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Granular cell tumors of the musculoskeletal system and peripheral nerves: A systematic review of clinical presentations, treatments, and outcomes

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Ipponi, E; D'Arienzo, A; Campo FR; Gentili, F; Cosseddu, F; Andreani, L; Parchi, PD.

Corresponding author:
Edoardo Ipponi

edward.ippo@gmail.com

Author Affiliation:
University of Pisa.

ADMINISTRATIVE INFORMATION

Support - None.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 February 2026 and was last updated on 9 February 2026.

INTRODUCTION

Review question / Objective This systematic review aims to synthesize the available evidence on musculoskeletal and peripheral nerve granular cell tumors, with a specific focus on clinical presentations, treatments, and outcomes, to summarize current knowledge and identify persistent gaps that warrant future investigation.

Condition being studied Granular cell tumor (GCT), also known as Abrikossoff tumor, is an uncommon soft tissue neoplasm composed of polygonal to occasionally spindle-shaped cells with abundant eosinophilic, finely granular cytoplasm.

METHODS

Search strategy A comprehensive search of the PubMed, MEDLINE, EMBASE, Web of Science and Scopus databases using the search line (granular cell tumor) AND ((musculoskeletal) OR (Limb) OR (Shoulder) OR (Arm) OR (Elbow) OR (Forearm) OR (Wrist) OR (Hand) OR (Hip) OR (Thigh) OR (Knee) OR (Leg) OR (Ankle) OR (Foot) OR (Muscle) OR (Articulation)). All papers published between 1975 and 2025, available as of the 1st November 2025, were included in our research. All the original articles reporting on patients diagnosed with granular cell tumors - arising from the peripheral nerves, localized in the musculoskeletal apparatus, and in the upper or lower limb - that required surgical treatment were included. Three independent reviewers (E.I., A.D., F.R.C.) conducted the research separately. Only articles from peer-reviewed journals were included. The investigators separately reviewed each publication's abstract and then closely read all articles, extracting data to minimize selection bias and errors.
Inclusion criteria were (1) a confirmed histological diagnosis of granular cell tumor, (2) a surgical treatment aimed to eradicate the neoplasm, and (3) data regarding the clinical presentation of the

disease or the oncological outcomes of treated patients. Exclusion criteria were (1) articles that did not mention or provide data on the surgical treatment, (2) articles that did not report on either patients' pre-operative clinical presentation or their postoperative outcome, (3) pre-clinical studies, (4) literature reviews without any new cases, and (5) papers written in languages other than English. During the review, authors also excluded (6) articles reporting on cases with diagnoses different than GCT, such as schwannoma or neurofibroma, and (7) cases whose lesions were localized solely in the skin or superficial subcutis so that neither the anatomical picture, the clinical presentation, nor the surgical treatment involved the musculoskeletal system. Conversely, cases in which the lesion or surgical treatment involved the muscular fascia or deeper layers were included.
All articles were initially screened for relevance based on title and abstract; articles without an abstract were excluded, and the full text was obtained if the abstract did not allow the investigators to assess inclusion and exclusion criteria. Considering the limited number of large-sized case series articles and the low level of evidence in the few available, we included in our study articles ranging from Level I to Level V, as well as detailed case reports.

Participant or population A comprehensive search of the PubMed, MEDLINE, EMBASE, Web of Science and Scopus databases using the search line (granular cell tumor) AND ((musculoskeletal) OR (Limb) OR (Shoulder) OR (Arm) OR (Elbow) OR (Forearm) OR (Wrist) OR (Hand) OR (Hip) OR (Thigh) OR (Knee) OR (Leg) OR (Ankle) OR (Foot) OR (Muscle) OR (Articulation)). All papers published between 1975 and 2025, available as of the 1st November 2025, were included in our research. All the original articles reporting on patients diagnosed with granular cell tumors - arising from the peripheral nerves, localized in the musculoskeletal apparatus, and in the upper or lower limb - that required surgical treatment were included. Three independent reviewers (E.I., A.D., F.R.C.) conducted the research separately. Only articles from peer-reviewed journals were included. The investigators separately reviewed each publication's abstract and then closely read all articles, extracting data to minimize selection bias and errors.
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Intervention All the original articles reporting on patients diagnosed with granular cell tumors - arising from the peripheral nerves, localized in the musculoskeletal apparatus, and in the upper or lower limb - that required surgical treatment were included.

Comparator None.

Study designs to be included Case series and case reports.

Eligibility criteria Inclusion criteria were (1) a confirmed histological diagnosis of granular cell tumor, (2) a surgical treatment aimed to eradicate the neoplasm, and (3) data regarding the clinical presentation of the disease or the oncological outcomes of treated patients. Exclusion criteria were (1) articles that did not mention or provide data on the surgical treatment, (2) articles that did not report on either patients' pre-operative clinical presentation or their postoperative outcome, (3) pre-clinical studies, (4) literature reviews without any new cases, and (5) papers written in languages other than English. During the review, authors also excluded (6) articles reporting on cases with diagnoses different than GCT, such as schwannoma or neurofibroma, and (7) cases whose lesions were localized solely in the skin or superficial subcutis so that neither the anatomical picture, the clinical presentation, nor the surgical treatment involved the musculoskeletal system.

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Information sources PubMed, MEDLINE, EMBASE, Web of Science and Scopus.

Main outcome(s) Forty-two articles describing 67 cases were included (50 females, 17 males). Tumors showed benign behavior in 50 cases and malignant features in 17 cases. The mean largest tumor diameter was 27 mm, and malignant lesions were significantly larger than benign ones. Thirty-one lesions were located in the lower limbs, 25 in the upper limbs, and 11 had central musculoskeletal localizations. Swelling was the most common presenting symptom (94%), followed by pain (41%). Surgical excision was performed in all patients except one, who underwent primary amputation. Adjuvant chemotherapy or radiotherapy was sporadically used in malignant cases (two cases each). Among the 15 malignant cases with reported oncological follow-up, eight (53%) developed distant metastases and two (13%) also experienced local recurrence, while the remaining cases were continuously disease-free (CDF). Only one benign GCT recurred (2%), whereas all others remained CDF (98%).

Quality assessment / Risk of bias analysis The Joanna Briggs Institute (JBI) Critical Appraisal tools were used to assess heterogeneity in study design and methodology across the selected cohort studies and case series, and to evaluate their quality for inclusion in this systematic review.
Dedicated bias assessment for randomized studies was not performed as there were no randomized trials.

Strategy of data synthesis Statistical analyses were carried out using Stata SE 13.1 (StataCorp LLC, College Station, TX, USA). The complication and local recurrence rates of each study were noted or calculated. The size, heterogeneity, and retrospective nature of the included studies discouraged us from conducting a meta-analysis. The rarity of bone tumors and the relative paucity of studies on the topic led to the inclusion of diverse study types, resulting in heterogeneous data on clinical presentation, tumor location and size, and therapeutic approaches. Furthermore, the focus of each study may vary, potentially affecting the reported outcomes. The absence of large cohorts or complex study designs precluded the use of Egger tests to assess the risk of publication bias. Generative artificial intelligence (GenAI) (ChatGPT 5.2, OpenAI Inc., San Francisco, CA, USA) has been used to generate graphics from our collected data and to double-check the statistical analysis. Tables and mean data.

Subgroup analysis Malignant and benign lesions were evaluated separately in terms of size, surgical treatment and oncological outcomes.

Sensitivity analysis None.

Country(ies) involved Italy.

Keywords Soft tissue tumor; Symptoms; Pain; Swelling; Recurrence; Metastasis; Survival.

Contributions of each author
Author 1 - Edoardo Ipponi.
Author 2 - Antonio D'Arienzo.
Author 3 - Francesco Rosario Campo.
Author 4 - Fabrizia Gentili.
Author 5 - Fabio Cosseddu.
Author 6 - Lorenzo Andreani.
Author 7 - Paolo Domenico Parchi.