An *in vitro* study on NUP62 as a potential target for radiosensitization in sarcoma

육종 세포주에서 방사선 민감제 타겟으로 NUP62의 이용 가능성에 대한 탐색 연구

Wan Lim Kim, MD, PhD[1]; Han-Soo Kim, MD, PhD[2]; Jong Seok Lee, MD[1]

[1]Department of Orthopaedic Surgery, Asan Medical Center, University of Ulsan College of Medicine, 86 Asanbyeongwongil, Songpa-gu, Seoul 138-736, Korea

[2]Department of Orthopaedic Surgery, Seoul National University Hospital, 101 Daehak-ro Jongno-gu, Seoul 03080, Korea

Background: Patients with unresectable sarcoma are often refractory to radiotherapy, leading to a poor prognosis. Outcomes of those patients can be improved if effective radiosensitizers are available. NUP62, a constituent of the nuclear pore complex, is known to have radiosensitizing effects in carcinoma cells; however, its effect in sarcoma has never been tested. In this *in vitro* study, we aimed to investigate the role of NUP62 as a potential molecular target for radiosensitization in human sarcoma cells.

Materials and methods: To test cell viability, we used a colony formation assay; NUP62 was silenced and exposed to ionizing radiation (IR) in 5 sarcoma cell lines and 1 fibroblast cell line. Apoptotic cell death and DNA double-strand breaks were then evaluated with fluorescence-activated cell sorting analyses, western blots, and gamma-H2AX assays.

Results: We identified the expression and silencing of NUP62 in 5 sarcoma cell lines and 1 fibroblast cell line. NUP62 depletion alone without IR did not affect cell viability and proliferation. We identified an increased rate of cell death by apoptosis, and decreased cell proliferation after NUP62 depletion following IR in synovial sarcoma and fibrosarcoma cell lines. Increased DNA damage was also observed in synovial sarcoma and fibrosarcoma cell lines after NUP62 depletion and IR. However, we noted that NUP62 depletion did not radiosensitize Ewing sarcoma, osteosarcoma, and normal human fibroblast cells.

Conclusions: We identified the feasibility of NUP62 as a potential target for radiosensitization in certain sarcoma cells, which have been considered radio-resistant tumors. Our preliminary results can be utilized as a basis for future screening and development of radiosensitizers in sarcoma.

Inorganic phosphate suppresses the proliferation of osteosarcoma cells

Young Jae Moon, **Jung Ryul Kim**

Departments of Orthopaedic Surgery, Jeonbuk National University Hospital

Introduction: The process of pre-osteoblast differentiation divided into three distinct stages: (1) proliferation, (2) matrix maturation, and (3) mineralization. *In vitro*, process of three distinct stages can be reproduced by treating with ascorbic acid and given a source of phosphate. There have been studied that inorganic phosphate may not only represent constituent of mineralization but also an important signaling molecule for pre-osteoblast proliferation. However, the cellular and molecular mechanisms by which elevated inorganic phosphate alters cell behavior remains to be elucidated. Furthermore, it remains largely unknown whether the process of osteosarcoma proliferation is affected by systemic phosphate.

Methods: To evaluate the role of inorganic phosphate in pre-osteoblast, we treated inorganic phosphate to MC3T3-E1 (pre-osteoblast cell line) and checked the morphology of pre-osteoblast and cellular signaling. To check the role of inorganic phosphate in the proliferation of osteosarcoma cells, we treated inorganic phosphate to osteosarcoma cell lines (U2OS, SaOS2). We performed soft agar assay, BrdU assay, and cell cycle analysis by flow cytometry.

Results: We found that inorganic phosphate triggered bone formation and mineralization but suppressed active β-catenin and inhibited its target gene, c-myc in pre-osteoblast. That results were not blocked by sodium-phosphate transport. These results could be considered that mechanisms other than the previously known mineralization mechanisms of inorganic phosphates affected the proliferation of pre-osteoblasts. Next, we observed inorganic phosphate suppressed proliferation of osteosarcoma cells lines through MTT, soft agar assay, and BrdU assay. We confirmed that the inhibition of proliferation of these osteosarcoma cells was G0/G1 cell cycle arrest using flow cytometry.

Conclusion: These data suggested that inorganic phosphate regulated progression of osteosarcomas. Although more mechanistic and clinical studies are needed, systemic inorganic phosphate treatment is expected to play a role in osteosarcoma.

Tumor microenvironments induce telomere maintenance mechanisms in MPNST

Jungwoo Lee,[1] Eunji Choi,[1] HyoJu Kim,[1] Young-Joon Kim,[1] Seong-Hwan Moon,[2] and **Seung Hyun Kim**[2]

[1] Interdisciplinary Program of Integrated OMICS for Biomedical Science, The Graduate School, Yonsei University, Seoul, 03722, Republic of Korea

[2] Department of Orthopaedic Surgery, Yonsei University College of Medicine, Seoul, 03722, Republic of Korea

A hallmark of complete oncogenesis is achieving cellular immortalization, which is implemented by telomere maintenance mechanisms (TMMs). To examine this process, neurofibroma (NF, a benign tumor) and malignant peripheral nerve sheath tumor (MPNST, a malignant tumor) associated with neurofibromatosis type 1 (NF-1) were compared as 21 pairs from 21 patients, where each NF-MPNST pair shared an identical genetic background and differentiation lineage and the changes that occurred during cellular transformation to overcome the Hayflick limit were structurally subtracted, since MPNST occurs in a preexisting NF. There was no difference in telomere length between NFs and MPNSTs, suggesting that MPNTs overcome replicative senescence (immortalization). 22 differently expressed genes (DEGs) were identified during immortalization. Only NELL2, BUB1, FOXG1, and PRIMA1 among them activated TMM. NELL2 activated RAD51, LIG4, and SLX4IP; BUB1 activated BLM; FOXG1 activated TERC and RAD52 and repressed POLD3; PRIMA1 activated TIMELESS. As a second cascade RAD9B, DAXX, COILIN, CTCFL, and BRCA2 were activated. These activated genes in TMM formed transcriptional regulation networks that transmitted DEGs-induced extrinsic signals to TMM through TIMELESS, COILIN, and CTCFL and activated RAD51-dependent homologous recombination (HR) machinery: BTR complex (BLM), Rad51 loader (BRCA2), and SLX complex (SLX4IP). In addition to, telomerase catalytic activation and repression of break-induced replication (BIR) were identified during immortalization. As a result, WRN-SMC complex-mediated intratelomeric HR in NF was replaced by Rad51-dependent intertelomeric HR and Rad51/Rad52-independent BIR in NF was repressed during immortalization. Our results identified and validated the transcriptional regulatory architecture needed to achieve immortalization in TMMs, which has not been described previously.

Feasibility of Novel In-situ Local Tumor Ablation and Recycling Machine using Radiofrequency Dielectric Heating

Min Wook Joo[1, *], Sangrok Jin[2], Gyeong-Jun Lee[2], Yong-Suk Lee[3], Yang-Guk Chung[4]

[1]Department of Orthopaedic Surgery, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea
[2]School of Mechanical Engineering, Pusan National University, Busan, Korea
[3]Department of Orthopaedic Surgery, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea
[4]Department of Orthopaedic Surgery, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea

Introduction

Standard operative treatment for malignant musculoskeletal tumors has been limb salvage surgery (LSS), which involves wide resection and reconstruction of resultant tissue defect. Common skeletal substitute includes tumor prosthesis, allograft and recycled autograft. The LSS procedure can vary depending on the reconstruction method, each of which has different disadvantages. Tumor-bearing autografts were treated by diverse ablation techniques such as extracorporeal irradiation, pasteurization, and freezing and thawing, however, all of them have the issues of long-term durability and non-union. Although pedicle frozen autograft was developed to overcome such complications, it still has possibility of insufficient tumor ablation. We devised a novel concept, in-situ local tumor ablation and recycling machine using radiofrequency (RF) dielectric heating, and intended experimental research to demonstrate its feasibility.

Materials and Methods

In all experiments, fresh femurs of 6-month-old three-way hybrid pigs were used after epiphyses had been cut off, and cancellous bone and bone marrow were curettaged. The distal part was contained in the dielectric heating device using RF generator and converter. Most distal part was located in the middle line of the electrode plate, and the length of the parts inside the machine was 10.75 cm. Two tips of fiber optic temperature sensors were inserted in the metaphysis, two in the meta-diaphysis, and one in the diaphysis, then, temperature change was measured during RF heating at 27.12 MHz and 50, 100, 150, 200, 250, 300 W five times, respectively.

Biomechanical study was also conducted to measure the change in the rigidity of the bone treated by RF heating. Compressive and bending rigidities were measured for the treated bones, pasteurized ones and untreated fresh ones six times respectively, and the results were statistically analyzed.

In addition, modeling and thermal analysis using COMSOL Multiphysics® software was performed. The subject was simulated to be heated at 600, 700, 800 and 900 V by the electrode in the same shape as the current experimental device, and at 2000 V by using another narrow bottom electrode.

Results

Under 300 W, the highest temperature and the time for the temperature to reach 70°C were 129.8 °C and 14 minutes in all regions of five subjects.

The RF-heated bones showed no statistically significant difference in compressive rigidity compared to the untreated bone (p=0.485). While the median compressive and bending rigidities were 2686.4 (range, 1479.2-4363.5) N/mm and 1856 (range, 1586.8-3717.7) N/mm, and 711.98 (range, 381.91-931.27) N/mm and 572.105 (range 448.7-748.42) N/mm in RF-heated and pasteurized bones respectively, no significant differences was revealed between them (p=0.31, and 0.589).

Simulation study showed that the temperature rise was inconsistent between regions under electrode in the same shape as the current experimental device, however, such discrepancy was alleviated at 2000 V by using a narrow bottom electrode.

Conclusion

This study demonstrated that it would be feasible to maintain the temperature at which tumor ablation can be expected and the favorable bone rigidity by in-situ local tumor ablation and recycling machine using RF dielectric heating. To apply the device to patients, clinical trials should be required after further improving its electrodes and appearance.

육종 혁신형 바이오뱅킹 컨소시엄 사업*

Sarcoma Biobank Innovation Consortium for Biomedical and Healthcare Research

김준혁[1], 강현귀[1], 박종웅[1], 김수지[1], 김은성[1], 김다영[1], 김정렬[2], 문영재[2], 주민욱[3], 서성욱[4], 유종우[5], 박석연[5], 김영주[6], 김경욱[6], 이경진[6], 손해정[6], 유혜진[7], 이은영[7], 김용연[8], 성지영[8], 최귀선[9], 박필립[9], 백연희[9], 김경민[10], 유창영[11], 정재환[12], 김수현[13], 이현수[13], 한일규[14]

국립암센터 정형외과[1], 전북대병원 정형외과[2], 가톨릭대병원 성빈센트병원 정형외과[3], 삼성서울병원 정형외과[4]
국립암센터 병리과[5], 국립암센터 바이오뱅크[6], 국립암센터 종양면역연구과[7], 국립암센터 암전이연구과[8], 국립암센터 암빅데이터센터[9], 전북대병원 병리과[10], 가톨릭대병원 성빈센트병원 병리과[11], 주식회사 셀레믹스[12], 한국제약바이오협회 인공지능신약개발센터[13], 서울대병원 정형외과[14]

목적

1차 연구목적: 육종에 대한 국가적 레지스트리 구축을 통해 환자들의 종양검체와 임상정보, 심층정보 들을 확보하여 육종 환자들의 생존률 향상을 위한 기초연구 및 임상연구에 활용한다.

2차 연구목적: 육종환자에 있어서 정밀의학을 구현하기 위한 육종 암유전자 패널(comprehensive genomic profiling test)을 수립 및 상용화 하고, 인공지능을 이용한 신약후보물질 검색을 통해 약물 설계 플랫폼을 개발한다.

대상 및 방법

전신적으로 발생하는 육종검체를 확보하기 위해 정형외과 외에 산부인과, 비뇨기과, 대장외과, 구강외과, 흉부외과 등의 전문의들을 참여시켰으며, 심층정보의 전문성 강화를 위해 영상의학과, 핵의학과, 병리과 전문의들 및 기초연구자들을 컨소시엄에 포함하였다. 2021년 7월부터 프로토콜에 따라 전향적으로 정상/치료전(treatment-naïve) 종양검체를 수집하였으며, 다기관 임상정보 수집을 위한 eCRF를 질병관리청의 KBN-CDM포맷에 맞추어 개발하고 이를 통해 각 검체에 대응하는 임상정보를 수집하였다. 기존 연구들을 통해 육종에서 유의하게 발현되는 유전자 및 전사체들을 대상으로 다중 암유전자 타겟 캡쳐 패널을 DNA/RNA 각 1종에 대해 개발하였다. 바이오뱅크 데이터를 활용할 수 있도록 전처리된 데이터를 사용할 수 있도록 하는 기초모델 수립을 진행하였다. PanCan Atlas 데이터의 전처리를 완료하고, GTEx/TARGET데이터를 확보하여 테스트하였다.

결과

1차년도에 총 117명의 육종환자에 대한 전향적/후향적 검체를 확보하였다. 수집된 바이알 기준 10퍼센트의 혈액 및 조직검체에 대해 정도관리를 시행하였다. 28예의 MRI영상 및 20예의 PET영상, 폐전이를 보이는 환자 9예에서 chest CT영상을 확보하였다. DNA, RNA 각 1건의 암유전자 타겟캡쳐패널을 제작하였다. 70예의 후향적 육종 검체를 분양받아 패널의 검증을 시행하고, whole exome/transcriptome 시퀀싱을 시행하였다. PanCan Atlas를 통해 육종을 포함하는 33개 암종에 대한 10,793개의 RNA 시퀀싱 샘플을 대상으로하는 pan-cancer VAE모델을 구축하고 학습하였다.

결론

육종과 같은 희귀암에 대한 정밀의학구현을 위해서는 국가적인 통합연구자원 수집을 위한 플랫폼 구축과 임상연구네트워크의 조성 및 운영이 필수적이다. 표준화된 운영지침을 통해 양질의 인체자원과 데이터베이스를 구축하고, 이를 활용한 기초 및 임상연구, 이행성연구를 진행하므로써 육종환자들의 치료성적 향상에 이바지하고자 한다.

Acknowledgments

This study was conducted with biospecimens and data from the Sarcoma Biobank Innovation Consortium for Biomedical and Healthcare Research, which was funded by the Korea Disease Control and Prevention Agency for the Korea Biobank Project (#6637-303)."

CLINICAL OUTCOMES OF ENDOPROSTHETIC RECONSTRUCTION FOR PROXIMAL FEMORAL RESECTION

이규평, 김용성, 공창배, 조완형, 전대근, 송원석

원자력 병원 정형외과

Abstract

Introduction: The proximal femur is a common site for primary sarcomas and metastatic lesions. Although the early results of tumor prostheses are promising, the long term results of reconstruction are unknown. The purpose of this study is to evaluate the prognostic factors affecting prosthesis survival and complications after proximal femoral resection and reconstruction.

Methods: We reviewed the results of 68 patients who underwent proximal femoral resection and reconstruction with a modular bipolar type tumor prosthesis between 2005 and 2017. The mean follow-up was 55.6 months (range, 6-172 months). There were 50 male and 18 female patients with a mean age of 41.5 years (range, 11–80 years). Cumulative survival analysis was performed to analyze the risk factors of prosthesis survival and complications after operation were evaluated.

Results: Fourteen (21%) patients required further surgery at a mean 37 months postoperatively (range, 5-125 months). There were three cases of infection (4%), six of local recurrence (9%), three of acetabular erosion (4%), and two of stem loosening (3%). The implant survival rates were 83.9% at 5 years and 59.8% at 10 years. Prosthesis survivals did not differ based on fixation method (p=0.085), age (p=0.329), or resection length (p=0.61). Acetabular chondrolysis was identified in 18 (26%) patients and longer resection length (≥20 cm) showed a trend for risk of acetabular wear (p=0.132).

Conclusion: The results of proximal femoral resection and reconstruction with a modular bipolar type prosthesis were found to be acceptable with infection and local recurrence as short-term complications and loosening and acetabular erosion as long -term complications.

Keywords: proximal femoral resection, tumor prosthesis, reconstruction, complications

골 거대세포종의 소파술 후 재발

Recurrence after extended curettage for giant cell tumors of bone

김재훈, 신승한, 정양국

가톨릭대학교 서울성모병원 정형외과

서론

골 거대세포종은 국소적으로 공격성을 보이며 확장형소파술 후 15-50%의 높은 재발율이 보고되고 있다. 최근 술 전 denosumab치료가 국소적으로 진행된 거대세포종에서 수술적 치료를 용이하게 한다는 보고가 있으나 반면에 술 전 denosumab 치료군에서 충분한 소파술이 어려워 재발율이 오히려 높다는 우려가 있다.

재료 및 방법

2009년 6월 이후 본원에서 단일 술자에 의해 골 거대세포종에 대하여 확장형 소파술을 시행받은 32예를 대상으로 국소 재발 유무와 국소 재발 관련 인자들, 즉 발생 부위, 술 전 denosumab 투여 여부, Campanacci grade, ABC change 동반 여부, 병적골절 유무, 재발성 병변, 재건 유형에 따른 재발율을 분석하였다. 남녀비는 14:18이었으며, 평균연령은 33.9(12-54)세였고 발생부위는 원위 대퇴골(15예), 근위 경골(8예), 원위 요골(3예) 순이었다. 술 전 denosumab 투여 군이 10예, 비투여 군이 22예 였으며 술 전 MRI 상 13예에서 ABC change를 동반하였다. 2예에서 진단시 병적골절을 동반하였으며 4예가 재발성 병변이었다. 소파 후 23예에서는 시멘트 충진술을, 5예에서는 골이식술을 시행하였으며 관절연골 가까운 병소 4예에서는 연골하 부위는 제한적으로 골 이식술을, 다른 부위는 시멘트 충진술을 시행하였다. 술 후 평균 추시 기간은 44.3 (9-112)개월 이었다.

결과

국소 재발이 6예(18.8%)에서 발생하였으며 폐 전이는 1예(3.1%0)서 보였다. 발생부위에 따른 차이는 없었으며 술 전 denosumab 투여 여부에 따른 차이도 없었다(20%/18.2%). Campanacci grade 1/2군에비해 grade 3군에서 재발율이 높았다(13.3%/23.5%). ABC change를 동반한 경우 높은 재발율을 보였다(30.8%/11%). 시멘트 충진술군이나 골 이식군에 비해 연골하부 골 이식술과 시멘트 충진술을 병행한 경우에 재발율이 높았으나(13%/20%/50%) selection bias와 관련될 가능성을 배제할 수 없었다. 재발성 병변 4예중 2예(50%)에서 재발을 보였으나 병적 골절 동반 2예에서는 재발이 없었다.

결론

Campanacci grade 3, ABC change 동반, 재발된 병변, 관절연골 근접병소에서 높은 재발율을 보였으나 시기를 달리하여 selection bias의 영향이 작은 본 연구에서 denosumab 투여 여부에 따른 재발율의 차이는 확인되지 않았다. 더 많은 증례에 대한 후향적 대조군 연구나 cohort 연구가 필요하다.

장관골 악성 골종양의 광범위 절제술 후 동종 이식골을 이용한 재건술의 치료 결과

Results of Allograft Reconstruction following Wide Resection of Malignant Bone Tumors in Long Bones

김갑중, 김하용, 최원식, **최효길**

을지대학교 의과대학 정형외과학교실

목적

장관골 악성 골종양의 광범위 절제술 후 동종 이식골을 이용한 재건술의 치료 결과를 분석하고자 하였다.

대상 및 방법

총 8예의 환자를 대상으로 하였다. 환자의 평균 나이는 40세(12~62세)였으며 남자 5예, 여자 3예였다. 평균 추시 기간은 100개월(12~174개월)였다. 기능적 평가는 MSTS 점수를 측정하였으며, 주기적 방사선 촬영을 통해 숙주골-동종 이식골의 유합 유·무와 수술 후 합병증을 분석하였다. 최종 추시 시 종양학적 결과를 분석하였다.

결과

이환 부위는 대퇴골 5예, 상완골 1예, 경골 2예였다. 조직학적 진단은 악성 골육종 5예, 다발성 골수종 2예, 법랑종 1예였다. 이식된 동종골의 평균 길이는 163㎜(110~195㎜)였다. 동종골 내고정은 금속정과 금속판 고정 4예, 골수강 내 금속정 고정 2예, 나사못 고정 1예, 금속판 고정 1예였다. 최종 추시 시 평균 MSTS 점수는 20점(16~26)였다. 수술 후 합병증으로는 불유합 3예, 내고정물 파손 2예, 감염 1예, 동종 이식골 골절 1예였다. 최종 추시 시 지속적 무병 상태 6예, 유병 상태의 생존 2예였다. 3예의 불유합 중 2예의 환자에서 자가골 이식술과 반 피질 동종골 보강술을 시행하였으며, 2예의 내고정물 파손 중 1예에서 내고정물 교체를 시행하였다.

결론

장관골에서 발생한 악성 골종양의 광범위 절제술 후 동종 이식골을 이용한 재건술은 매우 유용한 수술 방법 중 하나이다. 그러나, 숙주골-동종 이식골 경계 부위의 불유합 가능성을 염두해야하며, 숙주골과 동종 이식골 접촉면이 견고하고 넓을수록 숙주골-동종 이식골 유합율이 높을 것으로 사료된다.

골외성 점액성 연골육종의 임상 결과

The Clinical Outcome of Extraskeletal Myxoid Chondrosarcoma

이규평[1], 공창배[1], 송원석[1], 조완형[1], 고재수[2], 전대근[1]

1 원자력병원 정형외과학교실
2 원자력병원 병리학교실

Purpose

Extraskeletal myxoid chondrosarcoma (EMC) is an extremely rare malignant mesenchymal neoplasm. accounting for less than 3% of soft tissue sarcoma. This rare sarcoma is usually characterized by an indolent course. The aim of our study was to document the clinical manifestation and oncologic outcomes of EMC.

Materials and Methods

This study identified 17 patients who were diagnosed and treated for EMC between January 2008 and December 2018. The identified cohort was then reviewed regarding age, gender, symptom onset, tumor location, MR images, surgical margin and pathologic diagnosis. The time to local recurrence and/or metastasis, follow up duration, and the patients' final status were analyzed.

Results

The patients were comprised of 10 males and 7 female patients with a mean age of 54 (range, 31-79). The location of the tumor was in the buttock in 5, knee in 3, foot in 2, shoulder in 1, and back in 1. The average tumor diameter was 11.5 cm (range, 6-26 cm). At the time of diagnosis, 5 patients were AJCC stage II, 3 were IIIA, 3 were IIIB, and 6 were IV. Local recurrence occurred in 12 cases and distant metastasis occurred in 15 cases. The five-year overall survival of patients with EMC was 85%, and 2 patients died due to disease progression.

Conclusion

In spite of a high rate of local recurrence and distant metastasis, long-term survival rate in patients with EMC is quite high because of its' indolent characteristics.

Key Words: extraskeletal myxoid chondrosarcoma, pathology, prognosis, indolent

Myxofibrosarcoma of the extremity

Sungmin Kim, Sung Taek Jung

Department of Orthopedic Surgery, Chonnam National University Hospital

Aims

Myxofibrosarcomas (MFSs) are malignant soft-tissue sarcomas characteristically presenting as painless slowly growing masses in the extremities. Locally infiltrative growth means that the risk of local recurrence (LR) is high. We reviewed our clinical experience to investigate predictors of LR.

Patients and Methods

Patients with a primary or recurrent MFS who were treated surgically in our unit between 2001 and 2015 were included in the study. Clinical records and imaging were reviewed. A total of 25 patients with a median age of 71.4 years (interquartile range 61.6 to 81.8) were included. There were 15 men.

Results

The lower limb was the most common site (32/50, 64%). The mean size of the tumors was 8.95 cm (1.5 to 27.0); 9 (36%) were French Fédération Nationale des Centres de Lutte Contre le Cancer grade III. In total, 76% received radiotherapy postoperatively. All patients underwent surgery. Margins were negative in 52%, close/positive in 40%, and unknown in 8%. In total, 12% of patients received chemotherapy. Univariate Cox regression analysis was utilized to determine associations between clinical and treatment factors with LR. Local recurrence occurred in 13 patients (52%) at a mean of 21 months (3 to 33).

Conclusion

In this institutional series of MFS, older age and positive/close margins were significantly associated with a higher risk of LR.

Myxofibrosarcoma: Clinical and Prognostic features

Yong-Suk Lee, Min Wook Joo, Seung Han Shin, Yang-Guk Chung

The Catholic University of Korea

Introduction

Myxofibrosarcomas are misdiagnosed sometimes as benign tumor due to its superficial location and unplanned excisions are performed easily. The purpose of the study was to evaluate the clinical characteristics & oncologic outcome of myxofibrosarcomas (MFS).

Materials and Methods

This retrospective study reviewed 47 patients with histologically confirmed myxofibrosarcoma between 1994 and 2021. Follow-up period of all 47 patients were over 1 year, at least. We analyzed clinical characteristics and oncologic outcomes of myxofibrosarcomas. 24 cases were male and 23 cases were female, with a mean age of 65 years (ranged from 40 to 91 years). 5 patients were histologic grade I, 20 patient was grade II and 15 patients were grade III. Unplanned excision had been performed by other hospitals or other department in 15 out of 47 patients without regarding the possibility of malignancy, and transferred to our department and institute for additional treatment. All patients underwent wide excision except a patient who had retroperitoneal tumor. 34 out of 47 patients had negative tumor cell cut margins and 13 ones were not. 13 patients received postoperative chemotherapy and 4 patients pre- & post-operative chemotherapy. Postoperative radiotherapy performed for 31 patients, preoperative radiotherapy for 2 patients and pre- & post-operative for 2 patients. Average follow-up period was 60 months (ranged from 12 to 218 months).

Results: Local recurrence was occurred in 14 out of 47 patients (30%). 10 out of 15 patients who underwent unplanned surgery had tumor recurrence. For those who had positive surgical margin had 61.5% of local recurrence rate (8 out of 13). There were 6 case of distant metastasis to lung. Disease free survival rate was 83 % (39 out of 47). Oncologic result was 27 CDF, 12 NED, 5 AWD, 2 DOD and 1 DWOD.

Conclusion

Myxofibrosarcoma has high local recurrence rate and low distant metastasis rate. Even though it has high local recurrence rate, it still showed good survival. That might be related to their superficial location, in which the diagnosis was made early. Even after local recurrence, early detection and immediate secondary interventions are possible before the progression of disease.

Keywords

myxofibrosarcoma, local recurrence, surgery, prognosis

Double layer wide excision for the treatment of dermatofibrosarcoma protuberance

이중 층 광범위 절제술을 통한 융기피부섬유육종의 치료

이재영

가톨릭의대 부천성모병원 정형외과

서론

융기피부섬유육종(dermatofibrosarcoma protuberance)은 주로 진피층과 피하층에 발생하는 악성 종양이다. 조직학적으로 수지 상 침범(finger-like extension)의 형태를 보여 수술 후에도 종양이 잔존하는 경우가 많고 높은 국소 재발률을 보이고 있다. 이에 본 연구자는 이중 층 광범위 절제술(double-layer wide excision)을 통하여 종양을 제거함과 동시에 전방위 동결 조직 검사를 시행하여 안전한 종양 절제연을 확보하고자 하였다. 이를 바탕으로 이 수술 방법의 임상적 결과 및 조직학적 결과를 보고하고자 한다.

대상 및 방법

절개 생검술(Incisional Bx.) 또는 비계획성 절제(unplanned excision) 후 융기피부섬유육종으로 진단된 10례를 대상으로 하였다. MRI를 통한 수술 전 계획에 따라 2cm의 tumor margin 및 3mm 간격으로 double-layer wide excision을 시행하였다. Inner layer 및 outer layer 사이의 조직을 1시~12시로 세분화한 후 각각의 조직에 대하여 frozen Bx.를 시행하여 종양 조직의 유무를 판단하였다. 수술 후 6개월 및 1년 추시 MRI를 촬영하여 재발 여부를 확인하였다.

결과

10례 중 2례의 Double layer wide excision에서 frozen Bx. 상 종양 조직이 확인되었으며 추가적인 절제술을 시행하였다. 6개월 및 1년 추시 MRI 상 종양의 재발 소견은 관찰되지 않았다.

결론

융기피부섬유육종에 대한 광범위 절제술 시 2cm의 절제연은 비교적 안전하나 종양이 잔존할 수 있어 주의가 요한다. 이중 층 광범위 절제술을 통하여 추가적인 절제가 가능하였고 양호한 임상적 결과를 얻었다.

Myxoid liposarcoma: analyses of patients treated at single institution

Ilkyu Han, Yongsung Kim, Han-Soo Kim
Department of orthopaedic surgery, Seoul National University Hospital

Background

Myxoid liposarcoma is a homogenous subtype in regards with shared clinical features but is heterogenous histologically accounting for a mixed prognosis. Objective of this retrospective study was to investigate factors affecting survival, particularly importance of round cell content and grade over one another.

Methods

From 1993 to July 2017, 76 patients were diagnosed with Myxoid/Round cell liposarcoma (MRCLS). Clinicopathological and treatment related factors were investigated for influence on outcome by univariate and multivariate analysis.

Results

Out of 76 patients, 43 were pure myxoid liposarcoma (<5% Round cell component) and remaining 31 were round cell liposarcoma (>5% Round cell component). The mean age was 44 years (range, 12 to 74 years), the mean tumor size was 10 cm with 71% of them occurring in lower extremity and the median follow up was 57 months. All the patients underwent surgical resection, with radiotherapy being used in 60% (n=48) and 24% patients were given chemotherapy. The overall 5 years survival rate was 90%, and the local recurrence and metastases incidences were 17% and 19.7%, respectively. Margin status (P<.001) was significantly and strongly associated with local recurrence. Round cell component-RCC (P=.009) and grade (P<.001) were significant for metastases but on multivariate analysis.

Conclusion

Margin status is strongly associated with local recurrence. MRCLS patients with <5% and >5% Round cell component (RCC) have significantly different metastases rates, but it’s the FNCLCC grade which is a very strong predictor for metastases as well as overall survival.