SUPPLEMENTAL APPENDIX

a. Materials and Methods: search strategies, study selection, data extraction
b. Additional figure;
c. Additional table;
d. Publications included in the review;
e. Publications excluded for not having enough clinical, radiological and histological information;
f. Publications excluded due to the possibility of duplicated cases.
g. PRISMA checklist

a. Materials and Methods

Search strategies

An electronic search without time restrictions was undertaken in February 2018 in the following databases: PubMed/Medline, Web of Science, Science Direct, J-Stage, and Lilacs. The following terms were used in the search strategies:

("central giant cell lesion") OR ("central giant cell reparative granuloma") OR ("central giant cell granuloma") OR ("central giant cell") NOT ("elastolytic giant cell granuloma")


Study selection
The titles and abstracts of all reports identified through the electronic searches were read independently by the authors. For studies appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, the full report was obtained. Disagreements were resolved by discussion between the authors. The clinical and radiological aspects, as well as the histological description of the lesions reported by the publications were thoroughly assessed by one of the authors (R.S.G.) of the present study, in order to confirm the diagnosis of CGCL.

Data extraction

The review authors independently extracted data using specially designed data extraction forms. Any disagreements were resolved by discussion. For each of the identified studies included, the following data were then extracted on a standard form, when available: year of publication, number of patients, patient’s sex, age and race, follow-up period, for how long the lesion has been noticed before initial treatment, lesion location (maxilla/mandible), anterior/posterior location (three categories: [a] anterior: lesions in the incisors/canine region; [b] premolar region; [c] posterior: lesions in the molars/retromolar region), lesion size, perforation of cortical bone, locularity appearance in radiological exams (unilocular/multilocular), presence of radiopacities visible in the radiological exams, association of the lesion with a tooth, tooth displacement and/or tooth root resorption due to lesion’s growth, expansion of osseous region adjacent to the tumor, presence of clinical symptoms, classification in aggressive or non-aggressive lesion (see sub-item Analyses), treatment performed (curettage, debulking, enucleation, partial resection, resection with continuity, chemotherapy, radiotherapy, corticoid, calcitonin, interferon, monoclonal antibody, bisphosphonate), performance of curettage or peripheral osteotomy right after surgical excision, number of treatment steps, recurrence, recurrence period, number of recurrences, occurrence of spontaneous resolution, and blood exams (alkaline phosphatase, parathormone, calcium, phosphate). The lesion size was determined according to the largest diameter reported in the publications. Contact with authors for possible missing data was performed.
Figure S1. Study screening process.

2567 records identified through database searching

67 additional records identified through other sources

1765 records after duplicates removed

1238 records excluded

527 records screened

527 full-text articles assessed for eligibility

162 full-text articles excluded:
- 145 studies did not have enough clinical, radiological and histological information to confirm diagnosis of CGCL
- 17 studies were excluded due to the possibility of duplicated cases

365 studies included in qualitative synthesis

365 studies included in quantitative synthesis (statistical analysis)

c. Additional table
Table S1. Type of first treatment performed in lesions of different size ranges - for the lesions with available information about both treatment and size.

<table>
<thead>
<tr>
<th>Size (cm)</th>
<th>Curettage</th>
<th>Enucleation</th>
<th>Marginal resection</th>
<th>Segmental resection</th>
<th>Drug therapy</th>
<th>Debulking or radiotherapy</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-2.0</td>
<td>46 (48.4)</td>
<td>20 (21.1)</td>
<td>2 (2.1)</td>
<td>3 (3.1)</td>
<td>24 (25.3)</td>
<td>0 (0)</td>
<td>95 (100)</td>
</tr>
<tr>
<td>2.1-4.0</td>
<td>109 (41.1)</td>
<td>74 (27.9)</td>
<td>16 (6.1)</td>
<td>14 (5.3)</td>
<td>49 (18.5)</td>
<td>3 (1.1)</td>
<td>265 (100)</td>
</tr>
<tr>
<td>4.1-6.0</td>
<td>61 (35.7)</td>
<td>39 (22.8)</td>
<td>19 (11.1)</td>
<td>20 (11.7)</td>
<td>30 (17.5)</td>
<td>2 (1.2)</td>
<td>171 (100)</td>
</tr>
<tr>
<td>&gt;6.0</td>
<td>33 (44.6)</td>
<td>8 (10.8)</td>
<td>9 (12.1)</td>
<td>13 (17.6)</td>
<td>11 (14.9)</td>
<td>0 (0)</td>
<td>74 (100)</td>
</tr>
</tbody>
</table>

a Resection with continuity defect
b Therapy with a drug, which can be either corticoid, calcitonin, or monoclonal antibody

d. Publications included in the review

The 365 publications included in the review are listed below.


e. Publications excluded for not having enough clinical, radiological and histological information

The following excluded studies did not have enough clinical, radiological and histological information to confirm the diagnosis of central giant cell granuloma. The list also includes publications identified by other authors as presenting cases of these lesions, but which did not fulfill the inclusion criteria, as well as hybrid tumors containing parts of CGCG and a number of conditions that can present with lesions that histologically are indistinguishable from the CGCG (listed in the sub-item Inclusion and Exclusion Criteria of the text).


25


f. Publications excluded due to the possibility of duplicated cases

The following studies were excluded due to the possibility of duplicated cases, usually originated from clinical series from the same service or University.


### g. PRISMA checklist

#### PRISMA 2009 Checklist

<table>
<thead>
<tr>
<th>Section/topic</th>
<th>#</th>
<th>Checklist item</th>
<th>Reported on page #</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TITLE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Title</td>
<td>1</td>
<td>Identify the report as a systematic review, meta-analysis, or both.</td>
<td>Title</td>
</tr>
<tr>
<td><strong>ABSTRACT</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Structured summary</td>
<td>2</td>
<td>Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria; participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.</td>
<td>Abstract</td>
</tr>
<tr>
<td><strong>INTRODUCTION</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rationale</td>
<td>3</td>
<td>Describe the rationale for the review in the context of what is already known.</td>
<td>Introduction</td>
</tr>
<tr>
<td>Objectives</td>
<td>4</td>
<td>Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).</td>
<td>Introduction</td>
</tr>
<tr>
<td><strong>METHODS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protocol and registration</td>
<td>5</td>
<td>Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.</td>
<td>N/A</td>
</tr>
<tr>
<td>Eligibility criteria</td>
<td>6</td>
<td>Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.</td>
<td>Inclusion and Exclusion Criteria</td>
</tr>
<tr>
<td>Information sources</td>
<td>7</td>
<td>Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.</td>
<td>Search strategies</td>
</tr>
<tr>
<td>Search</td>
<td>8</td>
<td>Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.</td>
<td>Search strategies</td>
</tr>
<tr>
<td>Study selection</td>
<td>9</td>
<td>State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).</td>
<td>Study selection</td>
</tr>
<tr>
<td>Data collection process</td>
<td>10</td>
<td>Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.</td>
<td>Data extraction</td>
</tr>
<tr>
<td>Data items</td>
<td>11</td>
<td>List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.</td>
<td>Data extraction</td>
</tr>
<tr>
<td>Risk of bias in individual studies</td>
<td>12</td>
<td>Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.</td>
<td>N/A</td>
</tr>
<tr>
<td>Summary measures</td>
<td>13</td>
<td>State the principal summary measures (e.g., risk ratio, difference in means).</td>
<td>Data extraction and analyses</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>14</td>
<td>Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I² for each meta-analysis).</td>
<td>Data extraction and analyses</td>
</tr>
<tr>
<td>Section/topic</td>
<td>#</td>
<td>Checklist item</td>
<td>Reported on page #</td>
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<td>--------------------------------</td>
</tr>
<tr>
<td>Risk of bias across studies</td>
<td>15</td>
<td>Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).</td>
<td>Data extraction and analyses</td>
</tr>
<tr>
<td>Additional analyses</td>
<td>16</td>
<td>Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.</td>
<td>Data extraction and analyses</td>
</tr>
<tr>
<td>RESULTS</td>
<td></td>
<td></td>
<td>Literature search: Figure 51</td>
</tr>
<tr>
<td>Study selection</td>
<td>17</td>
<td>Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.</td>
<td>Descriptions of the Studies Tables 1-4</td>
</tr>
<tr>
<td>Study characteristics</td>
<td>18</td>
<td>For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.</td>
<td></td>
</tr>
<tr>
<td>Risk of bias within studies</td>
<td>19</td>
<td>Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).</td>
<td>N/A</td>
</tr>
<tr>
<td>Results of individual studies</td>
<td>20</td>
<td>For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.</td>
<td>N/A</td>
</tr>
<tr>
<td>Synthesis of results</td>
<td>21</td>
<td>Present results of each meta-analysis done, including confidence intervals and measures of consistency.</td>
<td>N/A</td>
</tr>
<tr>
<td>Risk of bias across studies</td>
<td>22</td>
<td>Present results of any assessment of risk of bias across studies (see Item 15).</td>
<td>N/A</td>
</tr>
<tr>
<td>Additional analysis</td>
<td>23</td>
<td>Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).</td>
<td>Not performed</td>
</tr>
<tr>
<td>DISCUSSION</td>
<td></td>
<td></td>
<td>Discussion</td>
</tr>
<tr>
<td>Summary of evidence</td>
<td>24</td>
<td>Summarize the main findings including the strength of evidence for each main outcome, consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).</td>
<td>Discussion</td>
</tr>
<tr>
<td>Limitations</td>
<td>25</td>
<td>Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).</td>
<td>Discussion</td>
</tr>
<tr>
<td>Conclusions</td>
<td>26</td>
<td>Provide a general interpretation of the results in the context of other evidence, and implications for future research.</td>
<td>Conclusion</td>
</tr>
<tr>
<td>FUNDING</td>
<td></td>
<td></td>
<td>Acknowledgements</td>
</tr>
<tr>
<td>Funding</td>
<td>27</td>
<td>Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.</td>
<td></td>
</tr>
</tbody>
</table>


For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).