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Unusual Protrusion of Conjunctiva in Two Neonates with Harlequin Ichthyosis

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Key Words
Ichthyosis · Chemosis · Conjunctival protrusion · Ectropion · Ultrasound echography

Abstract
Background: We present two patients who developed severe protrusion of the conjunctiva and chemosis secondary to Harlequin ichthyosis (HI).
Case Reports: Case 1 was a male infant diagnosed with HI who had parchment-like appearance and conjunctival protrusion with severe chemosis. Case 2 was a female infant on whom HI had been suspected before birth through ultrasonography. She showed thickened skin over the entire body and conjunctival protrusion with severe chemosis. For both cases, a vitamin A derivative was applied and the hyperkeratotic layer was peeled off every day. Great care was taken to sterilize and moisten the ocular surface. The conjunctival protrusion gradually improved and other systemic conditions were successfully treated. HI is a rare condition, but affected infants are surviving longer than previously and hence guidelines for ocular management are now required.
Conclusions: Gentle and patient debridement of the hyperkeratotic skin and moisturizing were important in treating the unusual conjunctival protrusion.

Introduction

Harlequin ichthyosis (HI, HIM 242500) is a severe disorder of keratinization caused by mutations in the *ABCA12* gene. The mutations lead to defective lipid transport which significantly affects the normal development and function of the skin [1]. HI is a severe, lethal form of keratinizing disorder [1], and there are less than 100 cases reported. The

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characteristic clinical features include: thick and plate-like scales over the entire body, ectropion, eclabium, and flattened ears [1]. We present two cases of HI with severe protrusion of the conjunctiva and chemosis secondary to HI. The protruded conjunctiva gradually improved without remnants and functioned normally following treatment of the palpebral hyperkeratosis.

Case Reports

Case 1

Case 1 was the second child of healthy non-consanguineous Japanese parents who was born at 37 weeks and 6 days of pregnancy by vaginal delivery. The male infant weighed 3,126 g with an APGAR score of 7/9. The infant was referred to the Ophthalmology Department for bilateral exophthalmus (**fig. 1**a). He had typical characteristics of HI, e.g. parchment-like appearance of the skin, deformities of the ears and mouth, ectropion, and conjunctival protrusion associated with severe chemosis (fig. 1a–c). Topical etretinate, a vitamin A derivative, was applied, and the hyperkeratotic layer was manually peeled off under aseptic conditions every day from the initial examination to early infancy: until approximately 90 days post partum. Other systemic conditions such as deformities of the ears and mouth were successfully treated with decrease of the abnormal skin turgor and the infant developed well.

Ophthalmologically, great care was taken to sterilize and moisten the ocular surface with antibacterial agent eye drops, hyaluronic acid, and eye ointment. The conjunctival protrusion and ectropion gradually improved until about 2 months after birth (fig. 1d, e). Finally, chemosis disappeared and the cornea could be kept clear.

Case 2

Case 2 was the second child of healthy Japanese parents. HI was suspected through the findings of ultrasonography (**fig. 2**a, b), and a Caesarean section was performed at 38 weeks and 0 days of pregnancy. Her birth weight was 2,566 g and the APGAR score was 8. The infant had the typical features of HI, e.g. thickened skin over the entire body with a number of fissures and rashes, face without mimicry, nasal hypoplasia, fixed open mouth, and conjunctival protrusion associated with severe chemosis (fig. 2c). The eyelids were completely everted with occlusion of the eyes bilaterally.

Intensive skin care was applied, especially moisturizing and lubrication with daily sterile dressings with liquid paraffin. The other systemic conditions were normal, and she developed well with systemic etretinate. The hyperkeratotic layer of the skin surrounding both eyes was hygienically peeled off very carefully and the surface was sterilized with an antibacterial eye drop every day. The protruded conjunctivae were protected by 0.3% ofloxacin ointment, and there was a gradual improvement accompanied by a decrease in the tension of the periocular skin (fig. 2d, e). The improvement enabled us to examine the anterior segment and fundus, and all findings were within normal limits. With time, the ectropion became more severe. The ocular surface was kept disinfected and moist with ointments and eye drops: 0.5% levofloxacin hydrate and 0.1% purified sodium hyaluronate 5 times a day. Thereafter, the ectropion did not worsen with further reduction of the tension on the periocular skin (fig. 2f).

Discussion

To date, the diagnosis of HI can be made by skin biopsy before 24 weeks of gestation but it is limited to families with a previously affected child [2]. Ultrasonographic diagnosis may be useful in some cases, but it is generally difficult because of the late development of the phenotype at mid-gestation and the rarity of the disease [3].

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HI is an inherited autosomal recessive trait, and the dysfunction of the epidermis begins prenatally. It has also been called: alligator baby, keratosis diffusa fetalis, malignant keratosis, and other descriptive names. It is associated with premature birth and is frequently fatal within the first days or weeks of life due to neonatal complications of fluid loss and sepsis. Recently, intensive care and skin treatment have improved the survival rate, although the mortality is still high and the exact life expectancy is unknown [4]. Only a limited number of cases have been reported on the ocular complications of hyperkeratosis such as ectropion [2, 3, 5, 6]. But with the improvement of treatment and longer life expectancy, it is expected that more and more cases of HI will require treatment or consultation with ophthalmologists [5–7].

Our two cases showed severe protrusion of the conjunctiva with chemosis and systemic hyperkeratosis but otherwise the infants were fit and well: musculoskeletal and visceral status as well as the eye ball itself were normal. For case 2, the prenatal diagnosis enabled a planned delivery and intensive local and systemic cares which contributed substantially to preventing sepsis. In our two cases, gentle and patient debridement of the hyperkeratotic skin, prevention against infection, and moisturizing were important in helping the unusual conjunctival protrusion and eyelid eversion from worsening.

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Disclosure Statement

No author has a proprietary interest in any material or method mentioned.

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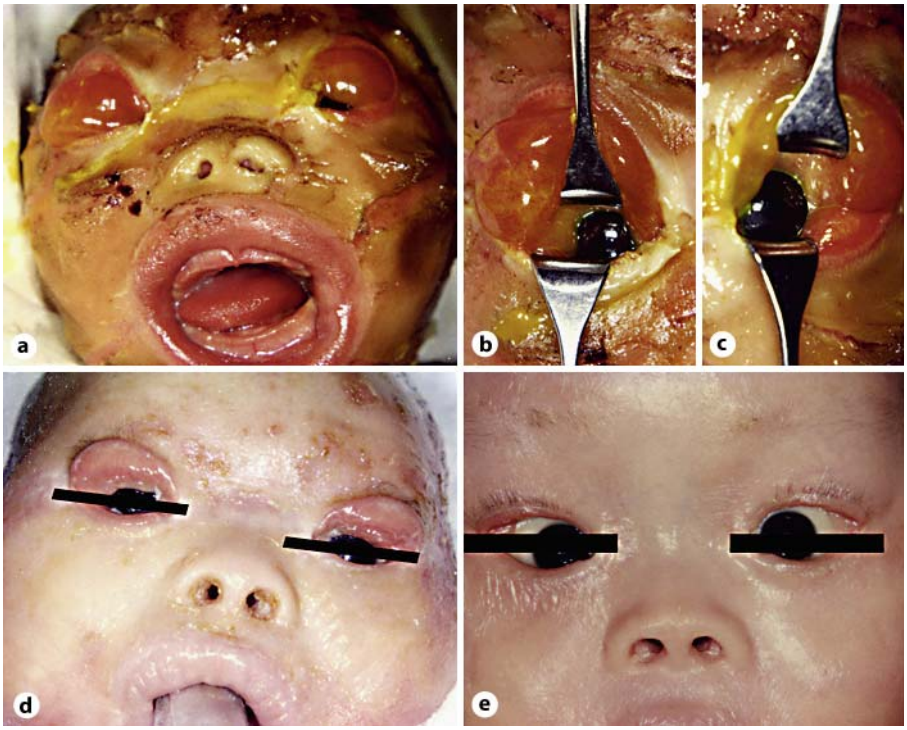

Fig. 1. a External photograph of case 1 with HI on the first day of life. The skin is parchment-like, deformities of the ears and mouth, ectropion, and conjunctival protrusion associated with severe chemosis can be seen. The protruding conjunctiva prevented a thorough examination of the eye. **b** External photograph of the right eye of case 1 on the first day of life. The protruding mucosal tissue can be seen to be the superior bulbar conjunctiva when the eyelid was retracted. Prominent protrusion of the superior bulbar conjunctiva is observed. **c** External photograph of the left eye of case 1 on the first day of life. Prominent protrusion of the superior bulbar conjunctiva is observed. The cornea is clear. **d** External photograph of the right eye of case 1 at 2 months after birth. Chemosis of the protruded conjunctivae are greatly improved leaving the ectropion more prominent. **e** External photograph of the right eye of case 1 at 7 months after birth. The protruded conjunctivae and ectropion are improved with a decrease in tension of the periocular skin.

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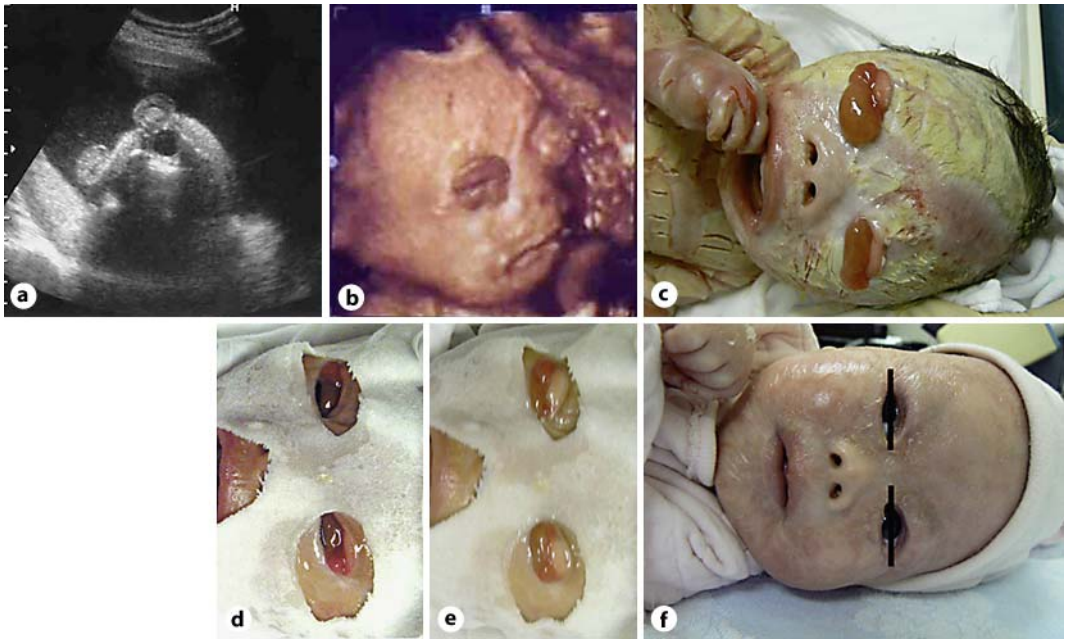

Fig. 2. a Two-dimensional ultrasound echography in the 30th week of pregnancy in case 2. The sonogram displays a flat profile with exophthalmos-like structures. **b** Ultrasound examination in the 30th week of pregnancy in case 2. The 3-dimensional picture reconstructed from the 2-dimensional pictures shows abnormal structures on the eyes. **c** External photograph of case 2 with HI immediately after birth. The skin over the whole body is thickened with a number of fissures and rashes, a face without mimicry, nasal hypoplasia, and a fixed and open mouth. Both eyes display extreme conjunctival protrusion associated with severe chemosis preventing the observation on the eyes. **d** External photograph of case 2 with HI immediately after birth. The protruding conjunctivae are improved with a decrease in the tension of the periocular skin. The facial skin was kept moist by a sterile gauze with holes for eyes and nose. **e** External photograph of both eyes of case 2 with HI 19 days after birth. The conjunctival protrusion was prominent when the infant held her breath. The protruding mucosal tissue was identified as superior bulbar conjunctiva because the palpebral conjunctiva can be seen. **f** External photograph of both eyes of case 2 with HI 3 months after birth. The ectropion has greatly improved with a decrease in the tension of the periocular skin.

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