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Punctal agenesis: Embryology, presentation, management modalities and outcomes

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ABSTRACT

Punctal agenesis is defined as the absence of the punctum occurring secondary to a failure of embryogenesis. This review synthesizes existing data on the embryology, anatomy, clinical presentation, symptomatology, management options and treatment outcomes of punctal agenesis. A foundational knowledge of the underlying embryologic and anatomical abnormalities is fundamental to understanding its clinical presentation and assists in choosing an appropriate management strategy. Existing outcomes data is generally favorable and suggests management with a step-wise approach can alleviate symptoms in patients across a spectrum of disease.

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1. Embryology and anatomy

First documented in 1846 by Blanchet, punctal agenesis is defined as absence of the lacrimal punctum secondary to a failure of embryogenesis (Ali, 2017a). In normal lacrimal outflow development, the nasolacrimal duct arises from canalization of surface ectoderm that begins as a solid cord of epithelium (Chambers et al., 2012). The process begins along the cleft between the lateral nasal and maxillary processes where a fold of thickened ectoderm extends downward into the mesoderm forming the naso-optic fissure. This fold subsequently separates to form a solid rod of epithelium representing the rudimentary lacrimal system (Duke-Elder, 1963).

Ectodermal outbudding progresses in a lateral direction terminating at the puncta. Canalization begins at 12 weeks of gestation with the canaliculi becoming patent during the fourth month (Hurwitz, 1996). The puncta open up onto an elevation of tissue at the lid margins called the papilla just before lid separation occurs at 7 months (Low et al., 2002). Duke-Elder described the canalization process as segmental, with disintegration of inner cells leading to isolated cavities followed by the formation of a continuous central lumen (Duke-Elder, 1963). In a 1981 serial anatomical examination of embryos and fetuses, Sevel disproved this theory and demonstrated that the canalization process occurs simultaneously throughout the length of the nasolacrimal apparatus, with the exception of the puncta and distal end of the nasolacrimal duct, which remain occluded for longer. Though the epithelium of the lacrimal canaliculi makes contact with the conjunctiva in embryos of 28–30 mm crown-rump length (9–10 weeks gestation), the puncta remain occluded by a combination of conjunctiva and canalicular epithelium until they become patent at 7-months gestation (Sevel, 1981).

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Disruption at any point in this developmental process can lead to punctal dysgenesis (Ali, 2015a). Punctal agenesis is less common than atresia, which refers to the presence of a thin membrane covering the punctum in the presence of well-formed canaliculi. Punctal dysgenesis with membranes has also been termed "incomplete punctal canalization," and can be further subdivided into cases with external or internal membranes. The external variety typically covers the puncta's external surface, giving the appearance of punctal agenesis, whereas the internal variety typically consists of a translucent membrane just at the entry of the puncta accompanied by blurred punctal margins. The architecture and shape of the pars lacrimalis tend to remain intact in these cases, as compared to punctal agenesis, where it is lost (Ali et al., 2013).

In contrast to the well-formed underlying canalicular systems present in cases of incomplete punctal canalization, punctal agenesis is variably accompanied by the presence of canaliculi. Lyons et al. (1993) reported absence of identifiable canalicular tissue in 86% of patients with bilateral punctal atresia. Modern imaging modalities such as OCT along with endoscopic studies have allowed better characterization of both the normal anatomy of the lacrimal punctal region as well as anatomical findings underlying lacrimal dysgenesis. For example, a case report of a patient with clinical unilateral punctal agenesis showed complete absence of punctum and canaliculus as well as a dilated lacrimal sac with thinned walls on endoscopy. Histopathology revealed crypt-like folds of thin columnar epithelium with goblet cells and apical snouts projecting towards the lumen, which together with the clinical features was suggestive of incomplete embryonic development (Ali et al., 2017b). OCT can help differentiate between lacrimal anomalies that may appear identical on external examination. For example, in cases of the external variety of incomplete punctal canalization that mimic punctal agenesis, Fourier-domain optical coherence tomography can be used to image the punctum and vertical canaliculus. OCT of incomplete punctal canalization is likely to reveal a hyper-reflective membrane with a distinct, anatomically normal underlying canalicular lumen, whereas punctal agenesis is more likely to reveal canalicular absence or pathology (Singh et al., 2017).

2. Clinical presentation

Congenital punctal agenesis is rare. In 1931, Goar identified a total of 23 cases of punctal and canalicular agenesis or atresia described in the literature, noting just one case in Mooren's series of 108,416 examinations (Goar, 1931). Lyons et al. (1993) observed the diagnosis of punctal and canalicular agenesis in 4% of new patients presenting to the lacrimal clinic at Moorfields Eye Hospital between the years of 1981 and 1990, which is a statistic consistent with reports from other institutions. However, the true incidence of punctal agenesis is difficult to estimate given that many patients are asymptomatic and thus may not present for evaluation (Yuen et al., 2004).

The condition is most commonly sporadic, although autosomal dominant inheritance with variable expression and penetrance has been reported (Ali, 2017a). It may be found in isolation or with associated ocular and systemic features. Associated ocular abnormalities include eyelid tags, absence of the caruncle, distichiasis, divergent strabismus, blepharitis, canaliculops, dacryocystocele and lacrimal fistula (Lyons et al., 1993; Han and Shin, 2013; Ali et al., 2015b). Associated systemic abnormalities that have been reported include choanal atresia, cleft lip and palate, developmental delay, anemia, hydrocephalus, low birth weight, epilepsy, agenesis of the parotid glands and ducts, preauricular fistula, branchial fistula and deafness due to otosclerosis (Lyons et al., 1993). A 2017 review (Ali and Paulsen, 2017c) identified 42 syndromes associated with congenital lacrimal drainage abnormalities. Examples of syndromes associated with punctal agenesis include Hay-Wells, Levy-Hollister, Rapp-Hodgkin, Robinow, Brachmann-de-Lange, ectodactyly-ectodermal dysplasia-clefting syndrome, and congenital rubella (Ali, 2015a; Rodini et al., 1990; Aguirre Vila-Coro et al., 1988a, b; Gupta et al., 2017). However, these syndromes may also present with other varieties of lacrimal anomalies. For example, ectodactyly-ectodermal dysplasia-clefting syndrome may also present with canalicular atresia, ectopic lacrimal opening, congenital lacrimal fistula, nasolacrimal duct stenosis, congenital nasolacrimal duct obstruction, membranous occlusion of the puncta, or even absence of the nasolacrimal ducts (Ali and Paulsen, 2017c).

Punctal agenesis encompasses a wide assortment of anatomical variations. Yuen et al. report that proximal lacrimal system dysgenesis involves a single punctum and/or canaliculus more commonly than both upper and lower structures, which corroborates existing data (Yuen et al., 2004; Welham and Hughes, 1985). In a review of 57 punctal agenesis patients who presented to the lacrimal clinic at Moorfields Eye Hospital, 20 patients had all 4 puncta missing, 13 had 1 punctum missing, 11 had 1 punctum missing from each eye, 7 had 2 puncta missing from the same eye, and 6 had 3 puncta missing (Lyons et al., 1993).

The clinical presentation may be variable based on the degree of lacrimal system agenesis. In a retrospective review of 50 patients with lacrimal outflow dysgenesis, epiphora was the most common presenting symptom; other presenting symptoms included discharge, conjunctivitis, dacryocystitis and mucocele. Discharge was more common in single proximal system involvement than in cases where both upper and lower systems were involved. In 36% of the patients in this study there was a positive family history (Yuen et al., 2004). Lyons et al. (1993) noted that in eyes with a single punctum, the most commonly reported symptom was discharge and occasionally redness and pain in the context of dacryocystitis. In eyes with no puncta, symptoms were limited mainly to occasional watering. Symptoms were noted at birth or soon after in all but four patients who noted symptoms at ages 5, 7, 11, and 25 years. A positive family history was noted in 13 (26%) of patients. Other ocular abnormalities were noted in 13 of the 50 patients in the study (Lyons et al., 1993).

In cases of punctal agenesis, slit lamp biomicroscopy reveals absence of the punctal papilla and transilluminant membrane, as well as absence of any dimple in the expected area of the punctum (Fig. 1a and 1b). Occasionally, eyelashes are found medial to the expected punctal location (Ali, 2015a). It is important to distinguish punctal agenesis from secondary causes of punctal stenosis, which include infection, trauma, inflammatory processes, neoplasms and topical medications such as miotics, antivirals, and intraocular pressure lowering agents (Lyons et al., 1993). Elucidation of these risk factors for secondary punctal stenosis is accomplished with a thorough history and review of medications, with the addition of OCT imaging or dacryocystography, if needed.

3. Management and outcomes

The management of punctal agenesis is dependent on the patient's symptoms and the extent of the obstruction. In addition to taking a thorough history and performing a careful slit lamp examination of the puncta, it is essential to define the extent of the anatomical abnormality both pre-operatively and at the time of intervention. If there is an ipsilateral patent punctum, the system may be preliminarily explored through diagnostic fluorescein dye tests and simple probing and irrigation (Lyons et al., 1993). Additionally, a non-barbed pigtail probe can be gently passed through a patent canaliculus to see if there is a communication with the

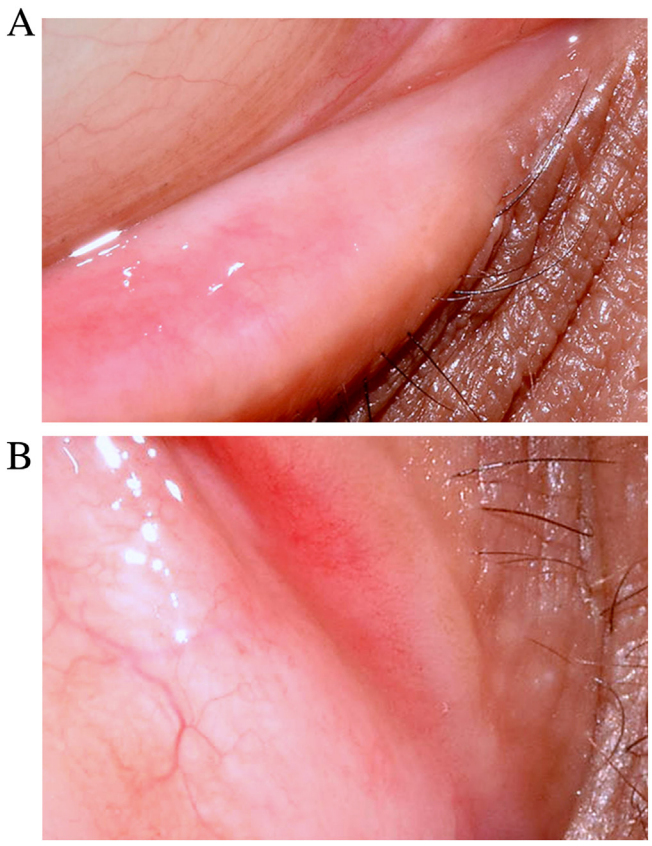

Fig. 1. (A) and (B): External photographs of the medial aspect of eyelids showing complete absence of puncta and punctal papillae surrounded by otherwise normal eyelid margin architecture, lashes and conjunctiva. (Photos courtesy of Mohammad Javed Ali, MD, PhD, FRCS).

opposing, occluded system (Cahill and Burns, 1991). Some advocate for pre-operative dacryocystography to better understand the extent of agenesis in complex cases. (Lyons et al., 1993; Yuen et al., 2004; Cahill and Burns, 1991; Boerner et al., 1995). With the addition of OCT imaging, the extent of the agenesis can be characterized in a non-invasive way. Using a combination of these modalities to characterize the anatomy, repair can be better directed toward the specific defects.

If a patient is asymptomatic, with no epiphora or infection, there is no indication for intervention, and observation may be considered. When a normal canalicular system is present in an eyelid with punctal atresia, it may be possible to exteriorize the canaliculus to the conjunctival surface directly (Ong et al., 2005). In this procedure, membrane lysis is performed using a punctal dilator, thus creating a direct passage to the underlying intact canalicular system (Yuen et al., 2004). Those with concurrent proximal canalicular obstructions may be managed with canalicular marsupialization. This procedure involves opening the conjunctiva in the punctal region followed by careful blunt dissection to identify the blind end of the canaliculus. The canaliculus is then opened with a punctal dilator and the soft tissue surrounding the now open canaliculus is trimmed to allow for creation of a neo-punctum. Injection of methylene blue into an opposing patent canaliculus or in cases with no patent puncta, transcutaneously into the lacrimal sac directly, has been suggested as an adjunct technique to identify the appropriate lid margin incision site (Katowitz, 1974; LaPiana, 1972; Cahill and Burns, 1991). Jones proposed retrograde probing as a means of improving localization in this technique. He described opening the anterior margin of the lacrimal sac in order to pass a 0 or 1 probe through the canaliculus to the punctal area, thus allowing the punctum or canaliculus to be opened along the conjunctival edge of the lid margin in a more controlled fashion than might otherwise occur in an unguided exploratory procedure (Jones, 1962).

Historically, several authors have described this exploratory cut-down and marsupialization technique without tube placement, but reported outcomes have been mixed (Beard, 1968; Putterman, 1973, 1979; LaPiana, 1972; Cahill and Burns, 1991; Rumelt, 2003). Beard (1968), who initially described the procedure, noted mostly failure in his own experience, finding the lumen only once. Putterman (1973) reported a 77% success rate with this technique, although his series included only one case of congenital punctal agenesis with the others being cases of secondary punctal stenosis from acquired causes. More modern literature advocates for punctoplasty coupled with intubation in cases where pre-operative assessment has confirmed the availability of sufficient canalicular tissue to do so (Yuen et al., 2004).

In cases of punctal agenesis accompanied by significant canalicular stenosis, canalicular trephination may also be considered to recanalize the canaliculus with placement of a lacrimal stent. The recommended duration of stent presence is quite variable, with some recommending 8–12 weeks and others 6–12 months (Zadeng et al., 2014). Canalicular microtrephination with stenting was first described by Sisler and Allarakhia (1990), who reported a success rate of 83.3% at 6–9 months of follow-up. Khoubian et al. (2006) reported a success rate of 55%, defined as at least partial relief of symptoms, in patients with proximal obstructions who were managed with trephination and silicone stent placement. Zadeng et al. (2014) advocate for the use of Mini-Monoka stents over standard silicone tubing, citing a success rate of almost 92% in their study. The purported advantages are that the Mini-Monoka is monocanalicular and self-retaining with a nonirritant collarette; they also note that the Mini-Monoka is more rigid, which facilitates passage through the small trephine-created opening in a less traumatic manner. Hussain et al. (2012) similarly note a success rate of greater than 80% in patients with punctal and/or canalicular stenosis who were managed with Mini-Monoka stent placement.

Given that the presence of a normal underlying canalicular system in punctal agenesis is uncommon, it may be necessary to consider more invasive therapy in patients with insufficient intact proximal canalicular tissue (Lyons et al., 1993; Yuen et al., 2004). Conjunctivodacryocystorhinostomy (CDCR) with Jones tube placement is the standard treatment in cases with irreparable canalicular obstruction (Sekhar et al., 1991). Wearne et al. (1999) describe an alternative technique in which a dacryocystorhinostomy with retrograde canaliculostomy and intubation is performed. In this not often employed technique, a standard external dacryocytorhinostomy approach is taken, but upon entering the lacrimal sac a blunt-tipped 0-gauge probe is inserted retrograde into the common internal punctum (common canaliculus) and passed in the direction of the proximal canalicular system. As the tip of the probe approaches the lid margin, a scalpel is used to cut down onto the probe tip and a canaliculostomy is performed followed by silicone intubation. Of the 123 lacrimal systems with proximal or midcanalicular obstruction that underwent DCR with retrograde intubation of canaliculi in this study, 73% were considered successful in that the eye was either not tearing or only mildly symptomatic after surgery. There were 22 cases of punctal agenesis included in the study and of these, 3 (14%) were considered failures. Overall, postoperative failure occurred in a higher proportion of cases with midcanalicular as compared to proximal canalicular obstruction.

Overall, the strategy for management of symptomatic punctal agenesis is strongly tied to the underlying anatomy of each case. There is a range of available treatment modalities that vary in invasiveness and are appropriate for different levels of dysgenesis. A foundational knowledge of the embryologic and anatomical abnormalities underlying punctal agenesis is thus fundamental

in choosing an appropriate management strategy. A stepwise approach from least invasive to most with consideration of the extent of dysgenesis leads to the highest rate of success. Outcomes data for symptomatic punctal agenesis managed in this way is generally favorable, and suggests that patients across the spectrum of disease can have satisfactory and lasting amelioration of symptoms.

Ethical approval

Not applicable.

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