Late-Onset Blau Syndrome: A Case of Misdiagnosis, Delayed Diagnosis, and the Impact of Social Challenges

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ABSTRACT

Blau syndrome is a rare, autosomal dominant, autoinflammatory disease caused by mutations in the NOD2 gene, characterized by arthritis, dermatitis, and uveitis. Symptoms typically appear in early childhood, before age 4, and later presentation is uncommon. We present a patient with late onset Blau syndrome, with symptom onset at age 10 and diagnosis at age 18.

CASE PRESENTATION

At age 10, our patient developed a severe, refractory generalized rash initially diagnosed as eczema, along with eye redness and irritation initially diagnosed as allergic conjunctivitis. These diagnoses were not challenged due to inconsistent follow-up. The rash was complicated by multiple superimposed skin infections leading to scarring.

Our patient was an excellent athlete, but at age 14, he developed thoracic back pain, hip and wrist arthritis, and malformations, including prominent bending of the fifth fingers and toes, which hindered physical activity.

The family suspected undiagnosed food allergies, leading to food withholding and resulting in protein deficiency over three years.

CASE PRESENTATION (continued)

A skin biopsy, planned several times, was delayed due to family hesitancy, but was finally performed at age 16, revealing granulomatous dermatitis.

At the same time, he was experiencing chronic diarrhea and bloating, but colonoscopy was never completed due to intolerance of the preparation.

Although his symptoms were concerning for inflammatory bowel disease, diagnostic pathology was never obtained for this reason.

However, an upper endoscopy revealed H. Pylori gastritis and changes suggestive of Celiac Disease, including blunted villi. Pathology demonstrated chronic duodenopathy.

At age 18, he was referred to allergy and immunology where genetic testing confirmed a pathogenic NOD2 mutation diagnosing Blau syndrome. Other laboratory findings, as shown in table 1, included low IgM (33), elevated IgE, but normal IgG and IgA, and fluctuating CRP. QuantiFERON was negative.

Table 1: Labs	
CRP	<3
ESR	2
IgG	930
IgM	33
IgA	104
QuantiFERON	Negative

DISCUSSION

A unique aspect of this patient's case is the delayed onset and the significant impact of social determinants of health on the patient's care. Since diagnosis, consistent in-person follow-up has been difficult to arrange due to frequently missed appointments for unknown reasons. Overall, a diagnosis of Blau syndrome can place significant financial and emotional burden on the patient and the patient's family. This can lead to gaps in care and more severe clinical course, resulting in physical disabilities including joint contractures and vision impairment or blindness, which can limit the child's functional status.

The incidence of Blau syndrome is only 1 in 1 million children worldwide, so it is not unreasonable that the diagnosis could be missed or delayed based merely on presentation. However, this underscores the importance of genetic testing and clinical vigilance in diagnosing and managing the disease if a clinician suspects Blau syndrome.

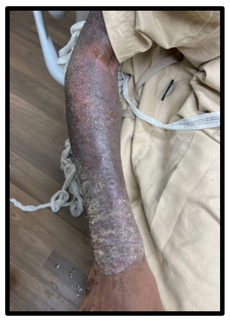

Figure 1: right arm

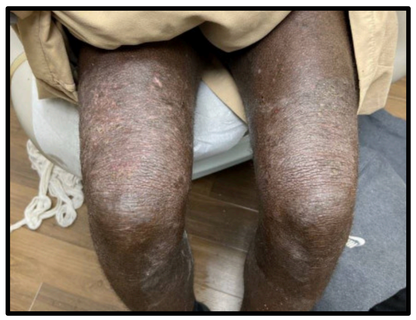

Figure 2: bilateral lower legs

DISCUSSION (continued)

Given the rarity and clinical complexity of Blau syndrome, patients and their families often find value in connecting with others who share similar experiences. Peer support networks can offer emotional encouragement, practical guidance, and up-to-date information on emerging treatments and research developments. Although dedicated support groups for Blau syndrome may be limited, broader organizations focused on rare diseases and autoinflammatory conditions can serve as valuable resources for community support and information sharing.

CONCLUSION

This case highlights the challenges of diagnosing late-onset Blau syndrome in the setting of inconclusive laboratory evaluation, and demonstrates the crucial role of social factors in medical management. The complexity, isolating nature of the symptoms, and unique challenges presented by the disease demonstrate a need for peer support networks in the comprehensive care of these patients.

REFERENCES

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