

Idiopathic facial aseptic granuloma: a multicentre prospective study of 30 cases

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Summary

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Conflicts of interest

None declared.

Background Idiopathic facial aseptic granuloma (IFAG) was recently described in a single-centre retrospective study as a skin condition that occurs specifically in childhood.

Objectives To improve our epidemiological, clinical and pathological knowledge on IFAG, to search for an infectious aetiology, and to assess therapeutic recommendations.

Methods Children presenting with one or several acquired nodules on the face, lasting for at least 1 month, with no evidence of any other recognizable clinical entity such as infantile acne, pilomatrixoma, furuncle, tumour or vascular malformation, were enrolled in a prospective multicentre study from June 2001 to June 2004, involving the main French paediatric dermatology outpatient units. We recorded clinical details about the nodule and its duration, ultrasound study pattern, cultures for bacteria and mycobacteria, and *Bartonella henselae* and *Afpia felis* antibody testing.

Results Thirty children (17 boys and 13 girls, mean age 3·8 years) were enrolled. Ultrasound studies revealed a solid well-demarcated hypoechoic lesion without calcium deposit. Cultures for bacteria were negative in 70% of cases. Cultures for mycobacteria and cat scratch disease serologies were negative. Antibiotic therapy was ineffective; the lesion healed spontaneously with a mean duration of 11 months. Histological examination, performed in five cases, showed a chronic dermal lymphohistiocytic granuloma with numerous foreign body-type giant cells. **Conclusions** IFAG is characterized by a painless facial nodule, presenting as a single lesion localized on the cheek, with a prolonged course but spontaneous healing. Oral or local antibiotics are usually ineffective. Regarding the pathophysiology, our study rules out a primary infectious disease, and allows considering IFAG either as a granulomatous process appearing around an embryological residue or as a manifestation to include in the spectrum of granulomatous rosacea in childhood.

Idiopathic facial aseptic granuloma (IFAG) was recently described by Roul et al.¹ as a skin condition that occurs specifically and not uncommonly in childhood. Because IFAG looks like an abscess with very slight inflammatory signs, we first proposed to name this condition *pyodermite froide* in French,² which means cold pyoderma/abscess. It is characterized by painless red nodules, often located on the cheeks, which heal spontaneously and usually without scarring after a benign course of a few months to a year. In our first

report, histological examination, performed in five cases, showed a dermal inflammatory granuloma similar to that observed after foreign body penetration or infections due to mycobacteria, but direct examination and cultures performed in selected cases were negative. In order to improve our epidemiological, clinical and pathological knowledge on IFAG, to search more extensively for an infectious aetiology, and to assess therapeutic recommendations, we performed a prospective multicentre study.

Patients and methods

The study was carried out prospectively at several centres in France (listed in the Acknowledgments) from June 2001 to June 2004. All children with a facial lesion suggestive of an IFAG, i.e. presenting with one or several acquired nodules or papulonodules on the face, lasting for at least 1 month, with no evidence of any other recognizable clinical entity such as infantile acne, pilomatrixoma, furuncle, tumour or vascular malformation, were enrolled. A standardized questionnaire detailing the medical history, the history of the lesion, epidemiological data and previous therapies was completed by the parents. Clinical examination provided clinical details about the facial nodule and possible associated conditions, with special attention to keratosis pilaris or comedones. This was followed by an ultrasound study of the lesion, *Bartonella henselae* and *Afipia felis* antibody testing, and cultures for bacteria and mycobacteria after minimal local incision. A liquid culture medium MB Redox (Heipha Diagnostika/Biotest Diagnostics, Heidelberg, Germany) was used for detection of mycobacteria.³ Histological examination of a skin sample from a punch biopsy or complete excision was proposed in cases of persistent lesions but was not strictly required by the protocol. Then, a 2-week therapy with amoxicillin-clavulanic acid (or with josamycin in cases of suspected allergy to penicillin) was systematically given. Follow-up visits were planned 1 month later and every 2 months until the disappearance of the lesion or for at least 1 year in patients with persistent lesions. Photographs were taken at each visit, and all the cases were jointly reassessed during meetings of our clinical research group.

Results

Forty patients were enrolled from seven of the 10 regional or university centres involved in the study. After a collegial evaluation, 10 were considered not to have IFAG and were excluded. Five of them were considered to have infantile acne, two had folliculitis, one had pilomatrixoma, one had pyogenic granuloma and one had atypical Spitz naevus. The remaining 30 patients (17 boys and 13 girls) had a mean age of 3.8 years (range 8 months–13 years). A single nodule was noted in 27 cases (90%; Fig. 1), two patients had two lesions, and one had three lesions. A previous similar lesion was reported for one child, with a slightly visible scar (Fig. 2), and the occurrence of a new lesion was observed in three patients during follow up, two involving the upper eyelid and one the contralateral cheek. Lesions were located on the cheeks in most cases, as shown in the summary drawing (Fig. 3). The mean size was 10 mm (range 3–25). A localized mild trauma preceding the lesion was mentioned by the parents in four cases. We observed no association with keratosis pilaris, found in five cases, or presence of comedones. No patient had recently travelled overseas. In two cases, the parents mentioned that the nodule was preceded by a slight but palpable subcutaneous lesion for at least 1 year. The ultrasound studies, performed in 14 cases, always revealed a solid



Fig 1. A single nonpainful nodule on the cheek with a course of several months in a 2-year-old boy.

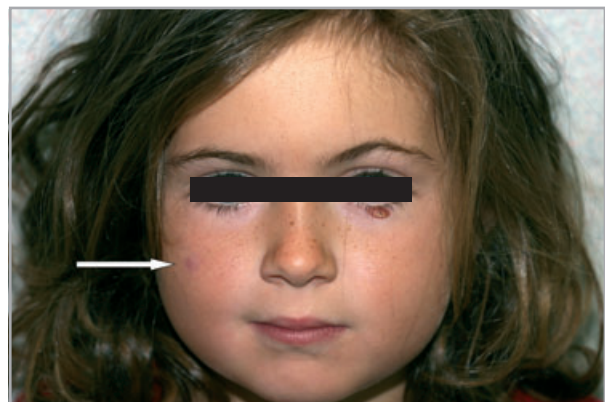


Fig 2. Appearance of a second lesion on the lower eyelid of a young girl, with visible scar of the previous lesion on the contralateral cheek (arrow).

and well-demarcated hypoechoic lesion, without calcium deposit or microcalcifications (Fig. 4). Cultures for bacteria, obtained in 27 cases, were negative in 19 cases, or showed *Staphylococcus aureus* (four cases), *Streptococcus* species (three cases) and *Enterococcus faecalis* (one case). In those cases with positive cultures for bacteria, a history of a recent modification or increase in size of the lesion was usually reported by the parents, leading consequently to a referral to our clinics. Cultures for mycobacteria were negative and antibodies to *B. henselae* and *A. felis* were not found. Antibiotic therapy, given in 26 cases, was followed by dramatic improvement only in four cases, but was considered as ineffective in the rest of the studied population. In most of the cases, the lesion healed sponta-



Fig 3. 'Hot spots'. This picture summarizes all the localizations of idiopathic facial aseptic granuloma lesions on the cheeks. The lesions involved the same triangular area in two-thirds of cases.

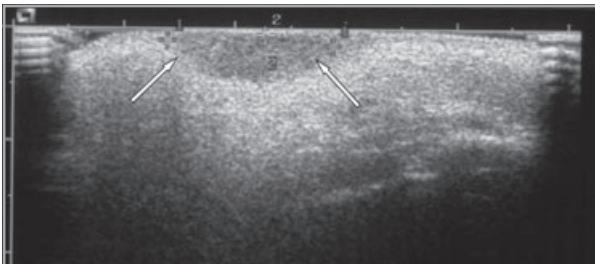


Fig 4. Ultrasound study of an idiopathic facial aseptic granuloma lesion, showing a solid and demarcated hypochoic lesion (arrows).

neously with a mean duration of 11 months (range 2–24), and required a surgical excision in two cases because of the long duration of the lesion, exceeding 1–2 years. Histological examination was performed in five cases, including three biopsies and two complete excisions, and showed a chronic dermal inflammatory granuloma mainly composed of lymphocytes, histiocytes, neutrophils and numerous foreign body-type giant cells. No calcium deposit or shadow cells were seen. In one case, the granuloma developed around a nonruptured epidermoid cyst (Fig. 5).

Discussion

IFAG is a newly recognized entity, defined by a chronic and painless facial nodule, presenting usually as a single lesion localized on the cheek, with a red or purplish appearance, and

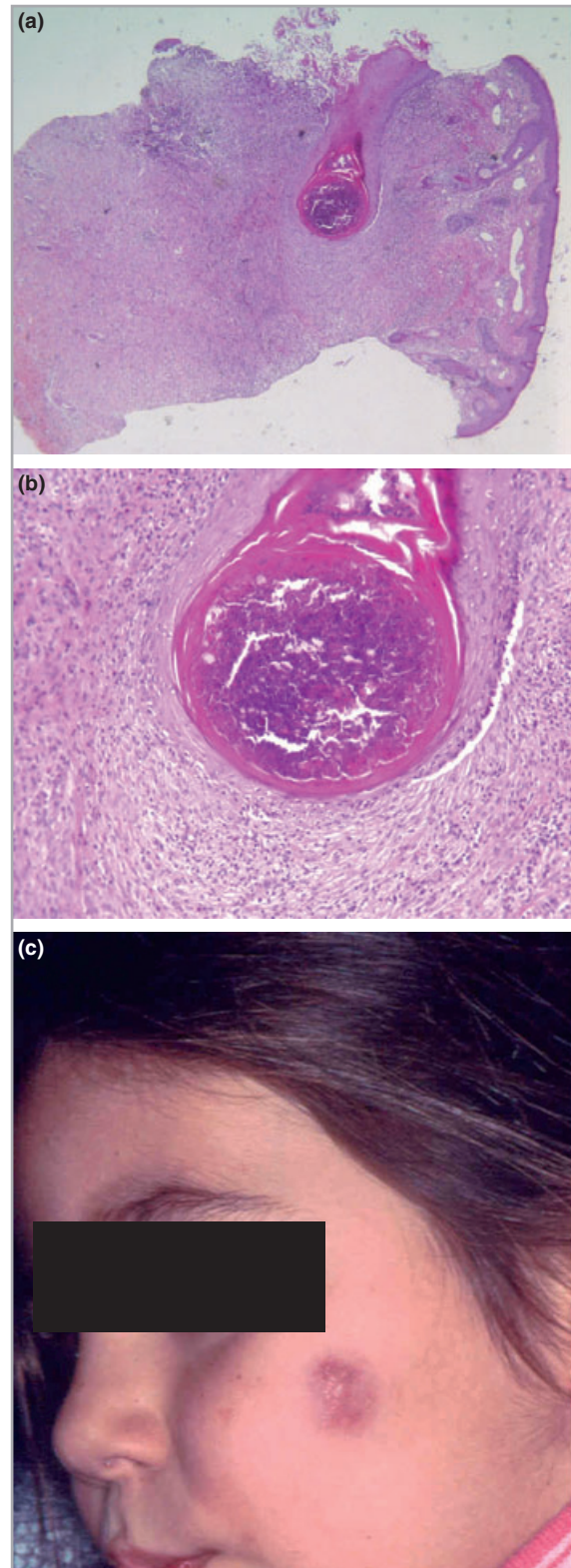


Fig 5. (a) Histological examination showing an inflammatory granuloma of the upper and deep dermis, with a ring of lymphocytes, histiocytes, neutrophils and rare eosinophils (haematoxylin, eosin and safranin; original magnification $\times 25$). (b) In this case, an epidermal cyst was present, filled with neutrophils (haematoxylin, eosin and safranin; original magnification $\times 100$). (c) Clinical appearance of this case.

a soft or elastic consistency. There is no common predisposing factor, no family history, and no associated clinical features, including no satellite lymph nodes. A local incision may discharge pus or a flow of blood mixed with pus, and cultures for bacteria are usually negative, except in cases of superinfection, which may be suspected when the size of the lesion increases rapidly. As illustrated in Figure 3, IFAG seems to involve selectively a restricted area affecting the middle part of the cheeks. Ultrasonography shows a well-demarcated hypoechoic dermal lesion without features suggestive of pilomatrixoma, i.e. an oval echogenic or hyperechogenic lesion with an acoustic shadow, a peripheral halo and calcifications.⁴

The main differential diagnoses are the following: localized infectious pyoderma, paucisymptomatic nodulocystic acne, pilomatrixoma, cutaneous leishmaniasis, botryomycosis and pyogenic granuloma. In contrast to pyoderma, IFAG is painless and perilesional inflammation is absent, and culture for bacteria remains negative except in cases of superinfection. In nodulocystic infantile acne, lesions appear between 6 and 16 months of age, especially in boys.⁵ Usual presentations of infantile acne with superficial inflammatory papules and comedones are quite easy to distinguish from IFAG, while cases with only one or two nodules or nodulocysts pose more problems. In those cases, a careful search for the presence of comedones may favour a diagnosis of acne. Pilomatrixoma is one of the most frequent benign tumours that may involve the face in children, usually as a bluish and firm single subcutaneous nodule. In rare cases, pilomatrixoma may appear as an ulcerated nodule, but pathological examination is specific.^{6–8} The cheek is a frequent location in cutaneous leishmaniasis, and a single nodule prior to a prolonged ulceration may be confused with an IFAG. Thus, in geographical areas where cutaneous leishmaniasis is common, cytological or histological examination and specific staining may be required to distinguish IFAG and leishmaniasis. Botryomycosis may exceptionally occur in young children and on the cheeks. The clinical and histological features differ from those observed in IFAG. In our cases, features suggestive of botryomycosis, including sinuses, fistulae, deeper abscesses, and small yellowish grains in the pus after a minimal incision were never seen.⁹ Moreover, the benign course of IFAG lesions argues against the diagnosis.

The pathophysiology of IFAG remains unclear. An infectious cause, including an inoculation disease such as cat scratch disease, seems highly unlikely according to this study. The late inflammatory manifestation of a naevoid condition or embryological residue was a hypothesis based on the frequent cheek location, suggesting the involvement of a cutaneous fusion line. The remnant of an epidermoid cyst found in one case is the only argument for this hypothesis in this series. As previously mentioned in our first report, eyelid involvement may be observed, either simultaneously or after some time of

follow up (Fig. 2). This association was also observed in several personal unpublished cases after the completion of this study, with a dramatic improvement after oral metronidazole therapy. These recent observations suggest that IFAG could belong to the spectrum of childhood rosacea.¹⁰

To summarize, IFAG is a paediatric condition characterized by a chronic painless nodule on the cheek, without identified predisposing factors and without evidence for a microbial cause, which should be recognized and managed nonaggressively.

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