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Case report

Anterior Segment-Optical Coherence Tomography features in Blau syndrome

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ABSTRACT

Blau syndrome (BS) is a rare granulomatous auto-inflammatory disease, characterized by the classic clinical triad of joints, skin and ocular involvements. Ocular manifestation usually consists in a bilateral insidious chronic anterior uveitis with a potential evolution to panuveitis. We describe the case of two siblings, an 8-years old female and a 5-years old male, with a diagnosis of BS, evaluated by Anterior Segment-Optical Coherence Tomography (AS-OCT). In the female patient, slit-lamp examination revealed bilateral anterior granulomatous uveitis and inflammatory sequelae. AS-OCT revealed high intensity reflective layers in the anterior cornea, hyperreflective dots both in the aqueous humor and in the posterior corneal surface. In the male, no signs of inflammation were detected both on slit-lamp examination and AS-OCT scans.

AS-OCT is a valuable, non-invasive tool that could improve the diagnosis of ocular involvement, better characterize and follow-up corneal alterations and anterior segment features in pediatric patients with BS.

1. Introduction

Blau syndrome (BS) is a rare granulomatous auto-inflammatory disease associated with an autosomal dominant mutation in the nucleotide-binding oligomerization domain-containing protein two (NOD2) [1]. Clinically, BS starts in early childhood and is characterized by the classic triad of granulomatous polyarthritis, dermatitis and uveitis. Arthritis, present in nearly all patients with BS, is a chronic, symmetrical and mostly painless polyarthritis with prevalent affection of peripheral joints [2]. Skin involvement usually represents the first symptom and it is characterized by non-confluent erythematous or pigment micro-papules on trunk and extremities [1]. Ocular involvement usually consists in a bilateral insidious chronic uveitis with a potential evolution to panuveitis [3]. Band keratopathy, cataract, glaucoma, macular edema could represent potential inflammatory complications [3]. Systemic therapy with steroids represents one of the main lines of treatment. Nevertheless, in case of steroids non-responsive patients or poor response, the use of biological drugs, such as Antitumour necrosis factor agents, MTX and interleukin-1 inhibitors, is a strategy described [4].

We describe the case of two siblings with diagnosis of BS, analyzing in detail corneal structural features with anterior segment-optical coherence tomography (AS-OCT).

Signed informed consent for patient's information and images to be published was provided by the parents.

2. Case 1

A 3-year-old female was referred to the Pediatric Unit for recent onset of lameness. The mother referred a diagnosis of rheumatoid arthritis and a history of visual loss due to several events of panuveitis at the age of 18. Clinical examination of the patient showed swelling, tenderness and limited range of movement of elbows, wrists, fingers' joints and knees. Treatment with naproxen and methotrexate (MTX) was started without significant improvement. Etanercept was added with clinical resolution. At the age of 4 years, the patient presented a papulo-

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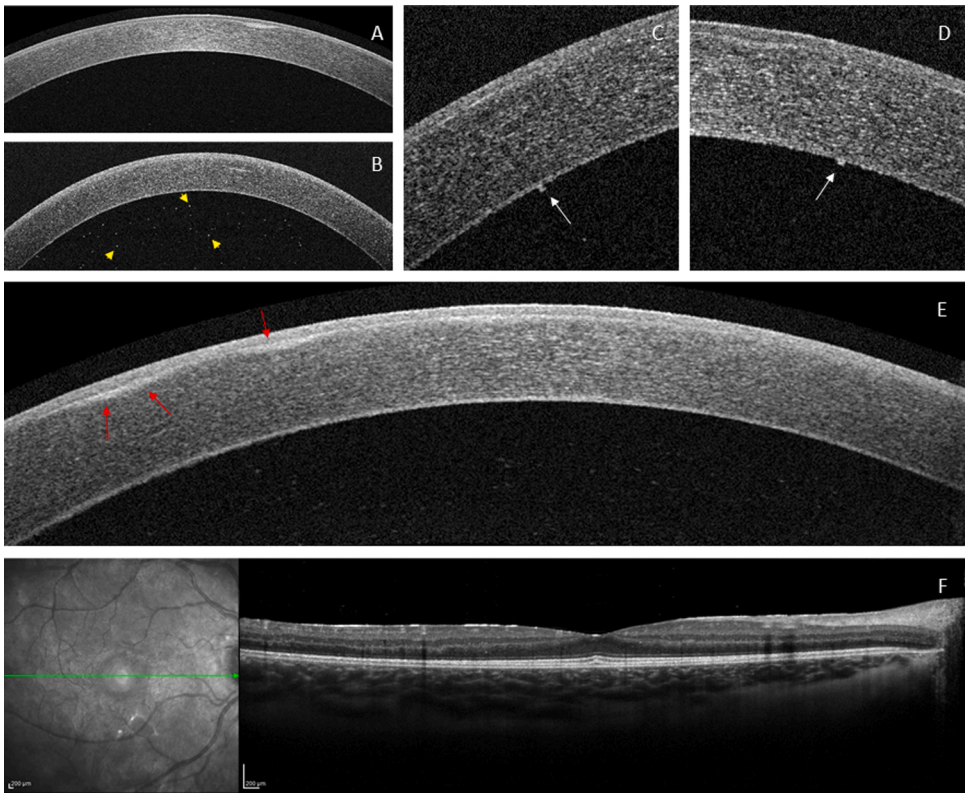

Fig. 1. Anterior segment-optical coherence tomography (AS-OCT) and spectral domain (SD)-OCT of 8-year-old female affected by Blau Syndrome (A—F): Hyperreflective dots (yellow arrows) in the aqueous are thought to represent anterior chamber (AC) cells, more evident in the left eye (B) than right one (A). Enlarged image of the AS-OCT scans show hyperreflective dots located in the posterior corneal surface that represent the keratic precipitates (white arrows) (C, D). AS-OCT of band keratopathy (red arrows) reveal a high intensity reflective layer in the anterior cornea (E). SD-OCT displays an epiretinal membrane in the right eye with no tractional effect (F).

erythematous rash on the trunk; skin biopsy was performed, showing sarcoid-like granulomatous features. In the suspect of BS, NOD2 genetic analysis was performed, revealing the pathogenetic c.1000C > T transition in exon 4. (p.R334W). BS was diagnosed. Treatment with MTX and Etanercept continued. Three years later, the patient complained of visual loss and was referred to Eye Clinic for ophthalmology evaluation.

Her best-corrected visual acuity (BCVA) was 20/200 in both eyes. Slit-lamp examination revealed bilateral anterior granulomatous uveitis and initial cortico-nuclear opacity of the lens in left eye. Intraocular pressure was normal and fundus examination was unremarkable in both eyes. The on-going anterior uveitis was treated with topical corticosteroids. Etanercept was interrupted and treatment with Adalimumab started. After 6-month follow-up, her BCVA was 20/30 in right eye and 20/200 in left eye. Slit-lamp examination revealed persisting uveitis and inflammatory sequelae such as band keratopathy, iris posterior synechiae, lens pigmented depositions in both eyes, dense cortico-nuclear cataract in left eye and partial lens opacity in the right eye. No increase of intraocular pressure was detected. AS-OCT, with the Optovue

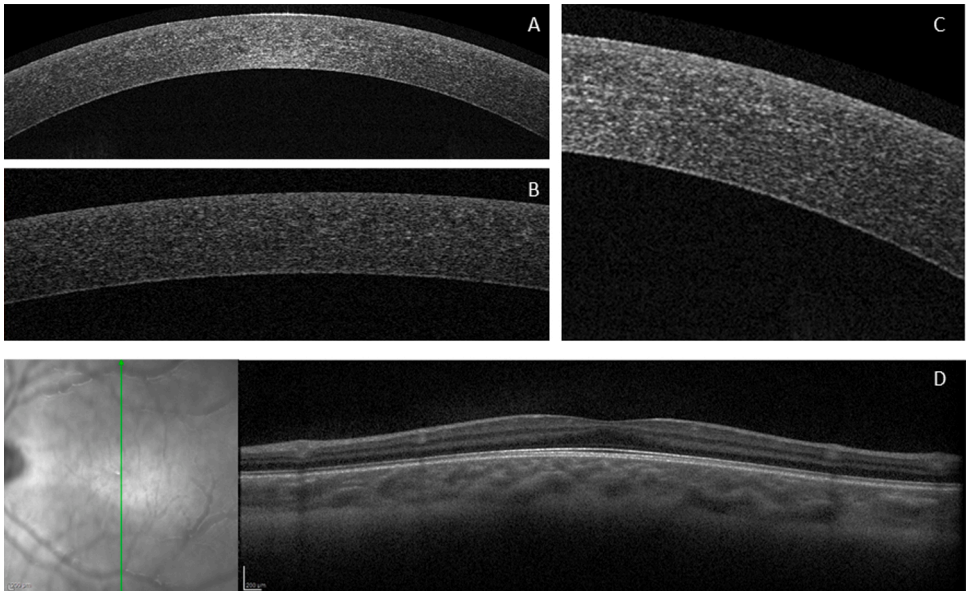

Fig. 2. Anterior segment-optical coherence tomography (AS-OCT) and spectral domain (SD)-OCT of 5-year-old male affected by Blau Syndrome (A-D): AS-OCT show no signs of inflammation in the anterior chamber (AC) in right eye (A) and in left eye (B). Enlarged image of the AS-OCT scans reveal no structural damage of corneal layers (C). SD-OCT displays normal retinal findings (D).

System (software RTVue XR version 2017.1.0.151, Optovue Inc., Fremont, CA, USA A) was performed. In both eyes, hyperreflective dots in the aqueous humor were found and thought to represent anterior chamber (AC) cells (Fig. 1A, B). Enlarged image of the AS-OCT scans showed the presence of various Keratic precipitates (KPs), that appear like hyperreflective dots located in the posterior corneal surface (Fig. 1C, D). Furthermore, like the slit-lamp examination revealed, the AS-OCT images showed the presence of high intensity reflective layers in the anterior cornea with variable degrees of posterior shadowing, that represent the signs of the band keratopathy (Fig. 1E). Fundus examination showed a mild semitranslucent aspect in the macular region of the right eye. Spectral domain-optical coherence tomography (SD-OCT - Spectralis HRA + OCT; Heidelberg Engineering, 21 Heidelberg, Germany) showed a hyper-reflective line on the inner surface of the retina without tractional effects, confirming the presence of a hint of epiretinal membrane in right eye. (Fig. 1F) Central Macular Thickness was within normal limits. Fundus examination and SD-OCT were unexplored due to the lenticular opacity in the left eye.

3. Case 2

The brother was referred to the Pediatric Rheumatology Unit at the age of 3, for limited range of movement and morning stiffness. Clinical examination revealed a widespread maculopapular rash, swelling of radiocarpal, metacarpal and metatarsal joints, with reduced movements dynamism. Genetic mutation analysis was performed and revealed the same mutation found in patient's sister and mother (p.R334W). BCVA was not appropriately evaluable for young age and poor compliance. Ocular examination showed no signs of inflammation in both eyes. Fundus evaluation was unremarkable. Treatment with Naproxen and MTX was prescribed. Due to persistence of articular symptoms and the appearance of eczematous lesions on the face, therapy with Adalimumab was started. One year later, no signs of uveitis were recorded. Intraocular pressure and fundus examination were normal in both eyes. AS-OCT showed no signs of inflammation or structural damage of corneal layers (Fig. 2A–C). No retinal alterations were present at SD-OCT (Fig. 2D).

4. Discussion

Ocular involvement represents the greatest feature for morbidity and functional impairment in BS [3]. AS-OCT allowed us to better analyze and measure both healthy and pathological features of the anterior segment that were not accurately observable with a slit-lamp microscope due to a limited magnification. To the best of our knowledge this is the first case of BS, described with AS-OCT, associated with signs of band keratopathy and with keratic precipitates, whereas OCT of posterior segment has been previously used to describe retinal involvement [5]. Presence of high intensity reflective layers in the anterior cornea with variable degrees of posterior shadowing, detected at AS-OCT, represents the signs of the patient's band keratopathy. Furthermore, KPs, that appear in our case as hyperreflective dots located in the posterior corneal surface, are corneal endothelial deposits that are frequently observed in association with anterior uveitis but cannot be used to estimate inflammatory activity [6]. Moreover, the hyperreflective dots in the aqueous humor are thought to represent AC cells [7]. The AC cells number is strongly associated with the severity of inflammation in uveitis [6]. Therefore, the presence of these pathological features, identified with AS-OCT, could justify the worsening of visual acuity in case 1. In this case, activity of uveitis persisted, although maximal local treatment and systemic therapy with steroids. Therefore, immune modulating drugs were prescribed [4]. No therapy guidelines have been defined for BS, because of its rarity and heterogeneity in severity of manifestations.

In conclusion, AS-OCT could represent a non-invasive tool, particularly useful in pediatric age, for diagnosis and follow-up of BS patients in order to evaluate with greater detail the pathological features in corneal layers and any abnormalities present in the anterior segment, which may correlate with worsening of visual acuity.

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Declaration of Competing Interest

The authors report no declarations of interest.

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