevated opening pressure of 350 mm H_2O (nl 70–180 mm H_2O), a glucose of 50 mg/dl (nl 50–75 mg/dl), and a protein of 44 mg/dl (nl 15–45 mg/dl) without white blood cells. A diagnosis of idiopathic intracranial hypertension was made.

Comment

Isoelectric focusing of serum transferrin is the most common screening technique for types I and II CDG.[1] Many congenital disorders of glycosylation have been identified based on mutational and enzyme analyses. Type I congenital disorders of glycosylation are caused by reduced functions of the genes for the assembly and processing pathways of N-glycosylation; a decrease in anodal fractions and an increase of disialotransferrin and asialotransferrin are suggestive of the diagnosis.

Ophthalmic features of the most common congenital disorder of glycosylation, type Ia (OMIM #2I2065) include myopia, attenuated retinal vessels, bone spicules, esotropia, and nyctalopia[3]; this disease subtype is caused by a deficiency of phosphomanomutase (OMIM #212065) encoded by phosphomannomutase-2 (PMM2; OMIM *601785) gene. In CDG type Ic, much less common, a homozygous amino acid substitution, A333V substitution, in the gene encoding α1,3-glucosyltransferase is the most common mutation.[4] There is no known biochemical link between CDG and idiopathic intracranial hypertension; the association in our patient may be coincidental. Grunwald and colleagues[5] found strabismus to be present in all eight patients with CDG type Ic; neither idiopathic intracranial hypertension nor retinal abnormalities were reported.

The developmental delay evident in our patient was severe. She possessed simple communication skills limiting her ability to complain of visual changes or symptoms of intracranial hypertention. No specific clinical presentation has been identified for the CDG group of diseases. Failure to thrive, unexplained seizures, hypotonia, and developmental delays are all frequently present.

In conclusion, we report an adult patient with CDG type Ic, confirmed by identification of mutations in the ALG6 gene, and describe new systemic and ocular features including idiopathic intracranial hypertension., optic

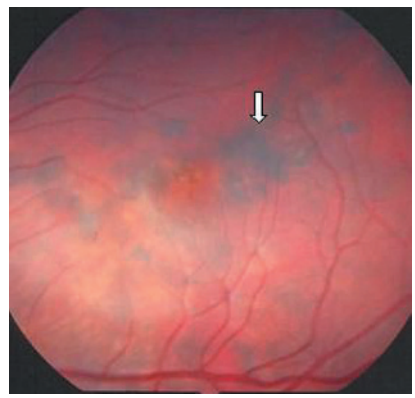

Figure 1 Left fundus showing attenuated vessels with retinal pigment cell granularity of the macula (white arrow).

Table 1 Reported ophthalmic manifestations in type I congenital disorder of glycosylation (CDG)

	CDG Ia	CDG Ib	CDG Ic
Strabismus	+	−	+
Retinopathy	+	−	−
Optic atrophy	+	−	−

atrophy, and a retinal dystrophy with abnormal electroretinography.

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References

1 **Jaeken J**. Congenital disorders of glycosylation (CDG): it's all in it! *J Inherit Metab Dis* 2003;**26**:99–118.
2 **Sun L**, Eklund E, Van Hove J, *et al*. Clinical and molecular characterization of the first adult congenital disorder of glycosylation (CDG) type Ic patient. *Am J Med Genet* (accepted).
3 **Jensen H**, Kjaergaard S, Klie F, *et al*. Ophthalmic manifestations of congenital disorder of glycosylation type 1a. *Ophthal Genet* 2003;**24**:81–8.
4 **Imbach T**, Burda P, Kuhnert P, *et al*. A mutation in the human ortholog of the Saccharomyces cerevisiae ALG6 gene causes carbohydrate-deficient glycoprotein syndrome type-Ic. *Proc Natl Acad Sci USA* 1999;**96**:6982–7.
5 **Grunewald S**, Imbach T, Huijben K, *et al*. Clinical and biochemical characteristics of congenital disorder of glycosylation type Ic, the first recognized endoplasmic reticulum defect in N-glycan synthesis. *Ann Neurol* 2000;**47**:776–81.

Woodhouse Sakati syndrome associated with bilateral keratoconus

Keratoconus is a non-inflammatory degenerative corneal disease characterised by a localised region of stromal thinning spatially associated with a cone-shaped deformation of the surface. It is most commonly an isolated sporadic condition.[1] Recent reports demonstrate genetic mapping to chromosomes 16q, 21q, and 18p, as well as association of HLA-A26, B40, and DR 9.[2 3] Keratoconus has been reported in clinical contexts with 36 other multisystem disorders.[1 2] We describe the first two cases of keratoconus in association with Woodhouse Sakati syndrome.

Case report

Two sisters (aged 14 years and 18 years) presented with history of bilateral progressive loss of vision over 8 years. Progeny of a first degree consanguineous marriage, they were the only members in the family of six siblings with a diagnosis of Woodhouse Sakati syndrome. Both sisters exhibited variable manifestations of the syndrome including hypogonadism, primary amenorrhoea, hypothyroidism, electrocardiographic abnormalities, and dysmorphic features. The elder sister also had a mild degree of mental retardation. None of their siblings or parents had eye complaints but a maternal aunt's daughter had bilateral keratoconus.

Ophthalmic evaluation of the elder sister revealed uncorrected visual acuity (UCVA) of 20/200 in both eyes. Her refraction was −19.0 −8.0×120 in the right eye and −9.0 −3.75×165 in the left eye. Spectacles improved only left eye vision slightly to 20/160. Slit lamp biomicroscopy showed bilateral central corneal protrusion and stromal thinning at the apex (fig 1A). Keratometry was 71.00/63.00 @ 68 in the right eye and 53.00/49.50 @ 135 in the left eye. Hard contact lens fitting failed and surgical intervention was not conducted.

Ophthalmic evaluation of the younger sister revealed UCVA of 20/40 in the right eye and 20/160 in the left eye, which improved to 20/80 with spectacles. Slit lamp biomicroscopy showed similar findings to her sister (fig 1B). Keratometry was 36.6 D/54.1 D @ 170 in the right eye and 49.2 D/56.6 D @ 48 in the left eye. She developed corneal hydrops in the left eye and contact lens fitting failed. Because of central corneal scarring and progressive deterioration of her left eye vision, she underwent penetrating keratoplasty (fig 1C). Fourteen months postoperatively, UCVA was 20/50, improving to 20/30 with pin hole.

Comment

Woodhouse Sakati syndrome (MIM 241080) is an extremely rare genetically determined autosomal recessive disorder. It was first described in two Saudi Arabian families,[4] and later reported in a single Turkish family.[5] Table 1 presents manifestations of the syndrome.[4 5]

We report a new association in our two cases. Such concurrence of early keratoconus and the syndrome raises the possibility of a genetic linkage, although a chance association cannot be excluded.

On one hand, either chromosomal rearrangements such as chromosome 7, 11 translocation or genetically determined syndromes such as this syndrome should be considered in cases where keratoconus is present during childhood.[6] That may explain the early presentation of keratoconus in our cases. An additional factor is that keratoconus tends to be more prevalent and diagnosed at a younger age in Asians than in white people.[3]

On the other hand, familial keratoconus in our cases cannot be excluded because of the presence of keratoconus in a single relative and parental consanguinity. Positive family history has been reported in 6% to 10% of keratoconus cases and is suggested to be caused by autosomal dominant inheritance with incomplete penetrance.[1-3]

To the best of our knowledge, this is the first report of bilateral keratoconus in association with Woodhouse Sakati syndrome. Ophthalmologists and endocrinologists should be aware that patients with this syndrome who complain of poor vision should be suspected of having keratoconus once other more common conditions are ruled out.

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References

1 **Rabinowitz YS**. Keratoconus. *Surv Ophthalmol* 1998;**42**:297–319.
2 **Tyynismaa H**, Sistonen P, Tuupanen S, *et al*. A locus for autosomal dominant keratoconus: linkage to 16q22.3-q23.1 in Finnish families. *Invest Ophthalmol Vis Sci* 2002;**43**:3160–4.

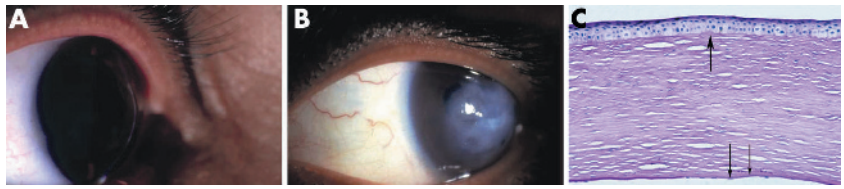

Figure 1 Features of keratoconus are seen. (A) Slit lamp biomicoscopy of the right cornea in the elder patient, showing advanced cone deformation and deep Descemet's membrane scarring. (B) Slit lamp biomicoscopy of the left cornea in the younger patient, showing dense central scarring following hydrops attack. (C) Histopathological section of left corneal button illustrating the fragmentation of Bowman's layer (large arrow) and large break in Descemet's membrane (small arrows) (periodic acid Schiff stain, ×200).

Table 1 Variable manifestations in the nine reported patients with Woodhouse Sakati syndrome

Delayed psychomotor development
Variable degree of mental retardation (very frequent sign)
Alopecia (very frequent sign), spare/absent scalp and eyebrow hair (frequent sign), dysarthria
Dysmorphic features: high forehead, flat occiput, triangular face, prominent nasal root, hypertelorism, and down-slanting palpebral fissures.
Hyper/hypogonadotrophic hypogonadism and late puberty (very frequent sign)
Sensorineural deafness (very frequent sign)
Electrocardiographic abnormalities and insulin dependent diabetes mellitus (very frequent signs)
No ocular manifestations