

Beyond the Lesion: A Retrospective Study of Idiopathic Facial Aseptic Granuloma in Children Focusing on Ultrasound Findings and Their Association with Chalazia

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ABSTRACT Introduction: Idiopathic facial aseptic granuloma (IFAG) is an uncommon granulomatous lesion associated with childhood rosacea. Affected children often experience recurrent eyelid chalazia.

Objectives: We present a single-center retrospective study of 16 cases of IFAG in order to assess their clinical course and discuss any therapeutic intervention.

Methods: Children presenting with facial lesions persisting for at least six weeks which exhibited clinical features of an (IFAG) were included in the study.

Results: There were 10 females and six males, with a mean age of 6.4 (\pm 4) years. The mean time from the onset of treatment to complete resolution of lesions was 11 months for the children treated with a topical regimen and 7.2 months for those children treated with both topical and systemic antibiotics respectively ($P < 0.005$).

Ultrasound examination revealed a solid, hypoechoic lesion with increased perilesional or intralesional blood flow in the hypodermis without any calcium deposit as an early finding. Skin biopsies were performed in seven children. Recurrent chalazia were reported in all 16 cases.

Conclusions: IFAG is a benign lesion that may persist for several months before resolution. Ultrasound examination is a valuable tool for establishing a diagnosis. Clinicians should monitor children with IFAG for potential ocular complications that may arise later in life.

Introduction

Idiopathic facial aseptic granuloma (IFAG) is an unusual granulomatous lesion that occurs in childhood. It is associated with childhood rosacea, as the lesions exhibit similar histopathological findings to granulomatous rosacea, and, moreover, affected children frequently present with recurrent eyelid chalazia [1]. IFAG, first described by Roul et al. [2], typically appears in children as a solitary or, less frequently, a few asymptomatic erythematous-to-violaceous nodules on the cheeks located within a triangular area defined by the outer limit of the orbit, the labial angle, and the ear lobe. This benign lesion primarily affects children between eight months and 13 years of age [3]. Specific predisposing factors for the disease have not yet been established [4]. Most cases are diagnosed clinically, but when the diagnosis is challenging, other examinations such as cutaneous ultrasound (US) and laboratory testing to rule out other conditions are implemented [5]. Occasionally, more invasive procedures such as skin biopsy and histological examination may be necessary for a definitive diagnosis. IFAG should be differentiated from other conditions such as nodular infantile acne, pyodermas, xanthogranulomas, Spitz nevus, bacterial, fungal, protozoan or mycobacterial infections, insect bites, pilomatricomas, dermoid and epidermoid cysts, and primary cutaneous lymphoproliferative disorders [6,7].

Objectives

This retrospective study included patients who were reviewed and followed up at the Pediatric Dermatology Unit of the First Department of Pediatrics, National and Kapodistrian University of Athens Medical School, at “Agia Sophia” Children’s Hospital in Athens, Greece. Data were retrieved from the medical files of patients diagnosed with an IFAG between May 2018 and November 2024. This study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was also obtained from our institutional ethics committee and board review.

Methods

Children who were documented to have a facial lesion suggestive of an IFAG lasting for at least six weeks were included in the study. Pyodermas, xanthogranulomas, Spitz

nevi, bacterial, fungal, protozoan, or mycobacterial infections, insect bites, pilomatricomas, and dermoid and epidermoid cysts were excluded as potential diagnoses upon initial assessment by two independent pediatric dermatologists at the outpatient clinic. Ultrasound (US) examination of the lesions was conducted for all patients, and cultures for any existing skin infections were also performed. Information such as demographic data, past medical history, location of the lesions, other clinical manifestations, diagnosis assessment, treatment, and follow-up was retrieved from their medical files. All patients were contacted retrospectively over the phone in order to investigate any potential relapses after the lesions had resolved.

Results

We examined 16 children in total (10 females and six males), with a mean age of 6.4 years. Their main clinical characteristics, therapeutic interventions, and disease duration are described in Table 1. Thirteen children (13/16) were referred to our clinic with a recent history of a solitary nodule on one cheek (Figure 1), one patient (1/16) presented with a single nodule on the tip of the nose, and another two patients (2/16) presented with two lesions at the same time on their face. Six children (6/16) had developed recurrent chalazia over the previous two years before visiting our clinic, while ten children (10/16) presented with chalazia upon their initial assessment. All patients were otherwise healthy, with no history of recent or previous travel to tropical areas, and their family history was unremarkable.

Ultrasound imaging of all patients revealed a well-defined hypoechoic solid oval-shaped lesion without any calcium deposits, with surrounding hyperechogenicity and venous and arterial flow on Doppler imaging. These findings are consistent with previous studies [8-10]. Children who were assessed before 2021 underwent both a skin biopsy and US during their initial assessment. Once it was determined that the ultrasound provided a reliable and definitive diagnosis, the skin biopsy was discontinued as a routine intervention for subsequent patients. Therefore, a skin biopsy was performed in seven children: five underwent a 2 mm punch biopsy, while the other two had their lesions completely excised for definitive management due to no response to initial treatment and extreme parental anxiety. Histopathology of all cases showed an inflammatory perifollicular

Table 1. Clinical characteristics and medical interventions of the study population.

Patient ID	Age (years)	Sex	Size (mm)	Chalazia (Yes/No)	Location	Ultrasound finding (Yes/No)	Therapy (Systemic / Topical)	Duration	Skin biopsy (Yes/No)	Surgical excision (Yes/No)
1	12	F	17	Yes	Right cheek	Yes	T/S	9	Yes	No
2	7	F	18	Yes	Left cheek	Yes	T/S	6	Yes	No
3	5	M	14	Yes	Right cheek	Yes	T	15	Yes	No
4	3	M	22	Yes	Right cheek	Yes	T/S	7	Yes	Yes
5	4	F	17	Yes	Right cheek	Yes	T	11	Yes	No
6	2	F	15	Yes	Left cheek	Yes	T	9	Yes	No
7	6	F	23, 19	Yes	2 Left cheek	Yes	T/S	6	Yes	No
8	11	F	7	Yes	Right cheek	Yes	T	11	No	No
9	13	M	19	Yes	Right cheek	Yes	T/S	5	No	No
10	4	F	17	Yes	Right cheek	Yes	T/S	8	No	No
11	7	F	8	Yes	Left cheek	Yes	T	13	No	No
12	7	M	7	Yes	Tip of the nose	Yes	T	9	No	No
13	0,7	M	10	Yes	Left cheek	Yes	T	10	No	Yes
14	2	F	15, 18	Yes	2 Upper left cheek	Yes	T/S	9	No	No
15	4	F	8	Yes	Left cheek	Yes	T	12	No	No
16	14	F	9	Yes	Right cheek	Yes	T	8	No	No



Figure 1. Clinical picture before treatment.

infiltrate consisting of lymphocytes, histiocytes, and reactive giant cells without necrosis. Immunohistochemistry revealed CD1a expression in mildly increased Langerhans cell populations in both the epidermis and hair follicles, excluding a primary cutaneous lymphoproliferative disorder (T CD4 type) (Figure 2, A and B).

Tissue cultures did not identify any microorganism (aerobic, anaerobic bacteria, fungus, and acid-fast bacilli), except in two cases, where there was a super infection with *Staphylococcus aureus*. Seven patients in total (5/7 patients with lesion sizes greater than 15 mm and another 2/7 patients having two lesions each) received systemic treatment with oral clarithromycin 15 mg/kg twice per day for two weeks, followed by 10 mg/kg once per day for 10 weeks. Concomitant treatment with topical metronidazole ointment twice per day for 12 weeks was also prescribed for these patients. The remaining nine patients were treated with either topical antibiotics (metronidazole) or topical retinoids for 12 weeks.

Although the patients who received both topical and systemic treatment (Group A, 6/16) had multiple and/or larger

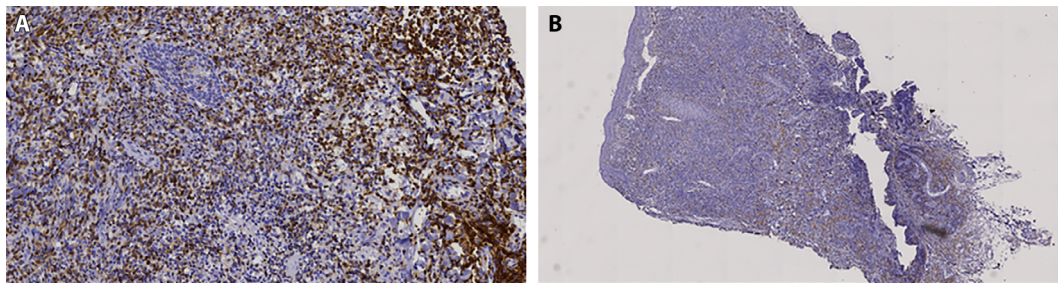


Figure 2. Skin biopsy/histopathology.



Figure 3. Clinical picture after oral antibiotic treatment.

lesions compared to those who received only topical treatment (Group B, 8/14), the time from the onset of treatment to compared to Group B (7.2 months versus 11 months, $P=0.005$).

All calculations for treatment response duration exclude patients No. 4 and No. 13, as their lesions were surgically excised three months after their initial assessment. IFAG lesions healed without scarring, leaving mild hypo- or hyperpigmentation (Figure 3). No relapse was reported in our study group.

Discussion

IFAG is a condition frequently observed in pediatric clinical practice but seldom reported. Females seem to develop this lesion more frequently, with a ratio of 2:1 [11].

The pathogenesis of IFAG is ambiguous. It has been suggested that IFAG may be related to skin trauma or insect bites, although the current hypothesis is that IFAG can be described as a granulomatous response due to embryonic domains or as an aspect of granulomatous rosacea in children [12]. A significant number of children with IFAG present with fundamental symptoms of rosacea, such as flushing and papules [13]. Moreover, most IFAG cases respond immediately to the same antibiotic and topical treatment used for rosacea [14]. Boralevi et al. performed histopathological analysis

in five IFAG cases, indicating a strong association between IFAG and rosacea [4]. Our histopathology findings in seven children similarly showed an inflammatory perifollicular infiltrate consisting of lymphocytes, histiocytes, and reactive giant cells without necrosis. This finding also demonstrates the strong association of this entity to rosacea, providing robust evidence that it belongs to the spectrum of granulomatous rosacea in childhood, as previously stated [15].

It is also reported that children with IFAG face a greater risk of developing rosacea, particularly ocular rosacea. A case series by Neri et al. showed that all children diagnosed with an IFAG had also presented with chalazia [16]. Additionally, Prey et al. concluded that up to 40% of their patients with one IFAG lesion had ≥ 2 criteria for rosacea, and when the lesions were multiple, the percentage exceeded 80% [13].

Similarly, in our study, all 16 children with IFAG either had presented or developed chalazia at a later stage in the disease course (100%). We also observed in our cohort that recurrent chalazia may precede IFAG manifestation by two years. Therefore, a high index of clinical suspicion should be maintained to accurately diagnose IFAG in patients who present with a facial nodule and who have a previous history of chalazia.

Furthermore, regarding ocular rosacea in the pediatric age group, it has been hypothesized that recurrent chalazia responding to classic topical medical treatment, such as metronidazole cream, should amplify suspicion for IFAG diagnosis in the presence of an existing facial nodule [17]. In our study, all our patients either had developed chalazia in the past or presented with chalazia at the time of examination. Additionally, the chalazia of patients who received systemic macrolides for the treatment of IFAG responded similarly and reduced significantly in size upon follow-up. Accordingly, when the diagnosis of IFAG is established, the patient should likely be referred to an ophthalmologist due to the increased risk of developing ocular rosacea [18].

Diagnosing IFAG can sometimes be challenging. Ultrasound (US) is a noninvasive examination that can be performed at the time the patient presents or during follow-up, providing a reliable diagnostic result. All children in our study underwent US examination, with results consistent

with previous studies [8]. Thus, US improves diagnostic accuracy in IFAG, supports differential diagnosis, and can supersede invasive techniques such as skin biopsy.

Furthermore, dermoscopy may serve as a valuable adjunct in the diagnosis of IFAG. In a study by Errichetti et al. [19], the most frequently observed dermoscopic characteristics included focal white structureless areas, blurred linear vessels, and focal orange structureless areas. Distinguishing IFAG from its clinical mimickers is particularly important. For instance, pilomatricomas commonly exhibit white coloration accompanied by linear and polymorphic vessels with a focal distribution, as demonstrated in a retrospective descriptive study of 35 pediatric patients conducted by Di Brizzi et al. [20]. Similarly, juvenile xanthogranuloma, another potential clinical mimic, typically presents with yellow-orange-to-pink-red coloration and focal distribution of linear and polymorphic vessels under dermoscopic examination [21].

IFAG is a clinical condition with a benign course that generally does not require aggressive treatment. According to some studies, these lesions may last for several months until they spontaneously resolve without scarring [18,22,23], or they may respond variably to prolonged, appropriate oral antibiotic therapy such as oral macrolides [24,25].

In younger children (≤ 8 years old), metronidazole cream/gel produced satisfactory results for smaller lesions [26]. Numerous reports have documented a satisfactory resolution of IFAG after systemic treatment with antibiotics, with variable treatment durations before resolution [9, 27, 28]. Unlike these reports, we concluded that patients with large or multiple lesions who received a 12-week course of systemic antibiotic treatment had a shorter clinical course compared to those who received only topical treatment.

Surgical excision should be avoided and is rarely recommended [29]. In our case series, two large IFAG lesions underwent surgical excision due to parental anxiety and the need for reassurance.

Conclusion

In conclusion, IFAG is a benign lesion that may persist for several months before resolution. Moreover, ultrasound examination and dermoscopy are valuable tools for establishing a diagnosis. Oral antibiotic therapy in selected cases appears to shorten the clinical course of this condition. Early surgical intervention should be avoided to prevent resultant scarring. Clinicians should monitor children with IFAG for potential ocular complications that may arise later in life.

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