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Case Report

Late-Onset Panuveitis in a Chinese Girl with Sporadic Blau Syndrome: A Case Report

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Keywords

Blau syndrome · Late-onset eye manifestations · Panuveitis · Case report

Abstract

Introduction: Blau syndrome (BS) is a rare autoimmune disease. We report here an atypical case of BS. ***Case Presentation:*** We present a case of late-onset eye manifestations in a Chinese girl of 18 years old with sporadic BS, presenting with panuveitis. We performed comprehensive ocular examinations including fluorescein fundus angiography and indocyanine green angiography for her. The oral hormone plus local anti-inflammatory eye drops have well controlled the inflammation of her eyes. ***Conclusion:*** Our case highlights the necessity of systemic medical history inquiry for every eye discomfort.

Introduction

Blau syndrome (BS) is a rare, autosomal dominant, and granulomatous autoimmune disease first described by Blau in 1985 [1, 2]. This syndrome is caused by mutation of the nucleotide-binding oligomerization domain containing 2 (NOD2)/caspase activation and recruitment domain member 15 (CARD15) gene [3] and classically presents as a triad of granulomatous dermatitis, arthritis, and uveitis [4]. It typically begins at the age of 3–4 years. Initial symptoms are cutaneous and articular, while eye symptoms usually start later, between 7 and 12 years of age. Ophthalmic manifestations are characterized bilateral uveitis that

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begins as granulomatous iridocyclitis and posterior uveitis, resulting in uveitis [3]. Except disseminated granulomas particularly in the liver and kidneys, eye involvement is usually the most relevant morbidity of BS. Here, we report a case of an 18-year-old girl with only mild ocular inflammation who has been initially diagnosed with suspected BS for 15 years until her eye symptoms appeared at the age of 18 years.

Case Presentation

An 18-year-old Chinese girl presented at our hospital with eye pain, photophobia, and blurred vision. Ocular preliminary examinations in our department revealed best-corrected visual acuity of 20/20 in the patient's both eyes. Anterior segment findings only included mild conjunctival hyperemia, mutton-fat keratic precipitates, and slight aqueous flare in the anterior chamber in her both eyes (Fig.1), while fundus examinations revealed only optic disc hyperemia in both eyes and focal punctate retinal infiltrations in the inferior peripheral retina of the left eye (Fig. 2). After a detailed medical history inquiry, we knew that she had been suffering from recurrent ankle and wrists swelling since she was 3 years old without any family history. Skin manifestations were not apparent except only roughness located on the trunk and forearms. Her past blood examinations showed only an elevated C-reactive protein level of more than 20 mg/dL (normal: less than 0.2 mg/dL). Between the ages of 3 and 6, the patient just had two fevers, each accompanied by joints swelling and pain involving wrists, right ankle, and proximal interphalangeal joints of feet. Methotrexate and prednisolone had been tried from 6 to 12 years old. Considering that the systemic symptoms were not very serious, the doctor asked her to stop methotrexate and continue prednisolone at a dose of 5 mg daily till now.

A synovial biopsy of her right ankle showed chronic synovitis with noncaseating granulomas at her age of 6. Until then, pediatric rheumatologists had been unable to give her a definitive diagnosis. Since then, she has never had fevers, and the only joint swelling left is on her right ankle and right wrist (Fig. 3). Genetic analysis revealed Met491Leu variant in the NOD2 gene in her 14 years old, but how it caused the disease is unclear.

The appearance of ocular symptoms this time accompanied by arthritis and skin lesions led to a preliminary diagnosis of BS for her. Since she was older and could cooperate well with the examination, we conducted a further fluorescein fundus angiography and indocyanine green angiography for her, which showed retinal vascular leakage in the nasal, inferior, and temporal retina of her right eye and inferior of the left, as well as hyperfluorescence in both optic discs (Fig. 4). No obvious abnormality was found in optical coherence tomography of macula (Fig. 5). Topical dexamethasone and compound tropicamide eye drops were used and controlled the inflammation. In the 2 years we observed, no serious ocular complications such as cataract or retina detachment occurred.

Discussion

It is sometimes little difficult to reach a definite diagnosis of BS. Ocular manifestations play an important role in the diagnosis of BS. Okafuji et al. [5] demonstrated that ocular lesions were seen in 18 of 20 patients with EOS (SBS)/BS. The reasons for the difficulty in the diagnosis of this patient maybe the late onset of ocular complications. In a study by Takeuchi et al., it was reported that the median ages at uveitis onset were 24 months and 4.5 years [5], while Wouters's research suggested that eye symptoms generally appear at around age 12 [6]. The ocular involvement in this patient occurred in her 18 years old. This has a big impact on her diagnosis of the disease.

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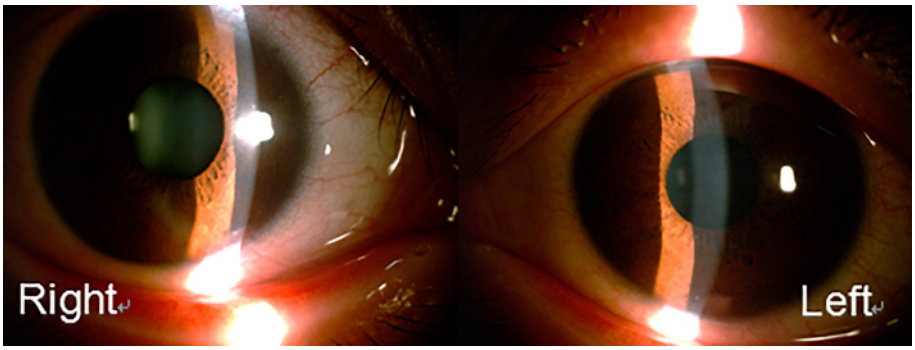

Fig. 1. Slit-lamp photography demonstrates mild conjunctival hyperemia, mutton-fat keratic precipitates, and slight aqueous flare in anterior segment in both eyes.

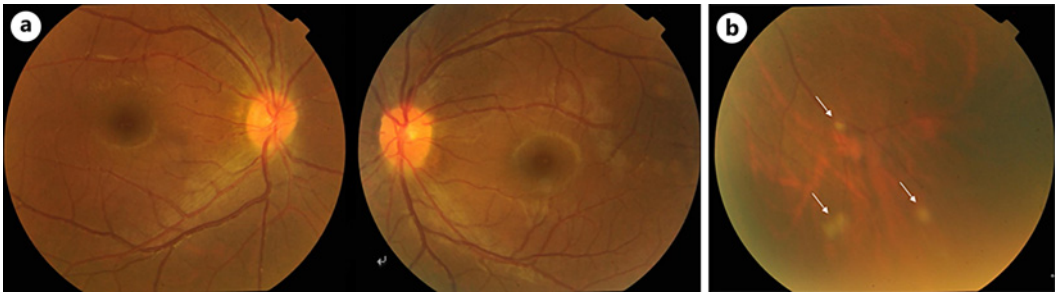

Fig. 2. Fundus photos show optic disc hyperemia in both eyes (**a**) and significant focal punctate infiltrations (arrows) in the inferior peripheral retina of the left eye (**b**).

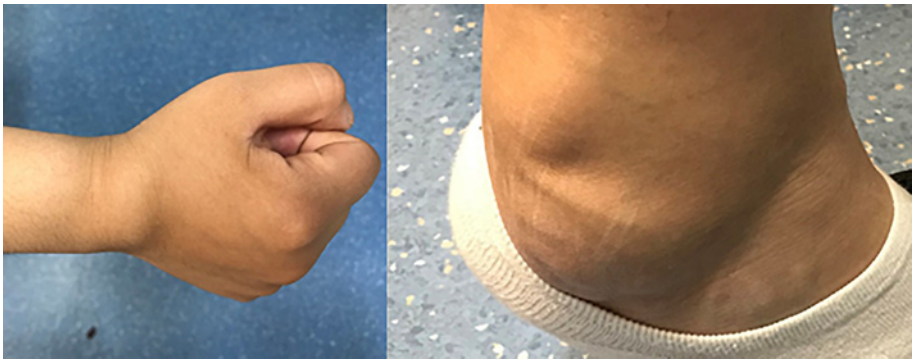

Fig. 3. Joint swellings left on her right ankle and right wrist at present.

Eye involvement is usually the most relevant morbidity of BS. The most frequent clinical manifestation was anterior segment involvement with a proportion of 99% [7]. At the same time, the inflammation can evolve into severe panuveitis, which can lead to cataracts and banded keratopathy, which often require surgery [8]. Marín-Noriega [9] has reported a 5-year-old boy of BS with bilateral cataracts and retinal detachment in his right eye. Despite the surgical treatment, his best-corrected visual acuity was no light perception in the right eye and 20/40 in the left. The ocular involvement in our patient presented as an insidious granulomatous iridocyclitis, shown as bilateral uveitis and focal punctate retinal infiltration in

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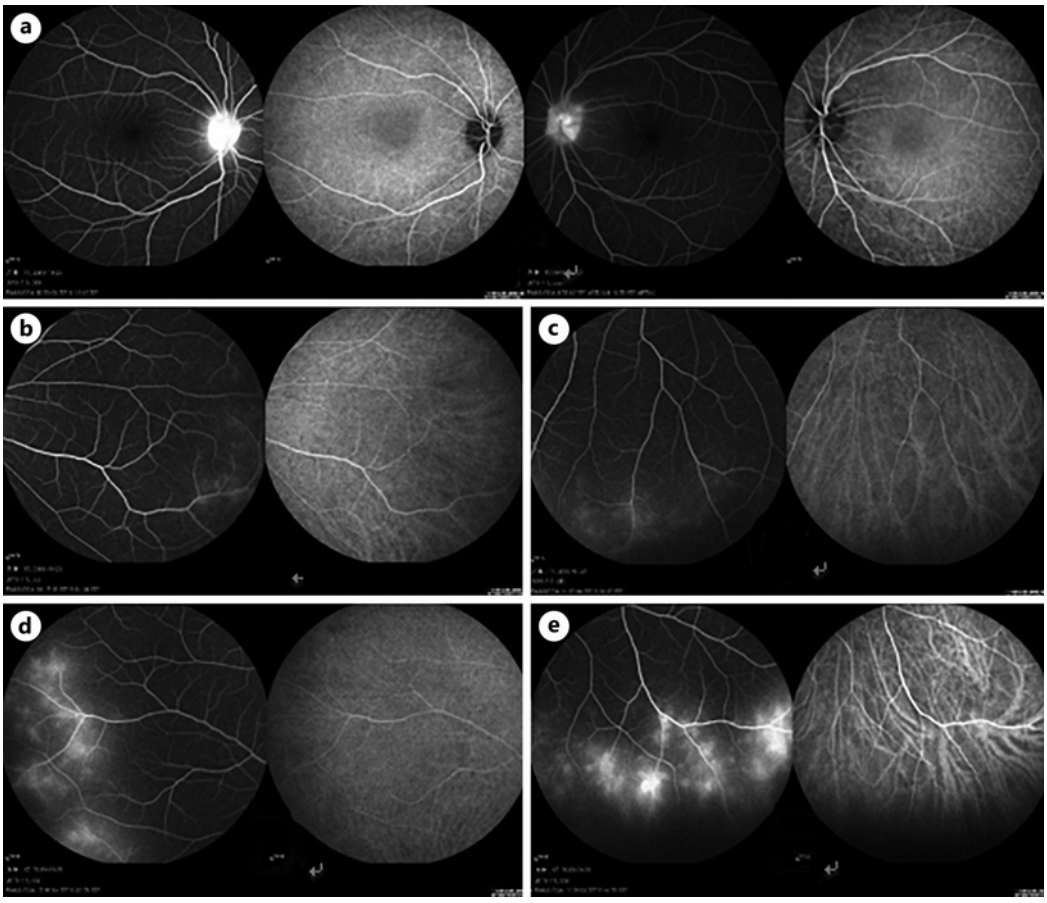

Fig. 4. FFA and ICG demonstrate vessel attenuation and optic disc hyperfluorescence (**a**) in early phase of both eyes, while late phase shows peripheral leakage in the nasal (**b**), inferior (**c**), and temporal (**d**) retina of her right eye and inferior of the left. **e** The leakage in the left inferior retina is the most serious, which is consistent with the result of fundus photo.

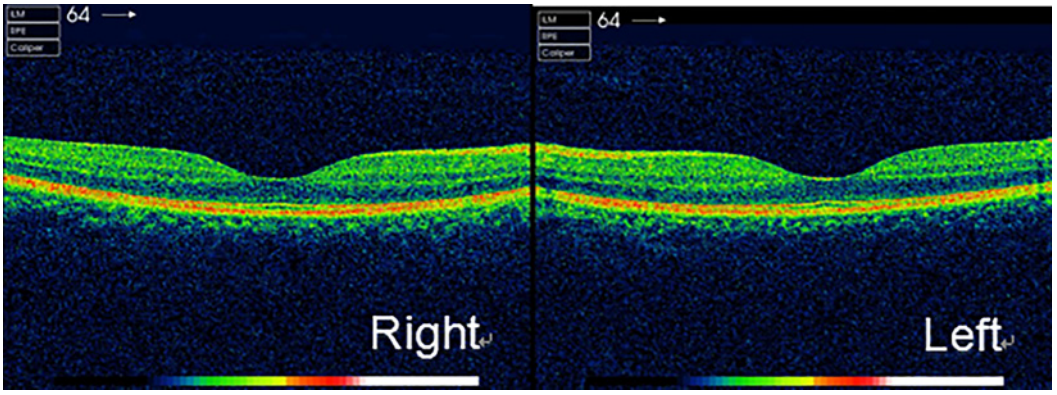

Fig. 5. OCT shows macula is normal in both eyes.

the fundus. A combination of topical steroid drops have controlled the low-level inflammation without serious ocular complications occurring so far, which may be related to the late onset of ocular symptoms so that the patient can find abnormalities more quickly, seek medical

treatment in time, and better cooperate with the treatment. However, because of this, doctors may be more likely to misdiagnose the relationship between eye problems and systemic diseases.

In conclusion, we report a case of late-onset eye lesions in an 18-year-old girl of BS. Timely detection of eye abnormalities and presenting to the hospital as well as better cooperation with comprehensive examination and medical treatment are easier for this relatively older patient, which may lead to better control of her eye lesions. At the same time, the clinical presentation of this patient highlights the necessity of systemic medical history inquiry in the clinical consultation work. The ophthalmologist must maintain a high degree of suspicion for the diagnosis of BS in the clinical work, despite its relative rarity. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000536005).

Statement of Ethics

This study protocol was reviewed and approved by the Ethics Committee of Beijing Anzhen Hospital, approval number 2020098X. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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Author Contributions

Z.M. and X.G. contributed to the design of the work. Z.M. has drafted the work, and X.G. and S.Z. have substantively revised it. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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