Idle gossip about validity of intralesional steroid injection in treating central giant cell granuloma

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Abstract
Treating central giant cell granuloma (CGCG) via intralesional injection of steroids was proven effective in some cases. Later, clinicians have preferred this treatment modality to surgical intervention for it avoids gnathic/bony disfigurement. Advocating this non-surgical therapy, several papers and reviews have recommended putting it into action as the first line of treatment, alone or combined with other treatment options, especially in treating aggressive CGCG. Other authors have reported inaccurate information to validate this approach. This paper scrutinizes, in retrospect, the infelicities about treating CGCG via intralesional injection of steroids and concludes that intralesional steroid injection is useful ONLY in treating non-aggressive CGCG and peripheral giant cell granulomas.

Keywords: Triamcinolone, cushing’s disease, giant cells, central granuloma, intralesional injection, intralesional steroid, CGCG

Introduction
Central giant cell granuloma (CGCG) of the jaw is a lesion characterized histologically by multinucleated giant cells in a background of ovoid to spindle-shaped mesenchymal cells. Since the WHO has approved the successful attempts of treating central giant cell granuloma (CGCG) via intralesional injection of steroids in some cases [1], this treatment modality was promoted to be preferred to surgical intervention for it avoids gnathic/bony disfigurement [2]. Moreover, Osterne et al., [3] have conducted a would-be “meta-analysis” of 14 papers to highlight the efficacy of using intralesional injection of corticosteroid, especially intralesional triamcinolone acetonide (ITA), and to recommend its use for it is totally safe and non-invasive. Complicating matters, the duration of recruiting ITA in treating has ranged from weeks to years with determining no standards [3].

Discussion
Recently, non-surgical treatment of CGCG has been advocated by some clinicians with varying degrees of success. Intralesional triamcinolone, alone or combined with denosumab, or interferon, was used to reverse the osteolytic effect of CGCG [4-7]. Other clinicians, however, have reported inaccurate information about treated cases of CGCG [8-10].

This paper aims at focusing light on some glaring errors in tackling the topic of non-surgical treatment of CGCG. First, the meta-analysis study was performed using a very limited number of cases. Its recommendation of recruiting intralesional steroid injection as the mainstay treatment cannot be accepted. Second, intralesional steroid injection failed to achieve the desirable effect in several cases. Thus, the intralesional steroid injection should be only a candidate. Third, fake cases of CGCG were reported and approved [8-10]. This allowed for fake serious complications of ITA to be considered. Fourth, overlapping between CGCG and giant cell tumor (GCT) thwarts the diagnostic issues and therapeutic implications. Tarasitano et al., [8] have reported unmatched clinical and radiological images for their treated case of CGCG. The provided panorex images of the submitted case show no trace of the orthodontic “METALLIC” wire and brackets which are present in the clinical picture. The CT images of the presented case do not show any metallic brackets either. At least, the initial radiographic pictures, if they belong to the described case, should have revealed such metallic brackets. This suggests that such radiograph images do not pertain to the giant-cell-containing figure.

El Hadidi [9,10] has reported treating a case by injecting, TWICE WEEKLY, what is equivalent to 30 mg of (ITA) for three months. There, the treatment was shifted to surgical removal after detecting a “cushinoid” appearance on the patient. Injecting 30 mg of ITA resulted in a monthly accumulation of 400 mg of ITA. According to Fredman and Tenenhaus [11], the optimal
dose of ITA should not exceed 30 mg per month in children. Thus, the authors may have iatrogenically induced an adrenal dysfunction but the patient, according to the manuscript, was never referred to any endocrinologist. The ACTH of the patient was, moreover, normal. Also, El Hadidi has turned a deaf ear to the Guidelines of the Endocrine Society’s Clinical Practice in diagnosing Cushing’s disease [12]. Such guidelines require basically ruling out any exogenous administration/ingestion of glucocorticoids and dictate running three screening tests to establish the diagnosis of Cushing’s diseases [13]. Dang et al., [14] have used El Hadidi’s case in their review. Therefore, there is no single unequivocal case of Cushing’s syndrome that has resulted from treating CGCG via ITA.

Accordingly, the literature, ad hoc non-surgical treatment of CGCG, should be underpinned with much care. There is no such a magic healing effect in treating CGCG via injecting ITA for weeks especially in treating aggressive CGCG. Also, glucocorticoids, calcitonin, and osteocalcin could not differentiate between aggressive and nonaggressive central giant cell lesions of the jaws [15].

Constantly, CGCGs and GCT of bone have been overlapped. Although both lesions share histopathological dominance of osteoclast-like giant cells, the giant cells, both in CGCG and in GCT, are not neoplastic. However, the neoplastic cells, which demonstrated high mitotic figures, are mononuclear. Moreover, CGCGs do not reveal, unlike GCT, high stromal cellularity or necrosis [16].

Cytogenetically, CGCGs do not demonstrate recurrent p. Gly34 Trp or p. Gly34 Leu mutations in the H3F3A gene [17]. However, the H3F3A mutation is evident, almost specifically, in GCT [18]. Immunohistochemically, the only salient differences between GCT and CGCG are expressed by neural and vascular markers. CGCGs demonstrate focal immunonegativity for SMA but GCT immunoreactivity for SMA is controversial. For vascular markers, CGCGs show moderate to strong expression for CD34 but GCT reveal no significant expression for the same marker. The intriguing fact about CGCG is that there is no reported metastatic CGCGs. However, GCT tends to metastasize [19].

**Conclusion**

To conclude, CGCGs must be differentiated from GCT. Therapeutically implicating, intralesional steroid injection is useful in treating non-aggressive central giant cell granulomas and peripheral giant cell granulomas.

**Competing interests**

The author declares that he has no competing interests.

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