Low-Grade Chondrosarcomas: Diagnosis and Treatment

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Abstract

Background: Multiple parameters are needed to distinguish between enchondroma and low-grade chondrosarcoma (LGCS). This study aimed to investigate the diagnosis, surgery type according to bone type, recurrence rates, and complications of LGCS in the appendicular and axial skeletons.

Methods: A total of 52 surgically treated patients with LGCS, between March 2007 and May 2019, were retrospectively examined. Following diagnosis, the patients were operated on with intralesional curettage for long bones or wide local excision (WLE) for axial bones. The retrieved data included demographics, tumor location, surgical treatment type, local adjuvants, complications, and Musculoskeletal Tumor Society scores.

Results: The final cohort included 52 patients (52 tumors; 35 female and 17 male). The male:female ratio was 1:2. The mean age was 44 ± 17 years. Forty of the tumors were treated with intralesional procedures (all with a high-speed burr and phenol), 6 with autograft, 8 with allograft, and 28 with cement augmentation, while 7 were treated with WLE.

Conclusions: The use of phenol as an adjuvant may reduce recurrence rates. Using a putty graft alone may result in nonunion. Applying a thin layer of putty on the cementum can create callus tissue on the cementum. Even in the upper limb, plate and screw fixation should be used to prevent fractures in metaphyseal–diaphyseal curettages.

Background:

Chondrosarcoma (CS) has three types according to histological grades determined by atypia, mitosis, and cellularity [1]. CS accounts for a quarter of malignant bone tumors; it is also the second most common tumorafter osteosarcoma [2,3]. The most used treatment for high-grade CS is wide resection because of resistance to chemotherapy and radiation [4,5,6]. Although it is relatively easy to diagnose a high-grade CS, multiple parameters are needed to distinguish between enchondroma and low-grade chondrosarcoma (LGCS) [7,8]. Grade I or LGCS is a primary bone tumor with low malignant potential [9,10]. However, in the case of a low-grade CS, the interobserver compatibility decreases even among experienced pathologists [7,11]. Especially in the distinction between enchondroma and grade 1 CS, radiology becomes a determinant [8]. In addition, recurrence rates are reported to be higher with intralesional procedures in the axial skeleton compared with the appendicular bones. Therefore, some authors recommended wide resection for the pelvis and other axial bones [12,13]. Diagnosis and therefore treatment should be determined according to radiology, pathology, and clinical findings in this type of tumor [14]. Chemotherapy and radiotherapy have no place in CS, and hence proper treatment is surgery. The indications for surgery of a low-grade cartilaginous lesion are recurrent pain, growth, or endosteal scalloping. Albeit very rare, distant metastases are troublesome due to adjuvant resistance [15,16,17]. Unlike high-grade CS, the preferred protocol for low-grade chondrosarcoma (LGCS) comprises intralesional curettage and some adjuvants like phenol or cryotherapy. After curettage cement/bone

grafting used [18,19,20]. Therefore, higher recurrence rates reported in axial bones led some authors to recommend wide resection for LGCS in the pelvis and other axial bones [12,13]. This study was performed to investigate the diagnosis, surgery type according to bone type, recurrence rates, and complications of LGCS in the appendicular and axial skeletons.

Methods:

The study was performed by the ethical standards of the Declaration of Helsinki. All patients provided informed consent before inclusion in the study. After approval from the Institutional Review Board, 52 surgically treated patients with LGCS, between March 2007 and May 2019, were retrospectively examined using clinical, surgical, and radiographic records from the senior surgeon's operating room. A hand search of operating room logs was performed for the records with the following terms: "enchondroma," "low-grade chondrosarcoma," and "'grade 1 chondrosarcoma." The diagnosis of LGCS was made with the recent onset of emerging pain, endosteal scalloping in radiology, and significant uptake on single-photon emission computed tomography/computed tomography, and finally was confirmed with a postoperative pathology report. Sixty-nine patients (69 tumors) were diagnosed with LGCS. Nine patients were lost to follow-up during a mean follow-up period of 2.9 years (range 2–5 years). All of them were treated with intralesional curettage ± cementation/graft or wide local excision (WLE). None of these had a postoperative complication. No local recurrence or metastases was confirmed in these nine patients. At the last follow-up, their MSTS score was 26.7 ± 2.3. Eight patients were lost to follow-up due to death for other reasons (last follow-up at 32.3 ± 5.7 months). Therefore, the final cohort included 52 patients (52 tumors), with a minimum follow-up of 24 months and a mean follow-up of 72.92 ± 39.13 months. Following diagnosis, the patients were operated on with intralesional curettage (IC) for long bones or WLE for axial bones. For IC, allograft/cancellous autograft or cement was used. IC was supported with a high-speed burr and phenol as adjuvant therapy. Following surgery, all patients received physiotherapy to obtain a full range of motion. The histopathologic diagnosis was made using the principles of Mirra et al., and the radiologic diagnosis was made using the principles of Murphey et al. [1,21]. The radiologic criteria were the evidence of endosteal scalloping, absent of cortical destruction/soft tissue mass on magnetic resonance imaging (MRI). On scintigraphy, the uptake of the lesion was greater than the spina iliaca anterior superior. The indications for surgery were radiographically low-grade cartilage tumor with pain/progressive enlargement or endosteal scalloping. The diagnosis was made with multidisciplinary approach including a musculoskeletal radiologist and pathologist. The retrieved data included demographics, tumor location, surgical treatment type, local adjuvants, complications, Musculoskeletal Tumor Society (MSTS) scores [22], and local recurrence. The follow-up was done every 3 months for the first year and annually for the following years. No patient had a metastatic disease or died because of chondrosarcoma.

Statistical analysis: Descriptive statistics were used to describe continuous variables (mean, standard deviation, minimum, median, and maximum). Independent variables with normal distribution were compared using the Student *t* test, while independent variables with non-normal distributions were compared using the Mann–Whitney *U* test. Two independent variables with non-normal distribution were

compared using one-way analysis of variance, while two independent variables with normal distribution were compared using the Kruskal–Wallis test. The chi-square or Fisher exact test was used to examine the relationship between categorical variables. Pearson correlation was used in correlation analyses for normally distributed variables, while Spearman's rho correlation analysis was used for continuous variables with a non-normal distribution. Analyses were performed using the MedCalc Statistical Software (version 12.7.7) (MedCalc Software BVBA, Ostend, Belgium; http://www.medcalc.org).

Results

The final cohort included 52 patients (52 tumors; 35 female and 17 male). The male:female ratio was 1:2. The mean age was 44 ± 17 years. The mean tumor size was 6.2 ± 2.8 cm at the greatest dimension. Forty-seven lesions involved the appendicular skeleton, and five involved the axial skeleton. Forty of the tumors were treated with intralesional procedures (all with a high-speed burr and phenol), 6 with autograft, 8 with allograft, and 28 with cement augmentation, while 7 were treated with WLE. No augmentation or implants were used for patients who underwent WLE. The mean follow-up was 72.92 ± 39.13 months (range: 24–171 months). One local recurrence occurred after 2 months from the initial surgery, which was in proximal humerus treated with re-curettage, high-speed burr, phenol, and cementation with plate fixation (Fig. 1). No other recurrence, including long-term follow-up, was seen in this series. Also, no metastatic disease was reported. The mean MSTS score at the final follow-up was 28.7 ± 1.7. In one case, a proximal femur fracture was encountered after trephine biopsy and treated with nail fixation (Fig. 2). In another case, the lesion in the second proximal phalanx of the foot was treated with curettage and putty allograft. After 5 months, a fracture was encountered and treated conservatively (Fig. 3). In another patient, the lesion in the fifth proximal phalanx of the hand was treated with curettage + allograft + putty graft. After pain for 3 months, swelling, redness, and nonunion occurred. Debridement was made, and autograft from the iliac crest, which was harvested using a mosaicplasty needle, was placed. Union was achieved after 6 weeks from this second procedure (Fig. 4). Despite these complications, the putty graft over the cementum provides a periosteal shell in the early stage. One of the disadvantages of using cement is that it cannot be covered with the cortex. However, in our series, we planted putty demineralized bone matrix (DBM) over the cementum and obtained a thin cortical shell in all patients treated with putty over the cementum (Fig. 5). In one patient, severe lower limb deformity due to multiple enchondromatosis was found. LGCS in proximal tibia treated with curettage and epiphysiodesis was made to contralateral epiphysis with eight plates (Fig. 6). Another six complications were also reported. In four patients, superficial wound infections were treated conservatively. Two patients who underwent an iliac wing wide resection experienced permanent limping due to gluteal insufficiency. These patients did not accept any other surgery. One case with a fourth proximal phalanx lesion in the hand was admitted with a pathological fracture. Secondary chondrosarcoma to osteochondroma was encountered in seven patients (13%). Further, 27 (52%) had scalloping and 14 (27%) cortical destruction. No other complication was encountered during the long-term follow-up (Table 1).

Discussion

Enchondroma and LGCS are categorized in the World Health Organization classification of bone and soft tissue guide as atypical cartilaginous tumor/chondrosarcoma grade I [23]. LGCS is a locally aggressive musculoskeletal tumor with a slow-growing pattern and potential for recurrence [24, 25]. Differential diagnoses between enchondroma and LGCS can be confusing. Surgery is the main treatment option because chemotherapy and radiotherapy are not effective. Generally, curettage without adjuvant therapy (phenol, cryotherapy, and argon beam coagulation) for appendicular skeleton and wide resection for axial skeleton are the choices of treatment [26]. The type of adjuvant used are still controversial. The current literature mainly consists of retrospective case series. In a retrospective series of surgically treated 164 patients with LGCS, 5 (3%) had distal metastases and 21 (13%) had a local recurrence. It was concluded that the local recurrence in long bones was associated with shorter overall survival and might indicate a more aggressive tumor [27]. Dierselhuis et al. reported 108 LGCS cases. They have treated patients with curettage and phenol as adjuvant. Mean follow-up was four years. In their series, no local recurrence was found. They reported five residual tumors. They concluded that residual tumors did not grow continuously and affect overall survival [24]. Shemesh et al. reported 2 (6%) patients with a local recurrence in their series of 33 patients. One of them had a recurrence after 2.9 years despite a wide resection [28]. The local recurrence was reported in several studies ranging between 2 months and 9 years after the initial treatment [20, 29]. The limitations of the present study were relatively small numbers of patients, patients lost to follow-up, and various types of graft/cement options. DBM powder is an osteoinductive and osteoconductive material. However, it is not stabile as cement or graft. [30].

In a pilot study, authors compared the DBM putty and bone marrow for treating long-bone fractures. They achieved complete union with DBM in 90% of patients (9/10). However rate was 75% (6/8) on the autograft side [31]. Several studies noted the efficacy of new-generation bone substitutes, but few studies evaluated their safety. Local complications rates were reported lowly. However, in a recent systematic review, immune system sensitisation rate with allografts was reported as 48% [32].

Eleswarapu et al. investigated the DBM and rhBMP-2 on 43 patients. Follow up time was 24 months. In rhBMP-2 group radiographic complication rate was 33% (7/21). However in DBM side complication rate was zero [33]. Despite these positive findings of DBM, two patients had complications in our series. One of them had nonunion of a foot phalanx in 5 months, and another had an inflammatory reaction that had to be debrided in the first 2 months.

Secondary chondrosarcoma may arise from the cartilaginous cap of an osteochondroma [34]. Osteochondroma may occur as soliter or multiple (hereditary) [35, 36]. Malign transformation rate of a sporadic lesion is < 1%. In multiple lesions this rate rises to 1–3% [37].

Andrea et al. reported 17 secondary chondrosarcomas transformed from sporadic osteochondromas. They found homozygous deletions of Exostosin (EXT1/2) [38]. The prevalence rate of chondrosarcoma secondary to osteochondroma in the present study was remarkably 14 in patients with multiple osteochondromatosis in our series.

Conclusions

The use of phenol as an adjuvant may reduce recurrence rates. Using putty graft alone may result in nonunion. Applying a thin layer of putty on the cementum can create callus tissue on the cementum. Even in the upper limb, a plate and screw fixation should be used to prevent fractures in metaphyseal–diaphyseal curettages. Limping due to abductor insufficiency is a frequent complication in pelvic wide resections. Further larger series with a longer follow-up are needed for choosing graft/cement and adjuvant type.

Declarations

Conflict of Interest: None.

Funding: None.

Consent for publication: Permissions were obtained from the patients.

Acknowledgements: Not applicable.

Ethics approval and consent to participate: This study was approved by the local ethical committee of Haydarpasa Numune Training and Research Hospital and informed consent has been taken from all participants. All methods were carried out in accordance with a guideline based on the CARE guidelines for case reports and case series.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions:

OE: Conception or design of the work, data collection and data analysis with interpretation.

SD: Data collection.

EK: Data collection.

GA: Data collection.

VG: Drafting the article critical revision of the article and final approval of the version to be published.

All authors read and approved the final manuscript.

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Tables

Due to technical limitations, table 1 is only available as a download in the Supplemental Files section.

Figures

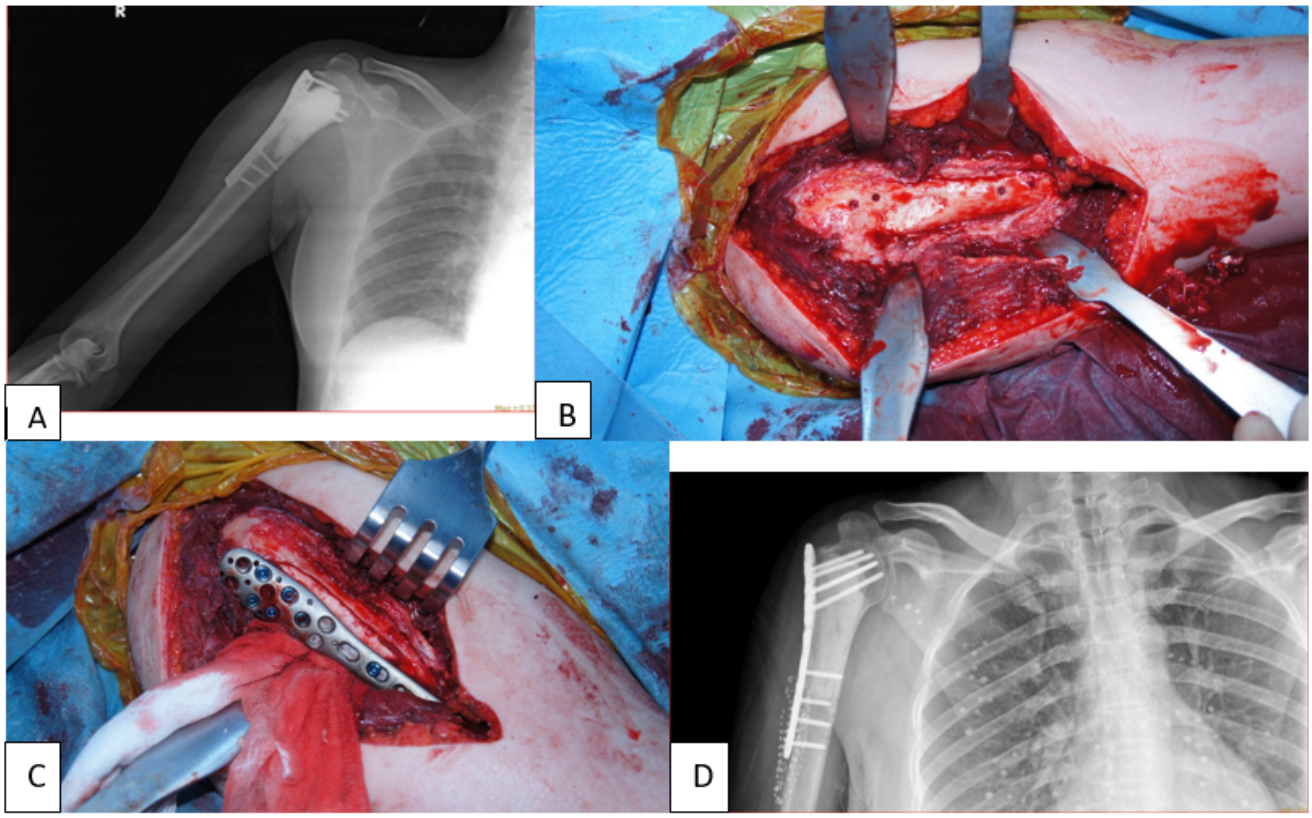

Figure 1. Patient with a recurrence. (A) Postoperative x-ray after the initial procedure. (B) Intraoperative image shows the recurrence focus beneath the plate. (C) After curettage and plate fixation. (D) X-ray after second intervention.

Figure 1

See image above for figure legend.

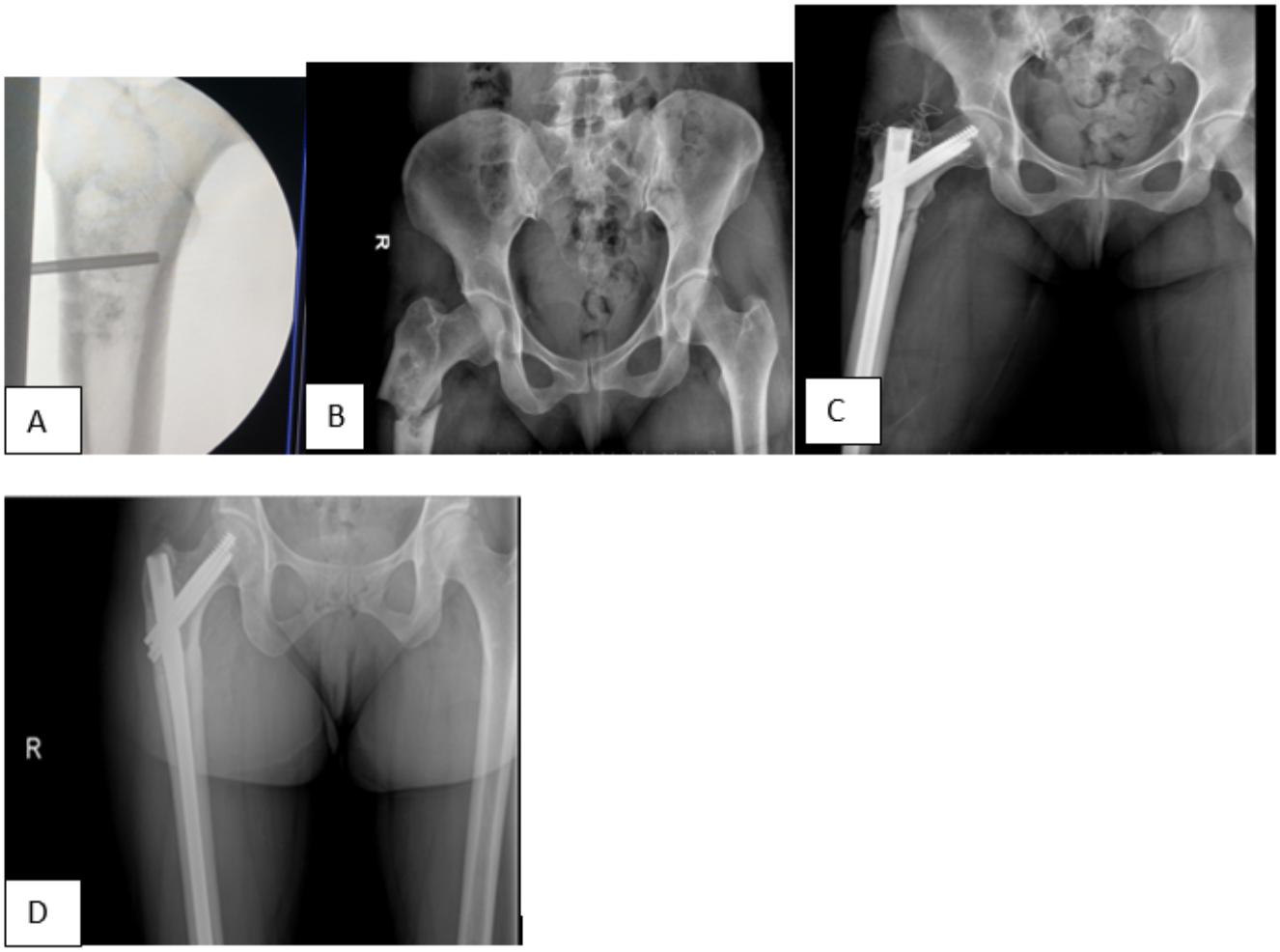

Figure 2. (A) Biopsy fluoroscopy image of a femur proximal lesion. (B) Femur proximal fracture 10 days after the biopsy. (C) Fixation with an antegrade femur nail. (D) X-ray shows bone union.

Figure 2

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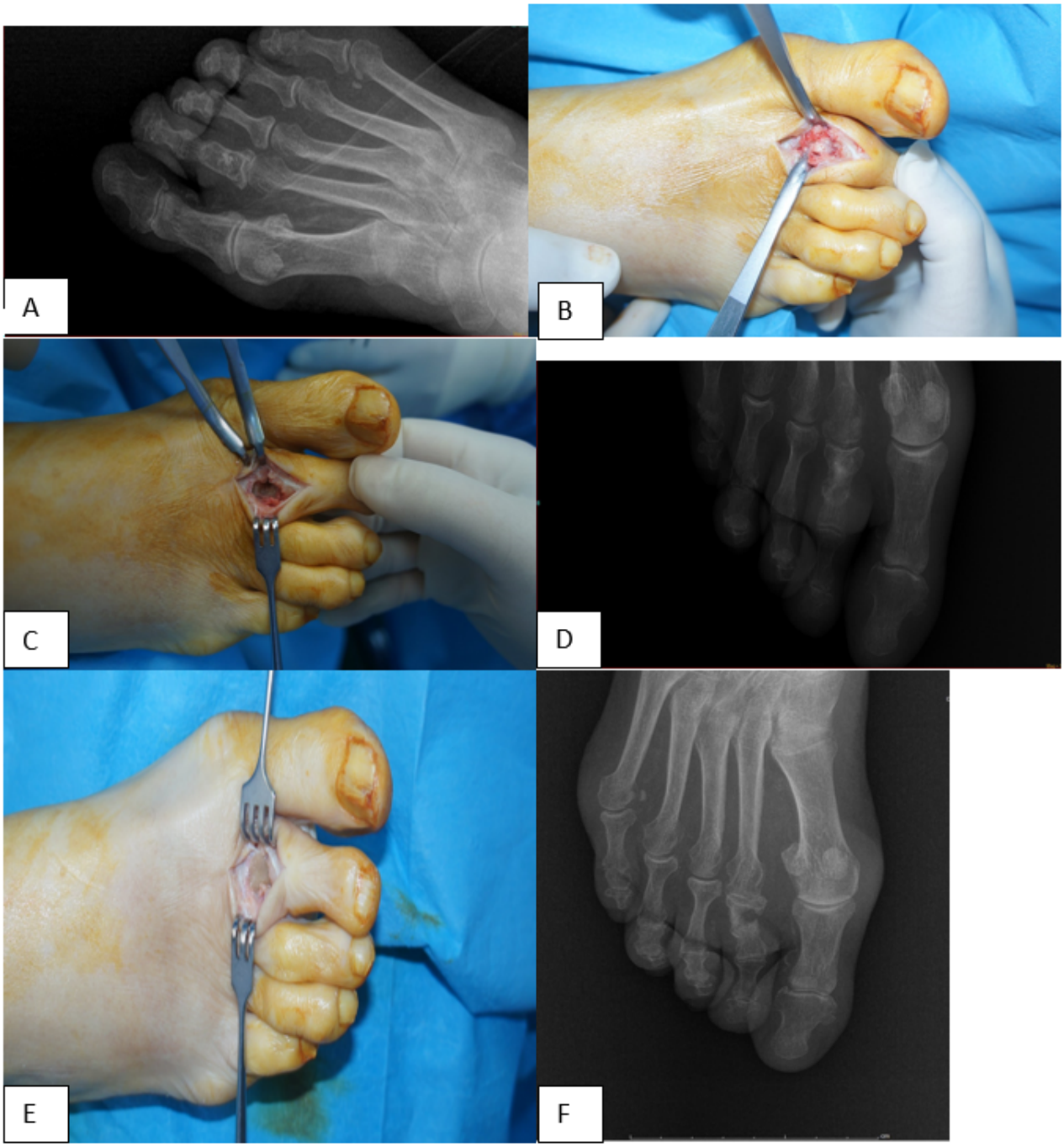

Figure 3. (A) LGCS at the second proximal phalanx. (B, C, and E) Intralesional curettage and pathological fracture. (D) Postoperative first day x-ray. (F) Fifth-month x-ray with nonunion.

Figure 3

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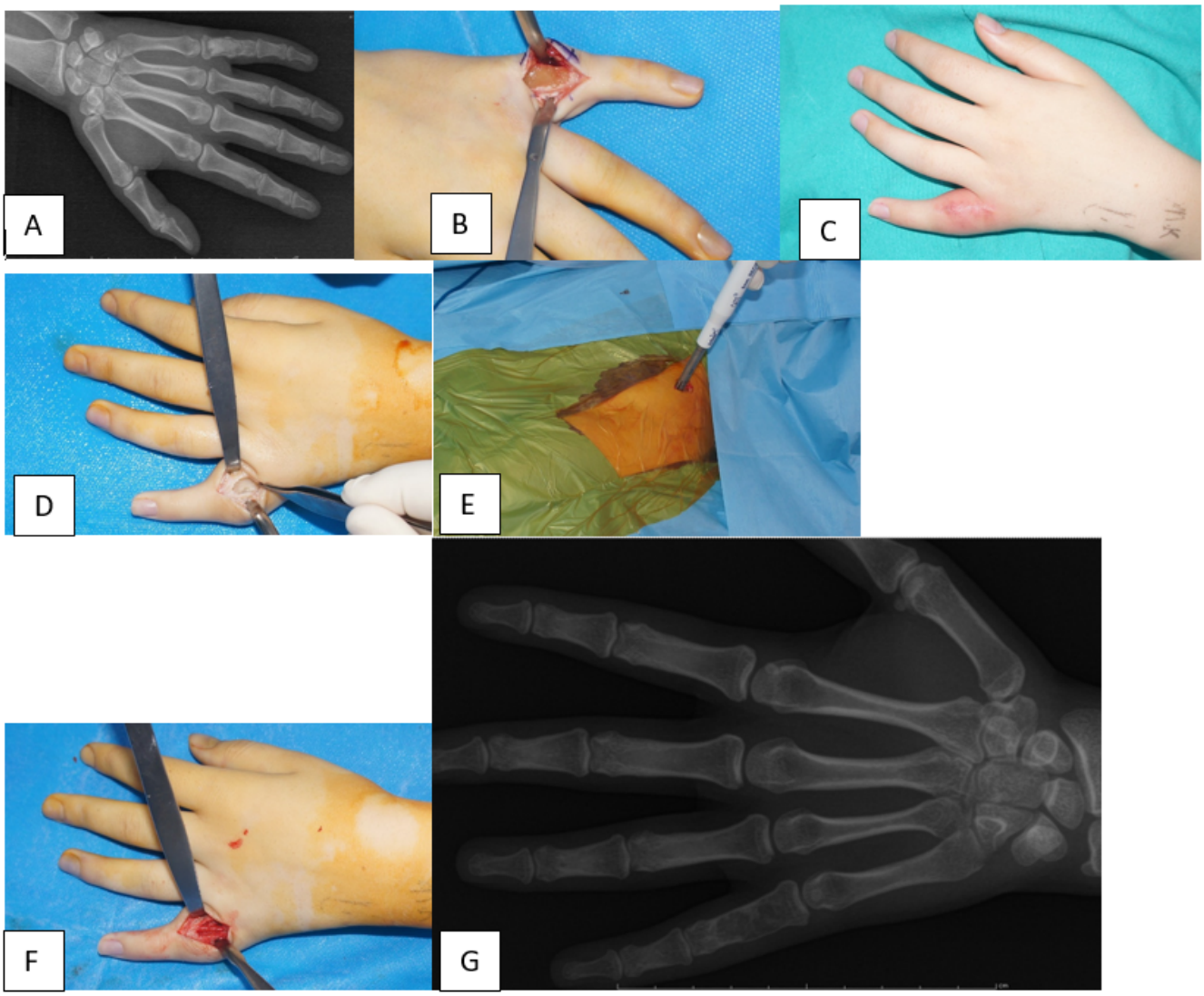

Figure 4. (A) LGCS in the fifth proximal phalanx. (B) Putty after curettage. (C) Inflammatory reaction after 1 month due to putty DBM . (D) Debridement. (E) Percutaneous iliac autograft harvesting with a mosaicplasty blade. (F) Autograft settled to the defect properly. (G) Postoperative x-ray.

Figure 4

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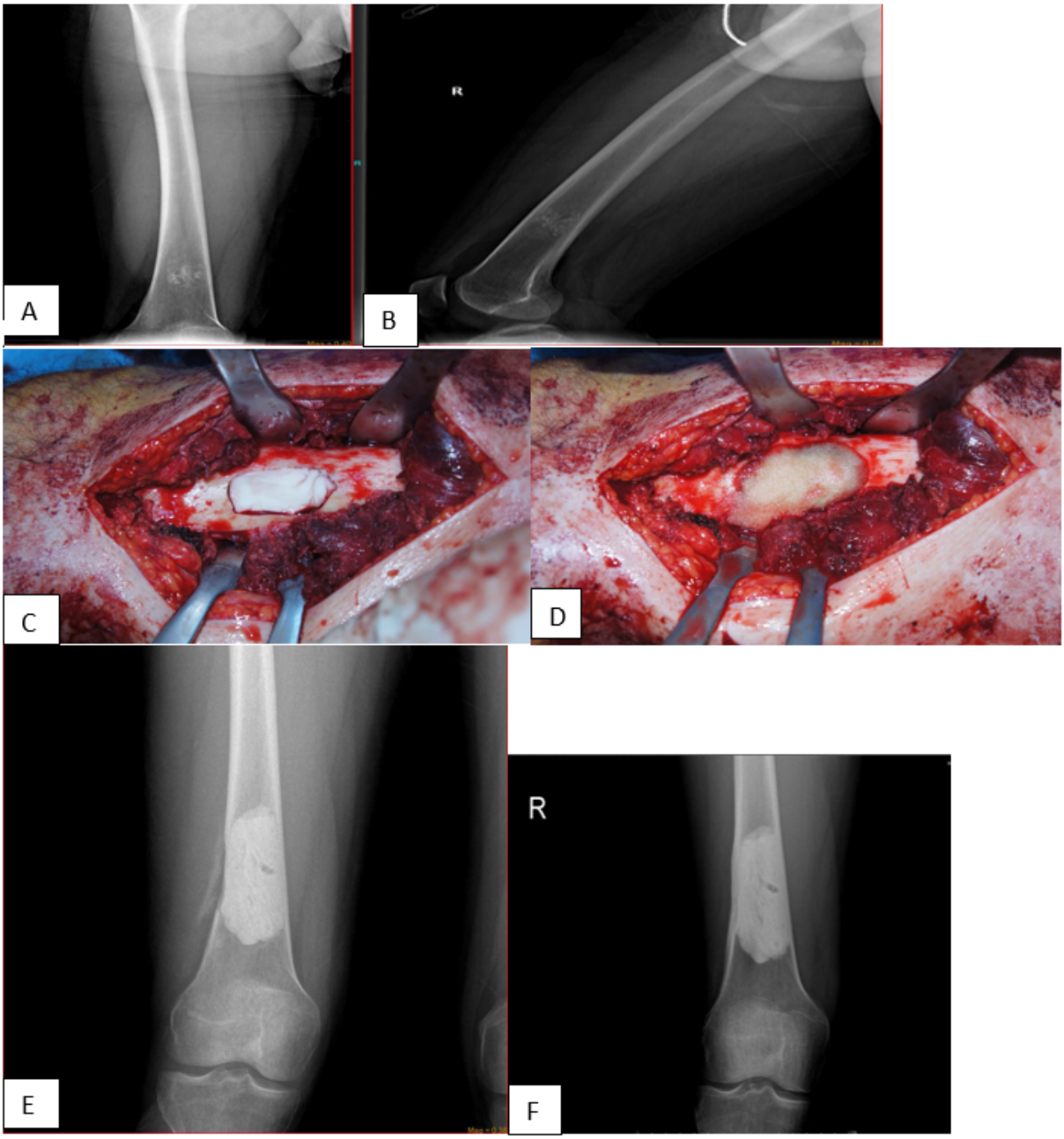

Figure 5. (A and B) AP and lateral x-rays of a 42 years old, male patient. (C) Curettage and cementation. (D) Putty allograft planting over the cementum. (E) Two months after the procedure. Cortical shell started to appear. (F) Three years after the index procedure. A new cortical bone formed and covered the cementum.

Figure 5

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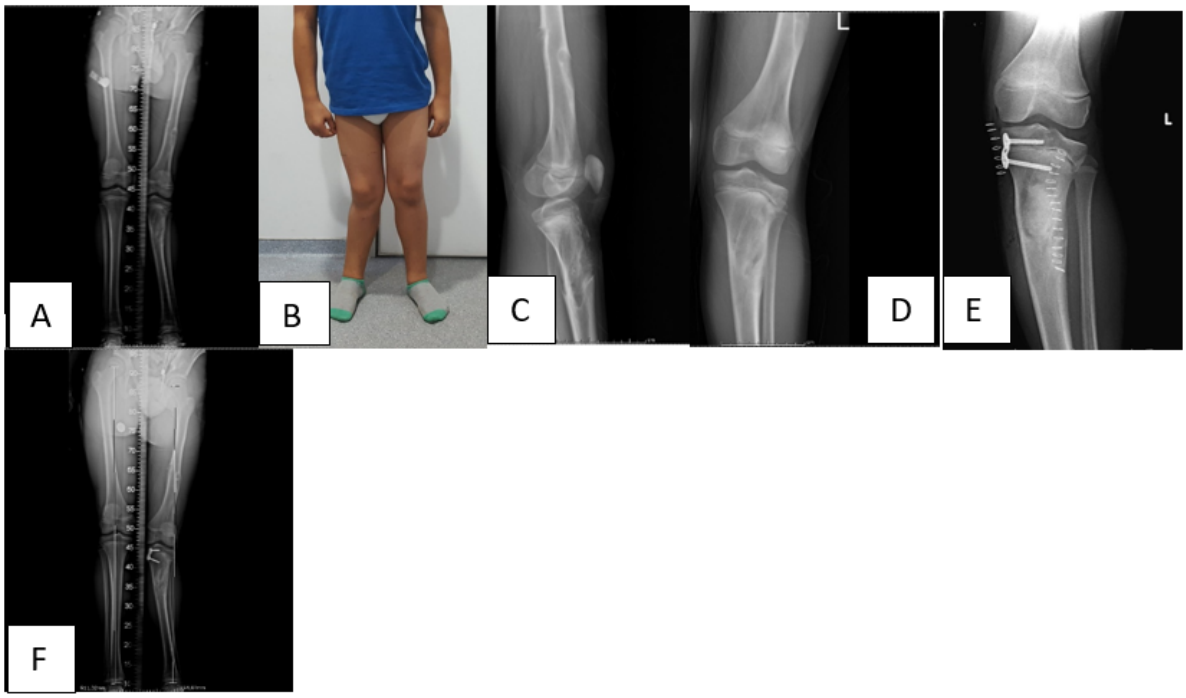

Figure 6. (A) Deformity and limb length discrepancy due to multiple enchondromatosis. (B) Clinical deformity. (C) Lateral x-ray. (D) AP x-ray. (E) Curettage and eight-plate epiphysiodesis. (F) Orthoroentgenogram after 6 months.

Figure 6

See image above for figure legend.

Supplementary Files

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- Table1.pdf