

Idiopathic facial aseptic granuloma: Report of successful treatment with low-dose isotretinoin in a pediatric patient with trisomy 21



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INTRODUCTION

This case report discusses a 7-year-old boy with trisomy 21 with an idiopathic facial aseptic granuloma (IFAG) of the cheek. IFAG is an uncommon entity that is thought to be part of the spectrum of juvenile granulomatous rosacea.¹ Only a few cases have been reported in the literature, as it is known to pose a diagnostic and therapeutic challenge. To our knowledge, this is the first pediatric patient with trisomy 21 reported in the literature treated with low-dose isotretinoin, who had a rapid, safe, and complete response to systemic retinoids.

CASE REPORT

A 7-year-old boy with trisomy 21 presented to our clinic with a 2-year history of a solitary tumor of the cheek. It was initially noted as a small violaceous papule that grew rapidly in the 3 weeks prior to his presentation to us. No punctum or pustular discharge was noted, and no symptoms were associated with it. The patient's mother reported the use of warm compresses with partial benefit. Aside from congenital nystagmus followed by Ophthalmology, the patient's medical history was noncontributory. Physical examination was notable for a large, soft, nontender, ovoid, red tumor on the medial aspect of the right cheek with subtle overlying xerosis, with no erosions or ulcerations (Fig 1). The remainder of his physical examination was unremarkable. An ultrasound scan was performed and revealed a subcutaneous hypoechoic heterogeneous ovoid structure measuring $2.2 \times 2.6 \times 1.2$ cm without internal flow.

Abbreviation used:

IFAG: idiopathic facial aseptic granuloma

With these results and the clinical picture, the diagnosis of an IFAG was made. The parents reported difficulty with administering medications, limiting our options of daily or twice daily treatment options. He was treated with low-dose isotretinoin 10 mg twice weekly (~ 1 mg/kg/week divided into biweekly doses). Significant improvement was noted at week 5 of the follow-up, and complete clearance of the lesion was achieved at 9 weeks, displaying minimal residual hyperpigmentation and complete flattening without any local or systemic side effects (Figs 2 and 3). At the 6-month follow-up, the patient remained clear despite no further intervention.

DISCUSSION

It is well known that patients with trisomy 21 commonly present with varied dermatological conditions. A recent retrospective review performed at the Mayo Clinic,² reported a pediatric cohort of patients with trisomy 21 presenting with varied dermatological conditions, including varied types of dermatitis, folliculitis, and soft tissue infections among others. To our knowledge, there is no specific data from pediatric patients with trisomy 21 diagnosed or treated for IFAG.

IFAG is an uncommon inflammatory and granulomatous lesion that classically presents as a solitary,

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Fig 1. Erythematous, soft, compressible, nontender nodule on the right cheek.



Fig 2. Idiopathic facial aseptic granuloma on the right cheek after 1 month of isotretinoin 10 mg twice weekly.



Fig 3. Idiopathic facial aseptic granuloma on the right cheek after 2 months of isotretinoin 10 mg twice weekly.

painless nodule located in the cheek of young children and adolescents.

Theories have hypothesized that this condition is a reactive process to insect bites or local trauma or a granulomatous response from an embryologic remnant³; however, its exact etiology and pathogenesis have not yet been confirmed. A small case series published histopathologic similarities between IFAG and rosacea, highlighting the presence of folliculitis and perifolliculitis with granulomas surrounded by lymphocytes and plasma cells.⁴ Another case series reported a prevalence of rosacea of 42% in their cohort, suggesting that IFAG might precede the onset of rosacea in some children.¹ The latest supports previous speculation of its relationship with juvenile rosacea.⁵

Facial nodules and tumors in the pediatric population can be distressing to caregivers and pose a diagnostic challenge to physicians. Differential diagnoses includes chalazions, bacterial, mycobacterial, fungal, and parasitic infections, vascular malformations or tumors (hemangiomas & pyogenic granulomas), pilomatricomas, dermoid/epidermoid cysts, xanthogranulomas, and Spitz nevi. An important clinical diagnostic clue suggestive of IFAG is the painless, soft, and compressible nature of the mass.

The majority of IFAG cases can be diagnosed clinically without any investigations. However, if the diagnosis is questioned, ultrasound imaging has been described in a multicenter prospective study,⁶ where a well-demarcated, hypoechoic lesion in the absence of microcalcifications or vascularity was indicative of IFAG, as in our patient's case. This is a noninvasive and cost effective diagnostic tool that can help obviate the need for skin biopsy, a potentially distressing and invasive procedure for children, with an added risk of scarring.

The prognosis of IFAG is favorable, and most cases resolve spontaneously without scarring by an average of 11 months.⁷ Nonetheless, patients are often treated with multiple courses of systemic and topical antibiotics, such as metronidazole, ivermectin, and doxycycline, with incomplete clearance. No treatment guidelines have been published.

Retinoids modify gene expression, induce cellular proliferation, and regulate apoptosis and lipogenesis, normalizing follicular keratinization.⁸ Isotretinoin is the treatment of choice for pediatric nodulocystic acne and for adult granulomatous rosacea, although its use in pediatric rosacea is off label and limited to expert experience. The safe use of isotretinoin for younger infants and children for infantile acne was documented recently.⁹

The documented use of isotretinoin in pediatric patients with IFAG remains limited but includes a

series of 4 patients aged 2-7 years (mean, 4.5 years) treated with low-dose isotretinoin (~0.25 mg/kg/day) biweekly with improvement in size and tenderness of nodules.¹⁰ Resolution was achieved between 6 and 9 months (mean, 7.5 months), and only 1 patient reported drug-associated xerosis 3 months into treatment that responded well to the use of emollients.

Our patient's clinical course supports the relationship between IFAG and granulomatous inflammation. The initial time to response and complete clearance with isotretinoin was considerably faster than that reported in previous publications, with notable changes of the lesion (flattening and shrinking) 5 weeks into treatment and by achieving complete clearance in 9 weeks' time, with no recurrence after stopping. No clinical or laboratory side effects were noticed during his regular evaluations.

In conclusion, this case highlights the effectiveness and safety of short and low-dose systemic isotretinoin therapy to treat IFAG in pediatric patients with trisomy 21. Additionally, we propose that this regimen could be broadly applied to other patients with IFAG. The authors acknowledge that further studies are required in order to establish treatment guidelines and protocols for the management of patients with IFAG.

Conflicts of interest

Dr Sibbald has received honoraria from Abbvie, Leo Pharma, Novartis Pfizer, Sanofi Regeneron, and UCB for work unrelated to this manuscript. Dr Sanchez-Espino has no conflicts of interest to disclose.

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