Case report: Ankyloblepharon-ectodermal dysplasia-cleft lip/palate (AEC)-like syndrome in a Holstein calf

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SUMMARY

Hay-Wells syndrome is a rare form of ectodermal dysplasia initially described by Hay and Wells in 1976. This autosomal dominant disorder leads to various congenital abnormalities of the skin, hair, teeth, nails and sweat glands. In the case report, a 20 days old Holstein calf exhibited a permanent bilateral congenital ankyloblepharon, skin erosions and oligodontia at birth which are considered as cardinal signs of this syndrome by most authors. Surgery was performed in order to reconstruct the palpebral fissure of both eyes. This manuscript reports the first case of an ankyloblepharon ectodermal dysplasia-cleft lip/palate (AEC)-like syndrome in a Holstein calf.

Keywords: Ankyloblepharon, Hay-Wells syndrome, calf, surgery.

Introduction

Hay-Wells syndrome, also known as AEC syndrome (ankyloblepharon ectodermal dysplasia-cleft syndrome), is a rare genetic disorder in humans, initially described by Hay and Wells [9] in 1976 in seven individuals from 4 families in whom multiple and complex malformations were associated with a pattern of autosomal dominant inheritance of varying degrees of penetrance. Sporadic cases have, however, also been described [16]. Later studies showed that this pathology is the result of a mutation in the p63 gene, a homologue of the p53 tumour suppressor gene (TP53) [14].

Most authors consider the presence of ankyloblepharon filiforme adnatum (tissue strands joining the upper and lower eyelid margins), cleft lip and/or palate and findings consistent with ectodermal dysplasia to constitute essential criteria for a diagnosis of Hay-Wells syndrome. Common ectodermal defects include alopecia, onychodystrophy, oligodontia and hypohidrosis [12].

Persistent congenital ankyloblepharon have been described in puppies [13] and foals [7]. To the author knowledge no description has been published of bilateral congenital ankyloblepharon in calves. This paper reports a case of ankyloblepharon ectodermal dysplasia-cleft lip/palate (AEC)-like syndrome in a Holstein calf.

Case Report

A 20-day-old Holstein female calf was presented for evaluation of persistent fusion of the upper and lower eyelids of both eyes since birth (figure 1). The history revealed that the calf had previously suffered from upper respiratory tract infection for two weeks and the referring veterinarian has prescribed medical therapy with systemic antibiotics (procaine penicillin G 1 500 000 units, sodium penicillin G 500 000 units, streptomycin sulphate 2.5g, Streptoveticilline, Eczacıbaşı, Turkey) at daily intramuscular injection for 2 weeks.

On physical examination, the calf was found to be underweight. Dermatological evaluation revealed sparse, fair hair with areas of alopecia in the nasolabial and temporal planum (figure 2) and crusting overall in the body. The absence of the mandibular second and third incisors (oligodontia) (figure 3) was noted during the examination of oral cavity. Evaluation of the extremities revealed punctuated carpal and tarsal keratoderma and erosions. Laboratory tests including complete blood count, electrolytes and liver, kidney function tests showed no abnormalities.
Surgical procedure

The calf was admitted to the University of Adnan Menderes, Faculty of Veterinary Medicine just after the initial examination. Surgery was performed to reconstruct the palpebral fissure of both eyes.

General anaesthesia was induced and maintained with an intravenous detomidine-ketamine-midazolam combination with an intravenous combined injection of detomidine (Demosedan; Orion Corporation Farmos, Finland, 100 pg/kg b.w.), ketamine (Alfamyne; Egevet, Turkey, 10 mg/kg b.w.) and midazolame (Demizolam; Dem, Turkey, 0.5 mg/kg) [10]. The patient was placed in dorsal recumbency; the head was turned laterally to expose the right or the left eye, and the ocular surface was cleaned with irrigating eyewash solution, followed by a dilute solution of 0.05% chlorhexidine gluconate. The skin covering the right globe was incised approximately 20 mm in length, and the underlying palpebral conjunctiva was sutured over the skin edge in a continuous simple suture pattern with 4-0 Dexon (Davis & Geck, Montreal, QC, Canada) on both newly formed upper and lower eyelids of both eyes (figure 4). Ocular examination revealed a normal movement of the third eyelid on both side. Both eyes had normal pupillary light and menace responses. No abnormalities were observed on ophthalmoscopy of the cornea and anterior chamber. Although a Schirmer tear test [18] or a phenol red thread test [8] was not performed on both eyes, adequate tear production was estimated because of the healthy glistening appearance of the both cornea.

Postoperative medication was limited to the use of a combination antibiotic-corticosteroid ophthalmic solution (Polymyxin B sulphate 6. 000 units, Neomycin sulphate 3. 500 units, Dexamethasone 1.0 mg; Maxitrol, Alcon Canada Inc, Mississauga, ON, Canada) applied to both eyes 3 times daily for 2 weeks. One month after the surgery, the palpebral fissures appeared healed and stable in length. No suture material was observed on eyelid margins.

Discussion

Hay-Wells or AEC syndrome is a rare, autosomal dominant disease in humans. Ankyloblepharon filiforme adnatum, ectodermal dysplasia and cleft lip and/or palate are considered as cardinal signs of this syndrome by most authors [12]. All these features were present in the animal case reported here.

Ankyloblepharon consists of partial or complete fusion of the upper and lower eyelid margins, and is often sporadic.
Normally, the eyelids remain fused until the fifth week of pregnancy in cows at which time they separate. Therefore, anomalies that occur between the 7th and 15th weeks of pregnancy may result in palpebral abnormalities [15]. Ankyloblepharon may also be present in trisomy 18 and CHAND (Curly Hair- Ankyloblepharon-Nail Dystrophy) syndrome, and is associated with cardiac defects, hydrocephaly, imperforate anus and glaucoma in humans [2, 3]; therefore, its presence should always serve as an alert to the possibility of another important concomitant disorder [19]. In calves, eyelid anomalies caused by congenital or acquired aetiologies may also occur [8] but to the author knowledge, there is no previous report about the existence of the persistent congenital ankyloblepharon in calves.

Ectodermal dysplasia refers to a group of diseases in which defects occur in the development of the hair, teeth, nails, sweat glands and other structures originating from the ectoderm [17, 20]. Patients with Hay-Wells syndrome may present various degrees of alopecia, sparse, fair hair, onychodystrophies, palmoplantar hyperkeratosis, skin pigmentation disorder [5], hypohidrosis, oligodontia, dental malformations and auricular abnormalities [3, 5, 11, 12]. In consistent with these findings, the calves in the present case had with various degrees of alopecia, sparse, fair hair and oligodontia.

In humans, the oligodontia in ankyloblepharon-ectodermal dysplasia-cleft lip/palate (AEC) syndrome was investigated in detail [6]. A higher incidence of missing permanent maxillary incisors and canines was founded and attributed to by the alveolar cleft defect. The relatively high incidence of maxillary hypoplasia is not normally seen in other ectodermal dysplasia syndromes and may be attributed to the facial growth problems related to the clefts. In the present case, examination of oral cavity has evidenced the absence of the mandibular second and third incisors.

This syndrome is caused by a mutation in the p63 gene, a homologue of the p53 tumour suppressor gene (TP53) [14, 16] which plays a role in the process of stratifying the epidermal epithelium, regulating the proliferative capacity of the basal keratinocytes. The evidence that an alteration in that gene may result in other pathologies such as the EEC (ectodermal dysplasia-cleft lip/palate syndrome) and Rapp-Hodgkin syndromes [1, 4] suggests highly pleomorphic effects of mutations in the p63 gene, the abnormalities associated with Hay-Wells syndrome originating specifically from the substitution of amino acids in the SAM (sterile alpha motif) domain [3, 14]. In the reported case, the genetic analysis was not performed, because of financial problem for the owner.

As a conclusion, the reported case is the first description of a bilateral congenital ankyloblepharon ectodermal dysplasia-cleft lip/palate (AEC)-like syndrome in calves.

References