

GAPO syndrome: a case associated with bilateral interstitial keratitis and hypothyroidism

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List of main features

Growth retardation
Alopecia
Pseudoanodontia
Interstitial keratitis
Hypothyroidism
Geriatric facies
Absent eyebrows and eyelashes
Telecanthus
Depressed nasal bridge
Anteverted wide nostrils
Long prominent philtrum
High-arched palate
Jaw recession
Rough thickened fingernails
Umbilical hernia
Undescended testicle

Introduction

Growth retardation, alopecia, pseudoanodontia, and optic atrophy (GAPO) syndrome is the acronymic designation for a complex of growth retardation, alopecia, pseudoanodontia, and optic atrophy. It is a very rare autosomal recessive disease, with approximately 30 cases reported worldwide (Andersen and Pindborg, 1947; Goloni-Bertollo *et al.*, 2008). Here we report a case with the novel findings of severe bilateral interstitial keratitis and hypothyroidism.

Case report

A 9-year-old boy presented to us during an ORBIS (the Flying Eye Hospital) program to Harbin City in north-eastern China because of bilateral, red painful eyes and blindness. He was the only child born to nonconsanguineous parents who were otherwise healthy. No other family member was similarly affected.

The patient was born at full term after an uneventful pregnancy by Cesarean section. At birth, his weight was 2400 g, length 46 cm, and head circumference 33.7 cm. His Apgar score was 9/10 at 1 and 5 min. Growth

retardation was first noticed when the patient was 6-months-old. He had recurrent episodes of bilateral eyelid swelling, photophobia, chronic tearing, and eye redness from 1 to 3 years of age. These eye symptoms resolved gradually after age 3 years when growth also improved.

At age 7 years, he lost all his hair, eyebrows, and eyelashes within a 6-month period. Bilateral red painful eye, eyelid swelling, and progressive severe vision loss ensued after 3–4 months. Review of symptoms revealed delayed teething, delayed psychomotor development, delayed speech development, and impaired sweating.

Examination under anesthesia showed an underdeveloped boy whose height (112 cm) and weight (16 kg) were both well below the fifth percentile for his age. His head circumference (49.5 cm) was small, reaching only the 50th percentile of a normal 3-year-old boy. He had total alopecia, as well as a high, convex, bossed forehead with prominent scalp veins (Fig. 1). An unusual old-appearing facies was noted, with absent eyebrows, telecanthus, depressed nasal bridge, anteverted wide nostrils, and long prominent philtrum. Intraoral examination revealed only two erupted permanent upper central incisors, extremely worn and irregularly erupted primary teeth, and high-arched palate. Jaw recession, rough thickened fingernails, a small umbilical hernia, and an undescended left testicle were also noted.

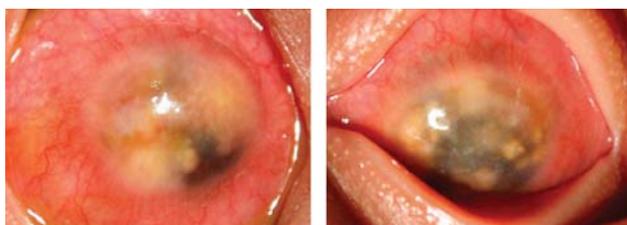
Ophthalmic examination showed complete absence of upper and lower lid eyelashes. Severe ocular inflammation, including ciliary injection, conjunctival hyperemia, and tarsal papillae were present. The corneal epithelium was intact, but bilateral, multiple, confluent, yellow nodules were present in the corneal stroma (Fig. 2). The anterior chamber was shallow bilaterally, with high intraocular pressure (37 mmHg in the right eye, and 24 mmHg in the left eye). Examination of the posterior segment, including optic nerve evaluation, was not possible because of severe keratopathy.

Fig. 1



Frontal and lateral view of patient. Note bossed forehead, telecanthus, depressed nasal bridge, anteverted wide nostrils, and long prominent philtrum.

Fig. 2

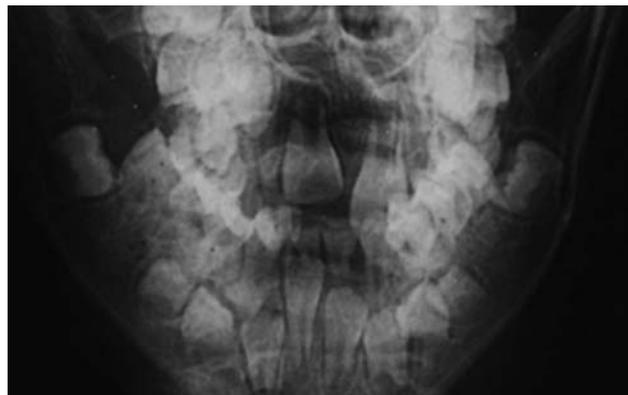


Severe ocular inflammation and bilateral corneal opacification from multiple, confluent, yellow nodules in the corneal stroma.

Conjunctival biopsy showed an abundance of inflammatory cells including lymphocytes, which were confined in the epithelium and superficial dermis. Blood vessels in the dermis were dilated and hyperemic. There was no abnormal accumulation of collagen, amyloid, or hyalin material. Corneal biopsy was not performed out of concern for lack of adequate follow-up care.

Brain computed tomograph at the age of 6 months and MRI at the age of 8 years were normal. At the age of 8 years, his bone maturation was equivalent to that of a 5-year-old boy. Dental radiographs (Fig. 3) showed unerupted permanent teeth except for two permanent upper central incisors. Thyroid function tests were normal at age 5 years; repeated testing at the age of 8 years, however, revealed decreased free thyroxin (0.78 ng/dl; normal range: 1.0–4.0 ng/dl), as well as positive thyroid microsomal and thyroglobulin antibodies. Karyotype was normal (46, XY). Blood counts, serum total cholesterol, and low-density lipoprotein cholesterol level, as well as urinalysis were normal. Metabolic workup including amino acids, organic acids, and acylcarnitine were normal when tested at age 7 years. Recent testing for syphilis (RPR), TORCH (ELISA), tuberculosis (PPD and chest X-ray) and sarcoidosis (chest X-ray) were all negative.

Fig. 3



Dental radiograph showing failure of eruption of permanent teeth except for two upper central incisors.

Discussion

Growth retardation, alopecia, and pseudoanodontia were present in all previously documented patients with GAPO syndrome. Optic atrophy, however, is the most inconsistent feature. In addition to optic atrophy, a number of ophthalmic findings have also been associated with GAPO syndrome. They include ptosis, nystagmus, strabismus, myopia, megalocornea, bilateral keratoconus, band keratopathy, unilateral corneal abscess, glaucoma (including congenital), hypermature cataract, retinoschisis, retinal vein dilation, and papilledema.

Our patient presented with severe bilateral interstitial keratitis and ocular inflammation. Three cases of GAPO with severe unilateral corneal opacity secondary to end-stage congenital glaucoma have been reported (Sayli and Gul, 1993; Mullaney *et al.*, 1997; Ilker *et al.*, 1999). The lack of buphthalmos and the absence of any sign of early visual impairment before the acute onset of red painful eyes at age 7 years, argued against end-stage congenital glaucoma as the cause of keratopathy in our patient. The elevated intraocular pressure we observed is most likely secondary to shallow anterior chambers as a result of the severe bilateral ocular inflammation and interstitial keratitis. The differential diagnoses of interstitial keratitis include congenital syphilis, severe phlyctenules from tuberculosis, sarcoidosis, and herpes simplex necrotizing keratitis, but testing for these conditions was negative in our patient. The presence of bilateral idiopathic interstitial keratitis in our case expands the spectrum of ocular manifestations seen in GAPO syndrome.

Another feature in our patient not previously reported in GAPO syndrome was hypothyroidism. Interestingly, infants and children with hypothyroidism can present with symptoms that resemble those of GAPO syndrome, including growth and mental retardation, sparse hair, large fontanel, puffy face, swollen eyelids, delayed tooth eruption, and umbilical hernia. Because thyroid status

was not specified in many earlier reports of GAPO syndrome, whether hypothyroidism plays any causative role in GAPO syndrome remains to be elucidated. We suggest that thyroid hormone deficiency should be closely monitored and treated in these patients.

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