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CASE REPORT

Aggressive central giant cell granuloma in a child treated with a conservative surgical: a case report with 10-year follow-up

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Abstract:

Central giant cell granuloma (CGCG) is a benign but sometimes aggressive intraosseous lesion that primarily affects the jaws. This report describes the clinical management and long-term follow-up of a 7-year-old male patient presenting with a refractory CGCG of the anterior mandible. Despite initial non-surgical treatment with intralesional corticosteroids, the lesion persisted and demonstrated expansion with cortical perforation and involvement of adjacent teeth. Conservative surgical excision was performed, requiring extraction of four teeth. Postoperative mandibular fracture occurred but healed with conservative management. The patient underwent orthodontic treatment and prosthetic rehabilitation, followed by alveolar ridge reconstruction with autogenous bone graft nine years later to allow dental implant placement. After 10 years of follow-up, no recurrence or new lesions were observed. This case highlights the challenges in managing aggressive CGCG in pediatric patients and supports conservative surgery combined with multidisciplinary rehabilitation as a viable approach.

Keywords: Central giant cell granuloma; Surgery; Neoadjuvant therapy.

INTRODUCTION

Central giant cell granuloma (CGCG) is defined by the World Health Organization (WHO) as "an intraosseous lesion, localized, benign but sometimes aggressive, characterized by osteolytic proliferation consisting of fibrous tissue with hemorrhage and hemosiderin deposits, and the presence of osteoclast-like giant cells with reactive bone formation"[1].

The pathogenesis of CGCG is now understood to be driven primarily by somatic, mutually exclusive activating mutations in genes such as KRAS, FGFR1, and TRPV4, which are found in the mononuclear proliferative parenchymal cell population. These mutations converge on the RAS/MAPK signaling pathway, leading to altered cellular behavior and lesion formation[2-4].

Clinically, CGCG can present in various ways, ranging from asymptomatic, indolent, and slow growing to aggressive and rapidly causing bone destruction, with cortical expansion, root resorption, and displacement of adjacent structures including teeth and nerves, often accompanied by pain[5,6].

Statement of Clinical Significance
This case highlights challenges in managing central giant cell lesions in pediatric patients. Conservative surgery, performed before denosumab became standard, along with multidisciplinary rehabilitation and long-term follow-up, achieved functional recovery and stability, with no recurrence after ten years.

CGCG is an intraosseous pathology that accounts for approximately 7% of non-neoplastic jaw lesions and is typically found in the jaw. It has a relatively high recurrence rate of 15–20%, the more aggressive the lesion, the higher the likelihood of recurrence. CGCG primarily affects young adults and occasionally children[6,7].

Treatment options vary depending on the clinical characteristics and behavior of the lesion, ranging from surgical excision or resection with a continuity defect,

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cryotherapy, to enucleation and aggressive local curettage with or without chemical cauterization[8,9].

Other alternatives are non-surgical or pre-surgical treatments with corticosteroid intralesional injection, calcitonin, interferon α-2a. And, most recently, denosumab has emerged as a pharmacological adjunct in selected cases, though not considered first-line for pediatric patients[7,10,11]. Also, in cases of lesion recurrence, there may be a combination of one or more therapeutic interventions[11]. Treating aggressive CGCG in children is particularly challenging due to concerns about facial growth, tooth development, and the risk of recurrence[8].

Given the rarity and variability in clinical behavior of CGCL, especially in pediatric populations, case reports are essential to expand understanding and guide clinical decision-making[11]. The aim of this study was to report a case of an aggressive central giant cell granuloma in a child treated with a conservative surgical approach.

CASE REPORT

A 7-year-old male patient was referred to the Department of Stomatology with a refractory mandibular lesion for evaluation of the indication of segmental mandibulectomy and reconstruction with an osteomyocutaneous fibula flap. He had no known comorbidities. During anamnesis, the patient's father reported a previous diagnosis of central giant cell granuloma, for which non-surgical treatment with intralesional corticosteroid injections was attempted without clinical response.

On clinical examination, facial asymmetry and increased volume in the mandibular region were observed. Intraoral examination revealed obliteration of the gingivolabial groove in the anterior mandible (Figure 1). The patient reported no associated symptoms, and the lesion had persisted for approximately one year. Additionally, the lesion presented firm consistency, smooth surface, and extended approximately 6 cm anteroposteriorly, causing visible vestibular bulging.

Computed tomography imaging of the face revealed an expansive osteolytic lesion with cortical perforation involving the anterior mandible and adjacent lower anterior teeth, measuring approximately 6 cm in greatest diameter (Figure 1).The tomographic evaluation also demonstrated internal hyperdense foci compatible with hemorrhagic or mineralized areas, and significant thinning of the remaining cortical plates. Based on clinical and radiological findings, the primary diagnostic hypothesis was consistent with an aggressive central giant cell granuloma.

Considering the size of the lesion, it was decided to perform a conservative surgical treatment (Figure 2). An intrasulcular incision was performed, followed by mucosal dissection over the residual lesion, extending to the mandibular base. Complete excision of the lesion was carried out, combined with curettage and peripheral ostectomy, with careful intraoperative hemostasis. The procedure resulted in the loss of four teeth, and the surgical wound was subsequently closed with primary closure. Histopathological examination of the surgical specimen confirmed the diagnosis of central giant cell granuloma (Figure 3).

Postoperatively, the patient experienced a mandibular fracture, which was closely monitored until complete consolidation. Subsequently, orthodontic treatment and rehabilitation with fixed prosthesis were carried out (Figure 4). After nine years, the patient underwent alveolar

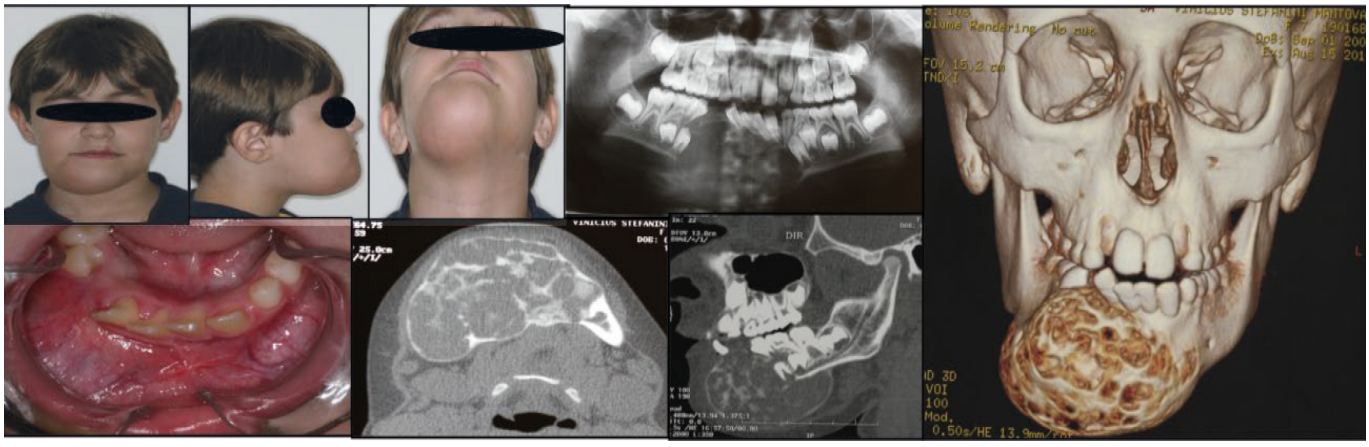

Figure 1. Baseline clinical and radiological characteristics. Legend expanded to improve clarity per reviewer request.

ridge reconstruction surgery using an autogenous bone graft to enable the placement of dental implants and free gingival graft for rehabilitation optimization (Figure 5).

Currently, the patient has been followed up for 10 years with no evidence of lesion recurrence or new oral pathologies (Figure 6).

This case report did not require approval by an institutional ethics committee because it describes routine clinical management with no experimental intervention. The patient's parent provided informed consent for publication, and all identifying information has been removed. All procedures performed in studies involving

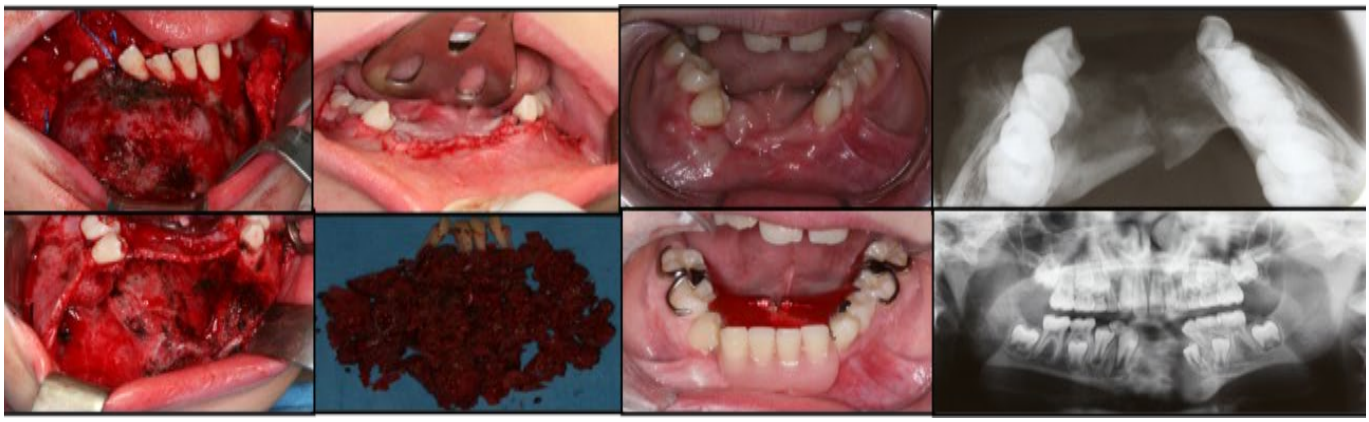

Figure 2. (A) Intraoperative findings during conservative excision and curettage; **(B)** Clinical aspect two months after surgery showing provisional prosthetic rehabilitation; **(C)** Postoperative mandibular fracture evident on occlusal view.

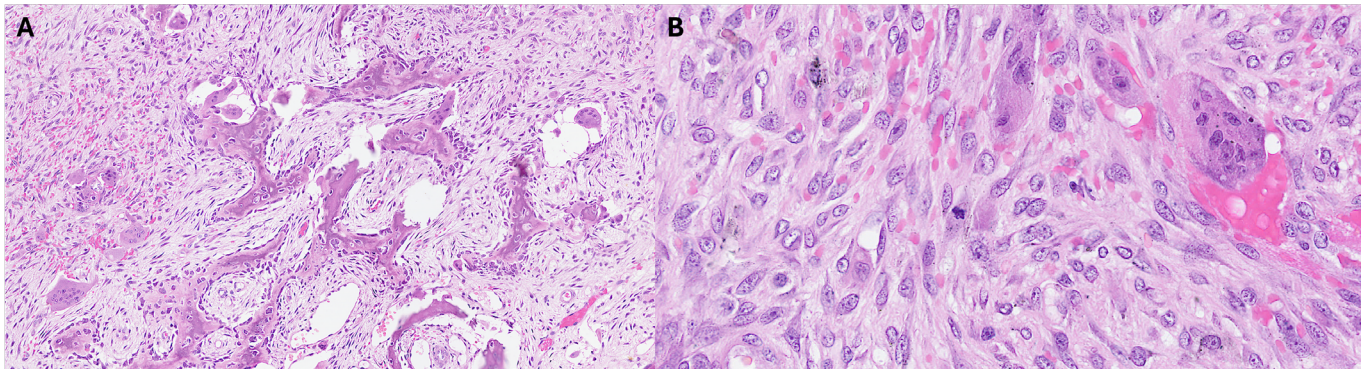

Figure 3. (A) Low-power photomicrograph showing multinucleated giant cells dispersed within a fibrous stroma; **(B)** Higher-power view highlighting hemorrhagic areas, hemosiderin deposition, and mononuclear proliferative cells (H&E stain).

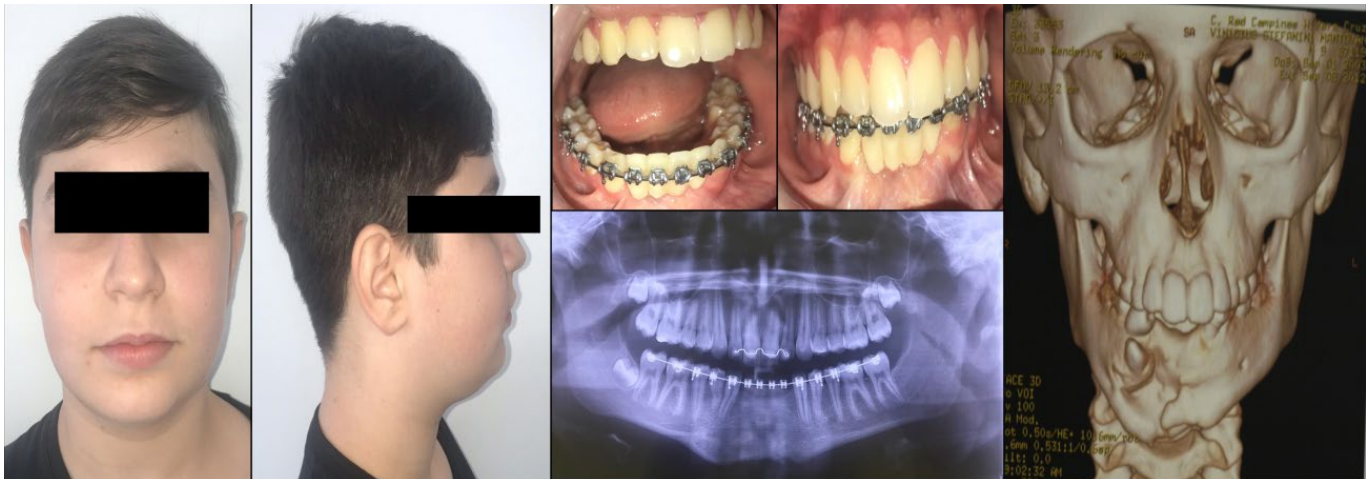

Figure 4. Clinical aspect, seven years after surgery, demonstrating long-term follow-up outcome.

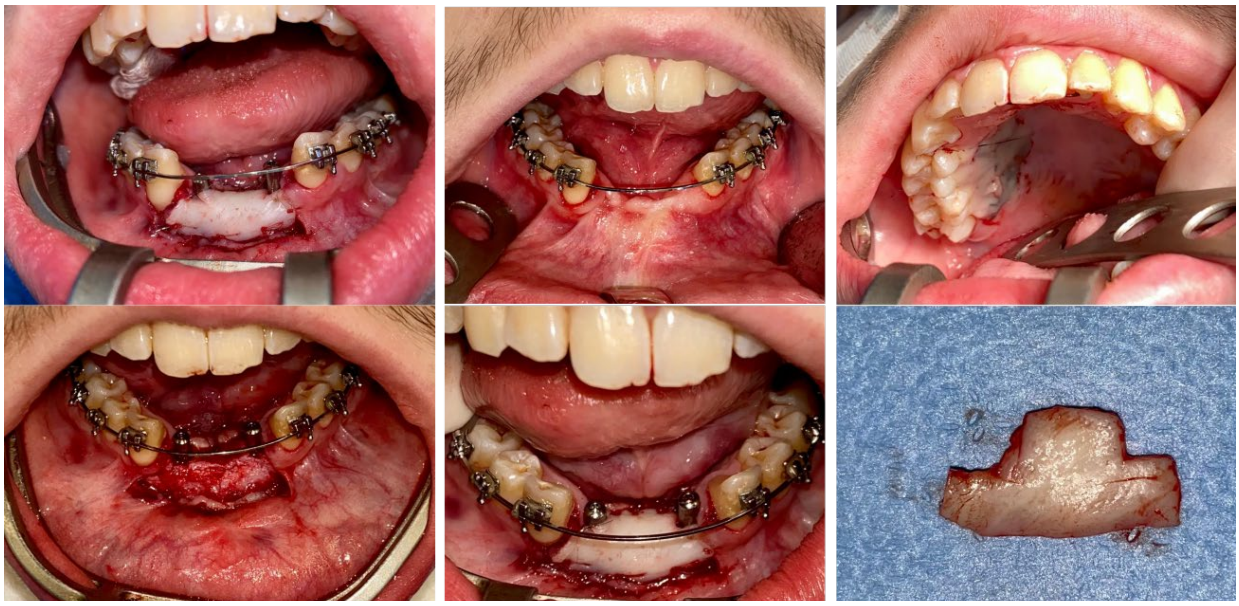

Figure 5. Intraoperative views showing **(A)** placement of an autogenous bone graft and soft tissue reconstruction and **(B)** subsequent installation of dental implants for definitive rehabilitation.

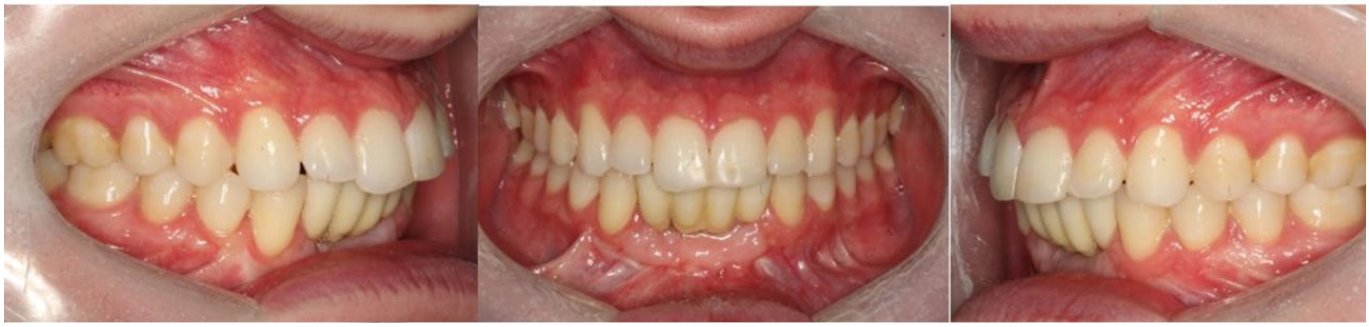

Figure 6. Final intraoral and extraoral aspect, seventeen years after treatment.

human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

DISCUSSION

This case report illustrates an aggressive central giant cell granuloma (CGCG) in a pediatric patient, presenting as facial asymmetry, swelling, and a 6 cm expansile osteolytic lesion of the mandible, typical features of this pathology[8,12]. The lesion's one-year duration without symptom improvement after conservative management highlights its aggressive behavior, a common finding in pediatric cases requiring timely surgical intervention[13,14]. Although the lesion was asymptomatic aside from swelling and asymmetry, systemic symptoms such as tumor-induced osteomalacia, caused by elevated fibroblast growth factor 23 (FGF23), have been reported in rare cases of CGCG[15].

Radiological evaluation revealed an expansile osteolytic lesion with cortical rupture, consistent with aggressive CGCG. These lesions may appear as unilocular or multilocular radiolucencies with cortical thinning or perforation, features essential for accurate surgical planning and prognosis estimation[12,16]. In this case, computed tomography was crucial to assess lesion extent and cortical integrity, guiding conservative surgery. The presence of internal hyperdense areas, as observed in this case, is frequently associated with hemorrhage or reactive bone, findings commonly reported in aggressive variants.

Histopathological analysis confirmed the diagnosis, showing multinucleated giant cells within a fibrous stroma with hemosiderin deposits, a hallmark of CGCG.

These findings are critical to differentiate CGCG from other giant cell–containing lesions such as brown tumors of hyperparathyroidism or giant cell tumors[8,17]. Differential diagnosis is particularly important in pediatric patients, in whom systemic conditions such as hyperparathyroidism must be excluded.

Several studies have demonstrated mutually exclusive activating mutations in KRAS, FGFR1, or TRPV4 within the proliferative mononuclear component, reinforcing the concept that CGCG represents a neoplastic rather than reactive process[18,19]. These mutations activate the MAPK pathway and may explain the aggressive clinical behavior observed in some cases. In addition, DNA methylation profiling has emerged as a diagnostic adjunct, demonstrating the ability to distinguish sporadic CGCG from other giant-cell–rich mimickers, such as aneurysmal bone cyst and giant cell tumor of bone, further supporting the biological distinctiveness of CGCG in challenging diagnostic scenarios[20].

Initial management with intralesional corticosteroid injections was unsuccessful, demonstrating the variability of response to non-surgical therapies, particularly in aggressive lesions. Surgical conservative treatment, including extraction of involved teeth, was necessary to achieve disease control. This aligns with studies showing that corticosteroid therapy may be less effective in cases presenting rapid growth, cortical perforation, or significant root involvement[21-23].

Intralesional corticosteroids, calcitonin, interferon-α, and bisphosphonates have demonstrated heterogeneous responses, and standardized treatment protocols remain lacking[24]. Denosumab, a RANKL inhibitor, has shown substantial radiographic and clinical responses in aggressive or recurrent CGCG in adults; however, its use in pediatric patients remains controversial due to concerns regarding skeletal maturation disturbances, rebound hypercalcemia, and insufficient long-term safety data[25]. The lack of response to corticosteroid therapy in the present case is consistent with studies indicating that large, rapidly expanding lesions with cortical perforation are less likely to respond to non-surgical pharmacologic strategies[24].

Postoperative mandibular fracture was a notable complication, reflecting the extensive bone involvement and fragility. Conservative management until consolidation, as performed here, is consistent with recommendations to minimize permanent morbidity and preserve function, underscoring the importance of multidisciplinary follow-up[16,17]. The long-term rehabilitation strategy, including orthodontic treatment, fixed prosthetics, and alveolar ridge reconstruction with autogenous bone grafting for implant placement and free gingival graft, illustrates comprehensive patient-centered care aimed at restoring aesthetics and function, especially in young patients with growth potential[21,26].

Recent multicenter studies have emphasized the importance of individualized treatment planning for CGCG, integrating clinical, radiologic, and biological factors to guide therapeutic decision-making. A 2025 European multicenter cohort demonstrated that long-term monitoring — preferably beyond five years — is essential due to the possibility of late recurrence regardless of treatment modality[27].

The absence of recurrence after 10 years emphasizes the effectiveness of the combined surgical and rehabilitative approach, although long-term follow-up remains essential given the reported 15-20% recurrence rate in aggressive CGCGs[14]. Continuous clinical and tomographic monitoring enables early detection and management of potential recurrences or complications, improving patient prognosis.

Understanding the molecular mechanisms involved in CGCG pathogenesis, such as mutations in the MAPK pathway and the role of RANKL, opens avenues for targeted therapies and personalized treatment plans, which may reduce the need for invasive surgery in the future[2,4,28]. Taken together, these molecular insights and evolving therapeutic strategies underscore the need for continued refinement of diagnostic and treatment guidelines for CGCG, particularly in pediatric populations. Until stronger prospective evidence becomes available, conservative surgery followed by vigilant long-term surveillance remains the most reliable approach for aggressive CGCG in children[18,27].

CONCLUSION

This case highlights the clinical challenges of managing aggressive central giant cell granulomas in pediatric patients. The failure of conservative corticosteroid treatment necessitated surgical intervention, which successfully controlled the disease and allowed for long-term rehabilitation and functional recovery. Comprehensive follow-up over ten years demonstrated no recurrence, emphasizing the importance of multidisciplinary care and vigilant monitoring. As advances in molecular understanding progress, targeted therapies may eventually complement or reduce the need for surgical intervention; however, surgery remains the most reliable approach in aggressive pediatric CGCG at present.

AUTHORS' CONTRIBUTIONS

DMAO: Conceptualization, Data curation, Writing – original draft. LLTS: Data curation, Writing – original draft. RNL: Writing – review & editing. EPS: Writing – review & editing. TBB: Writing – review & editing. MSNAM: Writing – review & editing. CALP: Writing – review & editing. ACR: Supervision, Writing – review & editing.

CONFLICT OF INTEREST STATEMENT

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Competing interests: The authors have no relevant financial or non-financial interests to disclose.

Ethics approval: Informed consent was obtained from the patient. The manuscript did not require ethical approval. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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