Case Report

A case of Hallermann-Streiff-François syndrome: an ophthalmological perspective

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Abstract

Hallermann-Streiff-François syndrome is a rare condition which offers multidisciplinary diagnostic and therapeutic challenges. The difficulty in dealing with these cases is compounded by the presentation at a very young age. The ophthalmologist has an important role in helping to establish a diagnosis and to recognize the need for early treatment to minimize amblyopia. This is a short report of the first documented local case which demonstrates many of the characteristic features of this syndrome and who has been followed up over three decades. A brief literature review is also presented.

Keywords

Hallermann syndrome, cataract, microphthalmia, amblyopia, Rubella

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Introduction

Hallermann-Streiff-François syndrome (HSF) is a sporadic congenital condition characterised by multiple dysmorphic features, including ocular abnormalities.[1] Prominent features include hypotrichosis, bird-like facies, brachycephaly with frontal bossing, dental anomalies, and proportionate dwarfism; mental retardation is uncommon.[1-3] From the ophthalmic point of view, microphthalmia is consistent with the generalised small dimensions; the condition has been typically associated with congenital cataract, especially membranous cataract.[2] There are numerous other ocular and systemic associations.

Case report

The medical notes of a 30-year-old female, who is a known case of Hallermann-Streiff-François syndrome, were reviewed. Her gestational history revealed that her mother had received the rubella vaccine at six months gestation.

Immediately after delivery she had multiple cyanotic attacks. Several dysmorphic features were noted early on: brachycephaly, facial hypoplasia, small nose and small nostrils with nasal congestion, low-set ears, and a small chest circumference (bell-shaped chest). Initial extensive investigations were normal, including karyotype, ECG, and echocardiogram.

Other general features that were documented over the following months included: frontal bossing markedly overhanging orbits, sunken eyes and down-slanting palpebral fissures, depressed broad nasal bridge with anteverted nostrils, small ear cartilages, small mouth, protruding tongue, early teeth eruption (noted at 20 days of age), micrognathia, prominent maxillae, long tapering fingers, pectus excavatum, sparse hair, hypotonia, psychomotor retardation, poor feeding and weight gain, with all growth parameters severely below the third centile. A clinical diagnosis of HSF was established at three months of age.

Her first ophthalmic review was requested at

five months. There were roving eye movements without fixation or following, aversion to bright light, microphthalmos, and leucocoria. An examination under anaesthesia was subsequently carried out and bilateral symmetical mature cataracts and unilateral posterior synechiae were also noted. Nystagmus was apparent at six months.

Sequential bilateral lensectomy and anterior vitrectomy were performed at one year of age without significant intra-operative complications. Surgery was delayed due to recurrent respiratory tract infections. Other features that became subsequently apparent were a unilateral peaked pupil from vitreous incarceration, blue sclerae, and pale fundal reflexes due to fairly large areas of macular chorioretinal atrophy. She was fitted with aphakic glasses, initially +18.00DS OU, to which there was good compliance, and subsequently there was a great improvement in the response to her surroundings.

At five years of age she was started on timolol eyedrops unilaterally in view of an intra-ocular pressure (IOP) in the high twenties on the side of vitreous prolapse in the anterior chamber. The ocular media remained clear. At six years, she had a left medial rectus recession and lateral rectus resection for esotropia. Over the years IOP remained stable, perimetry shows asymmetrical stable central scotomas, and she developed unilateral lateral superior forniceal conjunctival herniation. Figure 1 shows her current external features. The most recent appearance of the posterior poles with severe macular scarring is shown in Figure 2. Her latest refraction is: OD +14.00/-1.00x180 (6/20), OS +13.00DS (CFs to 6/120). The left eye is esotropic (Figure 3).

***Figure 1**: Profile View*

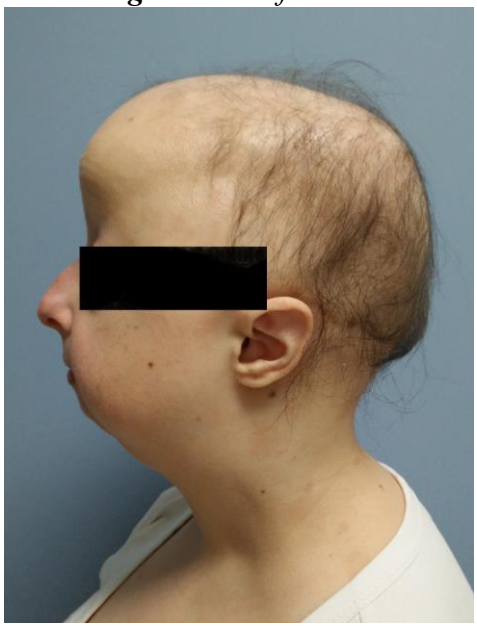


***Figure 2a:** Right fundus*

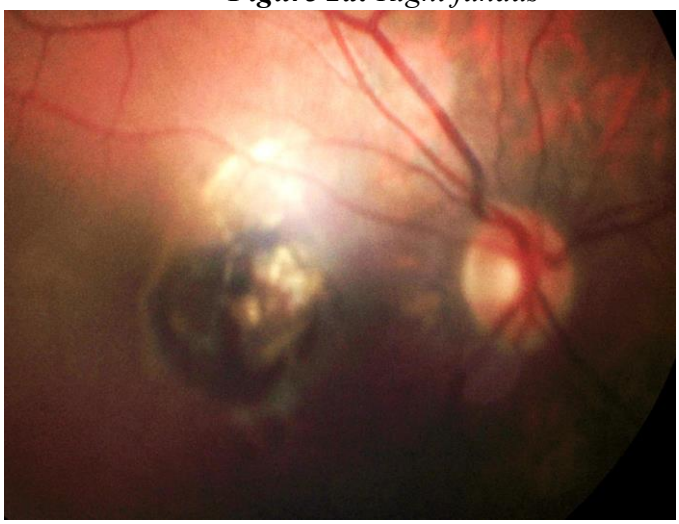
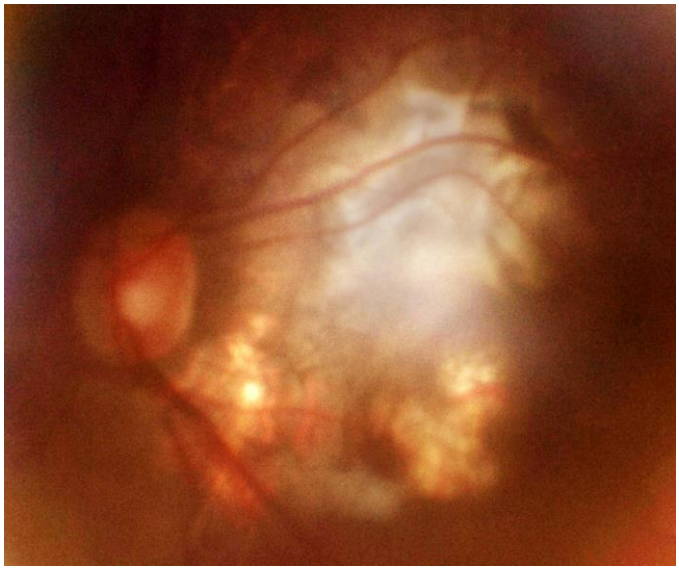


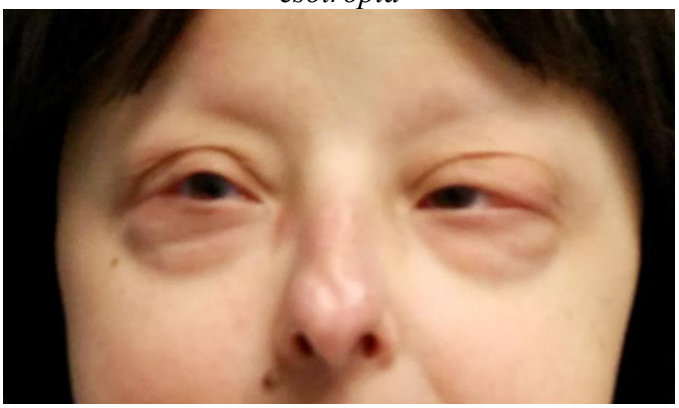
***Figure 2b:** Left fundus*



Discussion

This case describes the long-term follow-up of HSF. To our knowledge, this is the only documented case in Malta. HSF (HSS, oculomandibulodyscephaly with hypotrichosis, François dyscephalic syndrome, oculomandibulofacial syndrome) is rare with unknown prevalence and genetic basis.[2,4] A search on PubMed reveals around 200 reported cases. It is postulated that mutations are sporadic, autosomal dominant with variable expressivity, with occasional chromosomal abnormalities.[2]

***Figure 3**: Small palpebral fissures and left esotropia*



François proposed seven diagnostic criteria: dyscephalia with bird-like face, dental abnormalities, proportionate dwarfism, hypotrichosis, cutaneous atrophy, microphthalmos, and congenital cataracts.[3,5] However, as in this case, there are numerous other features that can occur and not all of the diagnostic criteria have to be present; the eyes may be spared in around 10% of cases.[2] Ophthalmic associations reported are listed in table 1. [2,5-11] The case outlined above also exhibited superior forniceal conjunctival herniation which possibly represents herniation of orbital fat secondary to the microphthalmos.

This patient was exposed to the rubella vaccine during her gestation (end of second trimester). There is a previous report of a case of HSF whose mother was treated for rubella in the third month of pregnancy.[13] Hence, it may be hypothesized that some of the ocular features seen in this case, such as the congenital cataracts and chorioretinal atrophy, may partly be due to the effect of the rubella vaccine.

In our case there was a delay between the diagnosis of HSF and ophthalmic referral, which shows that there could be a lack of awareness of the associated ocular features, and failure to recognize the importance of early treatment of any associated visually-significant cataracts. Cases of HSF are difficult to intubate and are prone to respiratory complications.[2] This is due to the inherent difficulty presented by paediatric cases and particular anatomical features of HSF including glossoptosis and tracheomalacia.[2,5] These issues can delay intervention which further reduces the visual prognosis in congenital cataracts and strabismus.

***Table 1**: List of ophthalmic associations*

Lids	ptosis
	down-sloping palpebral fissures
	entropion
	distichiasis
	enophthalmos
Eye movements	strabismus
	nystagmus
Anterior segment	blue sclera
	microcornea
	sclerocornea
	keratoglobus
	corneal opacities
	Brown-McLean syndrome
	later-onset cataracts
	aniridia/iris atrophy
	angle dysgenesis, peripheral anterior synechiae
	peristent pupillary membrane, posterior synechiae
	retrolental membrane
	buphthalmos
Posterior segment	posterior chorioretinal atrophy
	exudative retinal detachment
	choroidal neovascularisation
	uveal effusion
	cherry red spot in macula
	pale disc
	disc coloboma
	vitreous opacities
	retinal folds

There was also a late increase in IOP, which was successfully controlled medically. The associated perimetric defects due to the optic disc colobomas may mask glaucomatous changes. Glaucoma is a rare feature of HSF.[6] The elevation in intra-ocular pressure can be due to angle anomalies or inflammation. The latter may be

triggered by intra-ocular interventions such as cataract removal, hence post-operative anti-inflammatory treatment and follow-up are very important.[2,6]

In summary, a case of Hallermann-Streiff-François syndrome with long follow-up has been presented, with particular attention to the ophthalmic findings. These cases are diagnosed clinically, with bilateral microphthalmos and cataracts being primary initial clues. These cases require multidisciplinary treatment and multiple procedures. Early management of associated cataracts can limit the subsequent amblyopia, with patients generally being left aphakic. New issues can emerge over time and regular re-assessment is warranted.

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