**Clinical Outcome of Parosteal Osteosarcoma**

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**Purpose:** The purpose of this study was to evaluate the oncologic outcomes of parosteal osteosarcoma (POS) and to ascertain the fates of patients after local recurrence (LR).

**Materials and Methods:** The authors retrospectively reviewed 22 POS patients with an average follow-up of 114 months (range: 36-235 months). Seven of the 22 patients were referred after LR. There were 17 Stage IB and 5 Stage IIB (G2, 2; dedifferentiation, 3). Tumors were located in the femur (11) and in other locations (11). Initial surgical margins were wide in 10, marginal in 5, and intralesional in 7. Correlations between clinicopathologic variables and LR and clinical courses after LR were evaluated.

**Results:** The 10-year overall survival rate was 85.7%. Three (14%) patients developed distant metastasis and all of them succumbed to the disease. Nine (41%) patients developed LR. Tumor location, resection type, and surgical margin were found to be correlated with LR. At final follow-up, 7 of the 9 patients that experienced local failure achieved no evidence of disease.

**Conclusion:** A substantial risk of misdiagnosis exists, especially for POS in other than a femoral location. Recurrent tumor re-excision is possible in most cases; however, patients with an aggressive recurrence pattern deserve special attention.

**Key words:** parosteal osteosarcoma, local recur
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There were 8 males and 14 females. Patients ages ranged from 6 to 68 years (mean, 28 years). Seven of the 22 patients were referred for more than one local recurrence after surgery by other hospitals. Clinical data were obtained from the patient charts and medical records, preoperative roentgenograms, and pathology slides of consulting surgeon and pathologists. Radiographic imaging studies were available for all patients. Specific radiographic findings, including location, size, and the presence of medullary invasion and of a non-

Table 1. Patient Demographics and Treatment Outcomes

| Case number | Age/Gender | Anatomical site | Stage/Grade       | Medullary invasion | Soft tissue mass | Surgery               | Initial surgical margin | Recurrence | Outcome         | Follow up (months) |
|-------------|------------|-----------------|-------------------|-------------------|------------------|-----------------------|--------------------------|-------------|-----------------|-------------------|
| 1           | 20/M       | Distal femur    | IIB/dedifferentiated | +                 | +                | En bloc excision       | Wide                     | None        | CDF             | 98                |
| 2           | 21/F       | Proximal humerus | IIB/dedifferentiated | +                 | +                | En bloc excision       | Marginal                 | Local       | NED             | 209               |
| 3           | 22/M       | Distal femur    | IB/grade 1         | -                 | -                | Hemicortical excision  | Wide                     | None        | CDF             | 93                |
| 4           | 23/M       | Scapula         | IB/grade 1         | -                 | -                | En bloc excision       | Wide                     | None        | CDF             | 131               |
| 5           | 23/F       | Distal femur    | IB/grade 1         | -                 | -                | En bloc excision       | Wide                     | None        | CDF             | 84                |
| 6           | 23/F       | Proximal humerus | IB/grade 2         | +                 | +                | En bloc excision       | Marginal                 | Distant     | DOD             | 48                |
| 7           | 24/F       | Distal femur    | IB/grade 1         | -                 | -                | Hemicortical excision  | Marginal                 | None        | CDF             | 69                |
| 8           | 25/F       | Distal humerus  | IB/grade 1         | -                 | -                | Hemicortical excision  | Marginal                 | None        | CDF             | 112               |
| 9           | 27/F       | Distal femur    | IB/grade 1         | +                 | +                | En bloc excision       | Wide                     | None        | CDF             | 204               |
| 10          | 30/M       | Femur diaphysis | IIB/grade 1        | +                 | +                | Amputation             | Wide                     | None        | CDF             | 203               |
| 11          | 30/F       | Distal femur    | IIB/grade 1        | +                 | +                | Lumpectomy             | Wide                     | Local       | NED             | 94                |
| 12          | 34/M       | Proximal femur  | IB/grade 1         | -                 | -                | Lumpectomy             | Intralesional            | Local       | NED             | 235               |
| 13          | 34/M       | Distal tibia    | IB/grade 1         | +                 | +                | Lumpectomy             | Intralesional            | Local       | NED             | 73                |
| 14          | 37/M       | Distal femur    | IIB/grade 2        | +                 | +                | Hemicortical excision  | Marginal                 | Local/Distant| DOD             | 36                |
| 15          | 68/M       | Distal femur    | IIB/dedifferentiated | +                 | +                | Neck disarticulation   | Wide                     | None        | CDF             | 97                |
| 16*         | 6/F        | Talus           | IB/grade 1         | -                 | -                | Lumpectomy             | Intralesional            | Local       | NED             | 175               |
| 17*         | 18/F       | Proximal ulna   | IB/grade 1         | +                 | +                | Lumpectomy             | Intralesional            | Local       | NED             | 136               |
| 18*         | 18/F       | Distal femur    | IB/grade 1         | -                 | -                | Lumpectomy             | Intralesional            | Local       | NED             | 62                |
| 19*         | 27/F       | Proximal tibia  | IB/grade 1         | +                 | +                | Lumpectomy             | Intralesional            | Local       | NED             | 101               |
| 20*         | 31/F       | Proximal tibia  | IB/grade 1         | +                 | +                | Lumpectomy             | Intralesional            | Local       | NED             | 76                |
| 21*         | 37/F       | Proximal humerus | IB/grade 1         | -                 | +                | Lumpectomy             | Intralesional            | Local/Distant| DOD             | 49                |
| 22*         | 38/F       | Distal radius   | IB/grade 1         | -                 | +                | Lumpectomy             | Intralesional            | Local       | NED             | 104               |

*Referred patients.
CDF, continuous disease free; NED, no evidence of disease; DOD, dead of disease; AWD, alive with disease.
mineralized soft tissue mass, were noted. Locations of primary tumors were: femur (11), humerus (4), tibia (3), and one case each at talus, radius, ulna, and scapula. Tumor sizes ranged from 3 to 23 cm in maximum diameter (mean 7.1 cm). Nine (40.9%) patients had intramedullary tumor extension, and a non-mineralized soft tissue mass was observed in 11 (50%) patients by CT or MRI. Pathologic materials were analyzed to confirm the diagnoses. Five of the 7 referred patients were pathologically confirmed to have POS after intralesional excision and the other 2 were diagnosed to have a benign bone tumor at referral centers. Five of the 15 patients managed at our institute did not undergo biopsy and the remaining 10 patients underwent open biopsy. No patient showed metastasis at presentation, and no patient underwent initial chemo- or radiotherapy. Extent of surgery was decided by MRI or CT. Two types of resection methods were used: compartmental (en-bloc) resection and more conservative hemicortical resection. The indications for en-bloc resection were a large tumor, the presence of intramedullary invasion, and a local recurrence. Hemicortical resection was performed for small-to-moderate sized tumors with no intramedullary invasion. However, conservative resection was performed in two patients that underwent intralesional excision at another hospital. After surgery, surgical margins were evaluated using pathologic specimens: both bone and soft tissue margins were evaluated. A wide margin was defined as one with more than 3 millimeters of normal soft tissue and more than 2 centimeters of normal bone. Initial surgical margin was wide in 10, marginal in 5, and intralesional in 7 patients. Pathologic specimens were evaluated to determine the presence of high grade or dedifferentiated regions. The Musculoskeletal Tumor Society staging system was used to assess stage: Grade 1 lesions were assigned to Stage I and Grades 2 and 3 to Stage II. Dedifferentiation was defined as limited areas of high-grade tumor in a lesion that was predominantly low-grade. There were 17 Stage IB lesions and 5 Stage IIB lesions. Plain anteroposterior and lateral radiographic examinations were performed three monthly until 2 years, and bimonthly thereafter. Computed tomography of the chest and a whole body bone scan were performed bimonthly. For patients with lung metastasis, adjuvant chemotherapy was carried out using a modified T10 protocol, which included methotrexate (8–12 g/m²), adriamycin (60 mg/m²), and cisplatin (100 mg/m²). Follow-up duration was at least 36 months (average: 114 months, range: 36–235 months), and follow-up duration was defined as the time between the date of index operation to date of death or last visit. Patient survivals were...
plotted using the Kaplan–Meier method, and correlations between clinical variables and outcomes were evaluated using the chi–square test.

**Results**

1. Clinical outcomes of all study subjects

The 10-year overall and event free survival rates for the 22 study subjects determined using the Kaplan–Meier method were 85.7±5.1% and 54.6±10.6%, respectively (Fig. 1). Nineteen (86%) of the 22 patients were alive at a mean follow–up of 100 months. One patient (case 6) died of pulmonary metastasis at 48 months after index surgery. This patient developed pulmonary metastasis at 21 months after index surgery without evidence of local relapse, but despite metastasectomy and adjuvant chemotherapy, died 27 months later. The other patient (case 14) with marginal resection and high–grade POS developed local recurrence at 13 months after index surgery, and despite re–excision with wide margin, succumbed to another local recurrence and concomitant pulmonary metastasis. Remaining one patient (case 21) was initially misdiagnosed as Nora’s lesion and underwent four episodes of intralesional excision over 35 months. After referral, this patient received en–bloc resection of humerus, nevertheless, local recurrence and fulminant metastasis (lung, thigh, and lower leg) developed and eventually expired 49 months from initial intralesional procedure. A pathologic examination of the en–bloc resected specimen in this patient showed dedifferentiated POS (Fig. 2).

Nine (41%) of the 22 patients developed local relapse, and median time to first local recurrence was 22 months (range, 4–43 months). The clinico–pathological variables found to be correlated with lo–

| Variables                        | Recurred (%) | Not recurred (%) | p-value |
|----------------------------------|--------------|------------------|---------|
| Age                              |              |                  |         |
| ≤30                              | 5 (33.3%)    | 10 (66.7%)       | 0.38    |
| >30                              | 4 (57.1%)    | 3 (42.9%)        |         |
| Gender                           |              |                  |         |
| Male                             | 1 (12.5%)    | 7 (87.5%)        | 0.07    |
| Female                           | 8 (57.1%)    | 6 (42.9%)        |         |
| Initial stage                    |              |                  |         |
| IB                               | 7 (41.2%)    | 10 (58.8%)       | 1.00    |
| IIB                              | 2 (40.0%)    | 3 (60.0%)        |         |
| Histologic grade                 |              |                  |         |
| Grade 1                          | 7 (41.2%)    | 10 (58.8%)       | 0.93    |
| Grade 2                          | 1 (50.0%)    | 1 (50.0%)        |         |
| Dedifferentiated                 | 1 (33.3%)    | 2 (66.7%)        |         |
| Tumor volume                     |              |                  |         |
| Mean (range)                     | 91.9 (0.9–125)| 397.9 (12.6–4,552)| 0.48 |
| ≤50 ml                           | 6 (40.0%)    | 9 (60.0%)        | 1.00    |
| >50 ml                           | 3 (42.9%)    | 4 (57.1%)        |         |
| Location                         |              |                  |         |
| Femur                            | 2 (18.2%)    | 9 (81.8%)        | 0.03    |
| Others                           | 7 (63.6%)    | 4 (36.4%)        |         |
| Medullary invasion               |              |                  |         |
| Yes                              | 3 (33.3%)    | 6 (66.7%)        | 0.67    |
| No                               | 6 (46.2%)    | 7 (53.8%)        |         |
| Soft tissue mass                 |              |                  |         |
| Yes                              | 6 (54.5%)    | 5 (45.5%)        | 0.39    |
| No                               | 3 (27.3%)    | 8 (72.7%)        |         |
| Surgery                          |              |                  |         |
| En bloc/amputation               | 1 (9.1%)     | 10 (90.9%)       | < 0.01  |
| Hemicortical                     | 1 (25.0%)    | 3 (75.0%)        |         |
| Lumpectomy                       | 7 (100.0%)   | 0 (0.0%)         |         |
| Margin                           |              |                  |         |
| Wide                             | 0 (0.0%)     | 10 (100.0%)      | < 0.01  |
| Marginal                         | 2 (40.0%)    | 3 (60.0%)        |         |
| Intralesional                    | 7 (100.0%)   | 0 (0.0%)         |         |
| Total                            | 9 (40.9%)    | 13 (59.1%)       |         |
POS has better survival than classic high-grade intramedullary osteosarcoma, and often behaves in an indolent manner, even after inadvertent procedures. However, with the exception of POS of the femur, lack of familiarity with POS with knowledge of the aforementioned characteristics can cause surgeons to underestimate the risk of POS, which could result in a patient missing the opportunity of surgical cure. Although the conclusions that can be drawn from this small series are limited, this study reconfirms the importance of a sound surgical margin, and demonstrates that there is ample opportunity to undertreat POS, especially in a non-femoral location. Furthermore, it shows that re-excision to overcome further recurrence after an incomplete procedure is difficult to achieve.

This study is limited by its size and the use of heterogeneous patient populations, but it highlights the importance of a sound surgical margin and the need for further research in this area.

### Table 3. Treatment and Outcome of Patients with Local Recurrence

| Case number | Initial pathologic diagnosis | Type of initial operation | Time to 1st LR (months) | No. of intralesional or marginal procedure | Operation to achieve wide margin | Subsequent recurrence (months) | No. of subsequent recurrence | Metastasis (site) | Outcome | Follow up (months) |
|-------------|------------------------------|---------------------------|-------------------------|-------------------------------------------|---------------------------------|------------------------------|--------------------------|------------------|---------|------------------|
| 2           | Dedifferentiated POS         | En-bloc resection        | 18                      | 7                                         | Hemicortical excision & tumor prosthesis | 10                           | 1                        | -                | NED     | 16 months.      |
| 14          | POS G2                       | Hemicortical excision    | 18                      | 4                                         | None                            | None                         | NED                      | 21 (lung)        | NED     | 175 months.     |
| 16*         | Osteochondroma               | Lumpectomy               | 18                      | 4                                         | None                            | None                         | NED                      | -                | NED     | 136 months.     |
| 17*         | POS G1                       | Lumpectomy               | 18                      | 4                                         | En-bloc excision & recycled autograft | 21                           | 1                        | None             | NED     | 175 months.     |
| 18*         | POS G1                       | Lumpectomy               | 18                      | 4                                         | En-bloc excision & recycled autograft | None                         | None                     | NED              | NED     | 136 months.     |
| 19*         | POS G1                       | Lumpectomy               | 18                      | 4                                         | En-bloc excision & recycled autograft | None                         | None                     | NED              | NED     | 136 months.     |
| 20*         | POS G1                       | Lumpectomy               | 18                      | 4                                         | En-bloc excision & recycled autograft | None                         | None                     | NED              | NED     | 136 months.     |
| 21*         | Laos’ lesion                 | Lumpectomy               | 18                      | 4                                         | En-bloc excision & recycled autograft | None                         | None                     | NED              | NED     | 136 months.     |
| 22*         | POS G1                       | Lumpectomy               | 18                      | 4                                         | En-bloc excision & recycled autograft | None                         | None                     | NED              | NED     | 136 months.     |

*Referred case, †Months after initial treatment.

LR, local recurrence; POS, parosteal osteosarcoma; NED, no evidence of disease; AWD, alive with disease.
geneous surgical techniques. We acknowledge the heterogeneities caused by the different resection methods used and the relatively large proportion of referred patients. Nevertheless, our objective was to analyze the outcomes of various surgical conditions.

The overall survival achieved is similar to those of numerous previous studies (Table 4). The clinico–pathologic variables previously reported to be correlated with the oncologic results of POS include intramedullary invasion, histologic grade, soft tissue mass, and surgical margin. However, we were unable to determine the prognostic significances of these variables with the exception of surgical margin. All 9 local recurrences were associated with marginal or intracapsular procedures, which reconfirms that a wide surgical procedure should be viewed as the gold standard when treating POS. The local recurrence rate of 41% found in our study compares with that of the Mayo clinic report, in which referred patients constituted 41% (28/67) of the cohort. Interestingly, as compared with other reports, the proportion with a location other than the femur (50%) was high in the present study, and these sites were found to be associated with a significantly higher rate of local recurrence. Seven of the 9 patients that experienced local recurrence were referred due to an inadvertent procedure, and of these, 6 had a non–femoral primary site. Furthermore, although the diagnosis of POS is often believed to be relatively straightforward using plain radiographs, reported series suggest that risk of underdiagnosis is substantial. In those two studies, of the 21 patients that experienced local recurrence, 13 (72%) were initially misdiagnosed as having exostosis, myositis ossificans, osteoma, or osteitis, which suggests that primary physicians are unfamiliar with POS presenting with an aberrant location and radiologic pattern (case 21).

No matter what clinical situations lead to recurrence, in cases of local failure, the surgeon should decide on a type of surgery that results in a wide margin. Outcomes after local recurrence differ from those of classic high–grade osteosarcoma. Grimer et al. reported that 31 (41%) of 96 patients with local recurrence developed lung metastasis either before or at the time of recurrence, and 68 patients either aborted surgery (24 patients) or required amputation (44 patients). On the other hand, although there is a risk of dedifferentiation or an increase in histologic grade after repeated recurrence, the majority of patients can be successfully controlled. Therefore, in cases of local recurrence, resection with a wide margin, by whatever method, should be respected. In a meta–analysis of 21 locally recurrent patients, although a half of them underwent amputation, 90% of patients were free of disease at last follow up (Fig. 3). However, because these two studies were reported around 20 years ago, it is likely that the abilities of imaging modalities to define the extent of local

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Table 4. Summary of Publications Concerning Parosteal Osteosarcoma

| Author/Year | Patient number | Enneking stage | Histologic grade | Surgical margin (1st OP) | Local recurrence (%) | Metastasis (%) | Overall survival Mean FU duration (yr) |
|-------------|----------------|----------------|-----------------|--------------------------|---------------------|--------------|---------------------------------------|
| Temple et al. 2000 | 38 | 25/12/1 | 26 11 | 1 | 9 | 2 | 19 | 17 | 4 | 38% | 38/38 (100%) | 6.75 | (0.5-19) |
| Okada et al. 1994 | 226* | NA/NA/0 | 157 32 | 37 | 142 | 84 | 6 | 25 | 35 | 141% | 14/67 (21%) | 56/67 (84%) | 13 | (2-140) |
| Ritschl et al. 1991 | 33 | NA | 23 | 9 | 1 | 23 | 10 | 3 | 20 | 13 | 32/33 (98%) | 52/33 (157%) | 13 | (0-25) |
| Han et al. 2008 | 21 | 7/14/0 | 7 11 | 3 | 16 | 2 | 6 | 2 | 13 | 41% | 11/21 (52%) | 20/21 (95%) | 6 | (2-41) |
| Current study | 22 | 17/5/0 | 17 | 2 | 3 | 11 | 7 | 5 | 10 | 92/22 (86%) | 32/22 (41%) | 9.5 | (3-195) |

*226 patients were registered and outcomes of 67 (managed at that center patients) were presented.
recurrence would have been limited. Nowadays, surgical planning in recurrent patients is supported by the accuracy of MRI, which translates into a high rate of limb salvage. Nevertheless, patients with repeated recurrence after procedures that were presumed to achieve a sound margin should not be spared amputation.

In conclusion, we reconfirm the importance of achieving a sound surgical margin when treating POS, and emphasize that the risk of under-treatment not be ignored, especially for cases with a non-femoral location and without typical plain radiologic characteristics. Furthermore, we found that by using advanced imaging modalities, re-excision without a mutilating procedure was possible in the majority of cases with the exception of those with an aggressive disease pattern after repeated recurrences.

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방골성 골육종의 임상결과
승원석・전대근・조원형・공창배・조상현・이광열・이수용
원자력병원 정형외과

목적: 방골성 골육종 환자의 치료 결과와 국소 재발 후의 결과에 대해서 알아보고자 하였다.
대상 및 방법: 22명의 방골성 골육종 환자의 치료 결과를 후향적으로 분석하였다. 평균 추시기간은 114개월(범위: 36-235개월)이었다. 22명 중 7명은 국소 재발 후에 전원 되었다. 병기는 17명에서 IB였고, 5명은 IB (G2, 2명; 역분화, 3명)이었다. 종양의 위치는 대퇴골(11명), 기타 부위(11명)이었다. 최초 절제연은 광범위 절제연 10명, 변연 절제연 5명, 병소내 절제가 7명이었다. 여러 임상 및 병리인자와 국소 재발과의 연관성, 그리고 국소 재발 후의 임상 경과를 조사하였다.
결과: 10년 생존율은 85.7%이었다. 3명(14%)에서 원격 전이를 보였고 이들은 모두 사망하였다. 9명(41%)에서 국소 재발이 있었다. 종양의 위치, 절제 방법 및 절제연이 국소재발과 관련이 있었다. 국소 재발 후 수술 한 환자 9명 중 최종 추시 시 7명에서는 무병 상태였다.
결론: 방골성 골육종의 오진의 가능성이 높으며 특히 대퇴골 이외에 발생한 경우 오진이 많았다. 대부분의 재발성 종양에 대한 재절제는 가능하나 공격적 성향을 보이며 재발한 경우에는 주의가 필요한 것으로 생각된다.

색인단어: 방골성 골육종, 국소 재발