Structural and Vascular Features in Cavitary Congenital Optic Disc Anomaly Associated with Metaphyseal Acroscyphodysplasia

Journal:	*European Journal of Ophthalmology*
Manuscript ID	EJO-20-2025
Manuscript Type:	Case Report
Date Submitted by the Author:	15-Oct-2020
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Keywords:	Genetic Disease / Congenital Abnormalities < PEDIATRIC OPHTHALMOLOGY, Neuro Imaging < NEURO OPHTHALMOLOGY, Craniofacial malformations < PEDIATRIC OPHTHALMOLOGY, Neuro-Ophthalmic Disease < PEDIATRIC OPHTHALMOLOGY, Anatomy/Biochemistry/Physiology < RETINA
Abstract:	Purpose: To evaluate, using optical coherence tomography angiography (OCTA), the vascular network of the papillary region in presence of a cavitary congenital optic disc anomaly in a young patient with recessive autosomal metaphyseal acroscyphodysplasia. Methods: Observational case report. Results: A 17-year-old man, with diagnosis of metaphyseal acroscyphodysplasia was referred to Eye Clinic for fundus examination and multimodal imaging for retinal epithelium hypertrophy in the right eye. Clinical examination showed hyperthelorism and telecanthus. Fundus examination showed an optic disc coloboma in the right eye. Wide field en-face Optical Coherence Tomography (OCT) showed a hyporeflective area corresponding to the right optic disc coloboma. At OCTA examination, the whole papillary region revealed a general rarefaction of the vascular network, while the ganglion cell complex's and retinal fiber layers' parameters were normal in the right eye affected. Conclusion: The presence of a congenital defect linked to embryological abnormalities during the development process could pave the way for a wider understanding of the pathogenesis of metaphyseal acroscyphodisplasia by increasingly framing it as a systemic disease.

Structural and Vascular Features in Cavitary Congenital Optic Disc Anomaly Associated with Metaphyseal Acroscyphodysplasia

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Abstract

Purpose: To evaluate, using optical coherence tomography angiography (OCTA), the vascular network of the papillary region in presence of a cavitary congenital optic disc anomaly in a young patient with recessive autosomal metaphyseal acroscyphodysplasia.

Methods: Observational case report.

Results: A 17-year-old man, with diagnosis of metaphyseal acroscyphodysplasia was referred to Eye Clinic for fundus examination and multimodal imaging for retinal epithelium hypertrophy in the right eye. Clinical examination showed hyperthelorism and telecanthus. Fundus examination showed an optic disc coloboma in the right eye. Wide field en-face Optical Coherence Tomography (OCT) showed a hyporeflective area corresponding to the right optic disc coloboma. At OCTA examination, the whole papillary region revealed a general rarefaction of the vascular network, while the ganglion cell complex's and retinal fiber layers' parameters were normal in the right eye affected.

Conclusion: The presence of a congenital defect linked to embryological abnormalities during the development process could pave the way for a wider understanding of the pathogenesis of metaphyseal acroscyphodisplasia by increasingly framing it as a systemic disease.

Keywords: Acroscyphodysplasia; optic disc coloboma; cavitary congenital optic disc anomalies

Introduction

Metaphyseal Acroscyphodysplasia is a rare form of recessive autosomal metaphysical dysplasia (prevalence <1/1000000), first described in 1966 [1]. Also known as Bellini syndrome, it is characterized by a specific radiological sign: the cone shape of the upper femoral and tibial epiphyses that fit on the enlarged cup-shaped metaphyses [1,2]. The form of cone is observed in the epiphyses of phalanxes and metacarpus of the upper limbs. Metaphyseal acroscyphodysplasia is typically associated with short stature and micromelia [3]. In rare cases it has been associated with intellectual disability and alopecia [3]. In addition, Bellini syndrome is associated with craniofacial abnormalities most frequently characterized by hypertelorism, telecanthus, wide nasal bridge and prominent forehead. However, to the best of our knowledge, eye involvement had never been described in Bellini syndrome patients in scientific literature. Herein, we report a case of metaphyseal acroscyphodysplasia in a young boy with cavitary congenital optic disc anomalies.

Case Report

A 17-year-old man, with genetically confirmed (PDE4D variant) diagnosis of metaphyseal acroscyphodysplasia was referred to Eye Clinic for fundus examination and multimodal imaging for retinal epithelium hypertrophy in the right eye. No perinatal problems were present. There was no history of congenital abnormalities in his family. Clinical examination showed hyperthelorism and telecanthus. Best-corrected visual acuity (BCVA) was 20/20 in both eyes. Slit-lamp examination of the anterior segment was unremarkable in both eyes. Intraocular pressure was 12 mmHg in the right eye and 11 mmHg in the left eye. Dilated fundus examination and multicolor imaging showed an optic disc coloboma in the right eye (Fig. 1, A-D). The posterior pole showed normal profile and macular thickness in both eyes. Wide field en-face Optical Coherence Tomography (OCT) showed a hyporeflective area corresponding to the right optic disc coloboma (Fig. 1 -D). Ganglion Cell Complex (GCC) and retinal nerve fiber layer (RNFL) parameters were normal in both eyes

(respectively Average GCC: 111 µm in the right eye and 106 µm in the left eye; Average RNFL: 111 µm in the right eye and 107 µm in the left eye). OCT angiography (OCT-A) showed a rarefaction of radial peripapillary microvascular network corresponding to the optic disc coloboma in the right eye (Fig. 1 C). No structural and vascular anomalies were present at the left optic disc (Fig. 1, E-H).

Discussion

Bellini syndrome was first described in 1966 by Bellini and Bardare as a distinctive form of metaphyseal dysplasia [1]. In 1991 the term metaphyseal acroscyphodysplasia was first used to describe this unusual form of metaphyseal chondrodysplasia [3]. The term acroscyphodysplasia (‘acro’ = limb; ‘scypho’ = cup) describes the characteristic radiological features: cup-shaped metaphyseal deformities of the upper and lower limbs bones embedded in cone-shaped deformed epiphyses and central epiphyseometaphyseal fusion [4]. Advanced bone age is frequently found whereas other systemic defects such as mental delay and alopecia are less frequent. Short stature was always described in the previously reported cases [3,4]. In addition, Bellini syndrome is associated with craniofacial abnormalities most frequently characterized by hypertelorism, telecanthus, wide nasal bridge and prominent forehead. To the best of our knowledge, this is the first case of metaphyseal acroscyphodysplasia with eye involvement. Cavitary congenital optic disc anomaly was present in this patient in the form of optic disc coloboma in the right eye. Optic disc coloboma is the result of a defect in fetal closure fissure, may be associated with multiple congenital anomalies due to an alteration in the development of the fetus during the sixth week of gestation [5,6]. Primary structural dysgenesis involving the proximal embryonic fissure is at the basis of optic disc coloboma. Moreover, optic disc coloboma could be linked to an alteration of the differentiation process of astrocytes during the development process [7]. The study of the retinal and peripapillary circulation, performed by OCTA, showed rarefaction of the vascular texture of the

peripapillary radial plexus [8]. On the other hand, the absence of structural damage on the OCT examination, with normal GCC and RNFL parameters justifies the patient's excellent visual acuity. It should also be emphasized that the presence of impairment of the retinal peripapillary vascular complex could be linked to an involvement of the cerebral vessels as the retinal circulation is part of the cerebral circulation. In scientific literature some non-specific magnetic resonance imaging (MRI) abnormalities such as thin corpus callosum, delayed myelinisation and cortical atrophy, have already been described in metaphyseal acroscyphodysplasia [9]. Therefore, in the future it would be particularly interesting to be able to investigate this pathology, already known for intellectual disability, by means of MRI to evaluate any impairment of the cerebral circulation.

In conclusion, in this case coloboma is the result of a defect in fetal closure fissure but reduced vessel density of the peripapillary radial plexus and the presence of mental retardation could broaden our knowledge on the pathogenesis of metaphyseal acroscyphodysplasia, that could have both bone and vascular involvement.

Acknowledgment

None

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Consent for publication

A written consent was obtained by both parents of the young boy.

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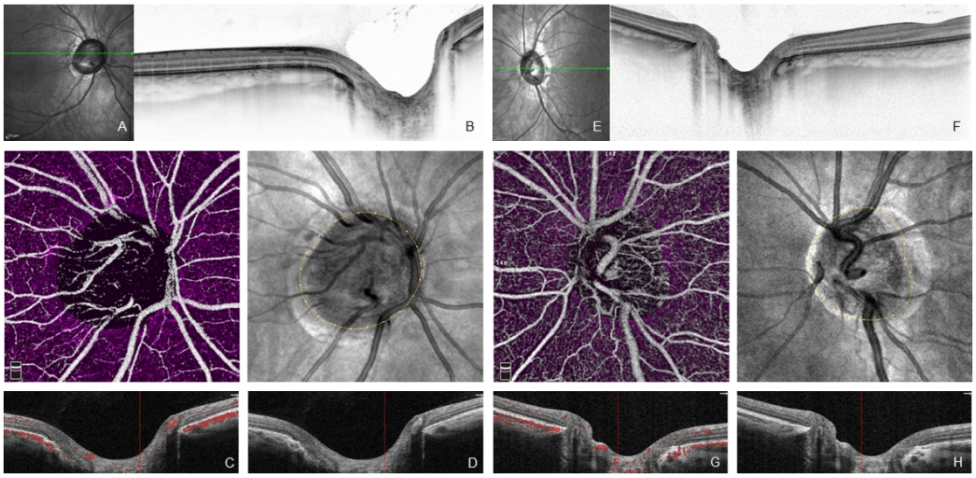
Figure legend

Figure 1. A 17-year-old metaphyseal acroscyphodysplasia patient with optic disc coloboma in the right eye (A-D). Structural spectral domain optical coherence tomography (SD-OCT) revealed an optic disc excavation (A-B). At OCT angiography (OCT-A), a rarefaction and a reduction of the radial peripapillary microvascular network was observed (C). Wide field en-face OCT showed a hyporeflective area corresponding to an optic disc coloboma (D).

Unaffected left eye of the same patient (E-H). SD-OCT (E-F), OCT-A (G) and wide field en-face OCT (H) revealed a normal optic disc and a normal radial peripapillary network.



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