

Case Report

Biological Reconstruction with Hydrogen Peroxide in Distal Osteosarcoma of the Femur: A Case Report

Jiva Yori Anugrah¹, Pamudji Utomo¹, Mujaddid Idulhaq¹, Ambar Mudigdo²

¹Department of Orthopaedic and Traumatology, Universitas Sebelas Maret, Prof. Dr. R. Soeharso Orthopaedic Hospital, Surakarta, Indonesia

²Department of Pathology Anatomy, Universitas Sebelas Maret, Surakarta, Indonesia

ABSTRACT

Osteosarcoma is commonly found in the metaphysis of long bones where the epiphyseal growth plate is very active; namely in the distal femur, proximal tibia and fibula, proximal humerus, and pelvis. Before the use of chemotherapy, osteosarcoma was treated with surgery in the form of amputation. Along with scientific developments, neo-adjuvant chemotherapy, and limb salvage surgery can be performed, one of which is with biological reconstruction. A 13 years old girl, with a diagnosis of osteosarcoma of the distal femur extra. The patient came with the main complaint of a lump on the left knee 5 months before control. Physical examination revealed a mass with indistinct borders on the left knee with a diameter Range of Motion (ROM) limited to 0° - 100°. The patient underwent neoadjuvant chemotherapy and showed a good response. Followed by limb salvage surgery in the form of biological reconstruction. The tumor tissue was resected and soaked in hydrogen peroxide liquid, then the bone tissue was replanted with plate and screw fixation. Limb salvage surgery with biological reconstruction using hydrogen peroxide was performed on the patient. On evaluation one week after surgery, good results were obtained. The patient did not feel pain, there were no signs of infection or neurovascular disorders. There were no complications in the surgical wound and implant fixation was good. Evaluation after one year showed good results in the physical examination and laboratory findings. There was no sign of infection or recurrence of the tumor. The evaluation also assessed the Musculoskeletal Tumor Rating Scale (MSTS) to evaluate the physical function of the patient. Limb salvage surgery with biological reconstruction using hydrogen peroxide may be an alternative treatment option for distal femur osteosarcoma patients with favorable clinical conditions.

Keywords: osteosarcoma, limb salvage surgery, biological reconstruction, neo-adjuvant chemotherapy
<https://doi.org/10.31282/joti.v5n1.88>

Corresponding author: Jiva Yori Anugrah, MD. Email: jivayori@gmail.com

INTRODUCTION

Osteosarcoma, also known as Osteogenic Sarcoma, is a malignant neoplasm that originates from primitive cells (poorly differentiated cells) in the metaphyseal region of long bones in children.¹ It is called osteogenic because it develops from osteoblastic series of primitive mesenchymal cells. Osteosarcoma is the most common primary neoplasm of bone after multiple myeloma.^{1,3,10} Osteosarcoma is the third most common cancer in adolescents, with an incidence of 5.6 cases per 1,000,000 children under 15 years of age. The incidence is highest in the second decade of life. Before the age of 5 years, osteosarcoma is rare.¹⁰

Osteosarcoma is usually found in the metaphysis of long bones where the epiphyseal growth plate is very active; i.e. distal femur, proximal tibia, fibula, proximal humerus, and pelvis. In the elderly over 50 years of age, osteosarcoma can result from malignant degeneration of Paget's disease, with a very poor prognosis.^{1,3,4}

Osteosarcoma is a bone tumor with a mortality rate of 80% after 5 years of diagnosis. Classic osteosarcoma is defined as a spindle cell sarcoma with a high degree of malignancy and very distinctive osteoid matrix production. Osteosarcoma is found in approximately 3 people per 10,000 in the United States.^{5,11}

The location of the tumor and the age of the patient in the rapid growth of the bone suggest an influence on the pathogenesis of osteosarcoma. It starts either inside the bone or on the bone surface and progresses to the soft tissues surrounding the bone. The epiphysis and joint cartilage act as barriers to tumor growth into the joint.³ Osteosarcoma metastasizes hematogenously, commonly to the lung or other bones and approximately 15%-20% have metastasized at the time of diagnosis. Lymphogenous metastases are almost non-existent.³

CASE

A 13 years old girl with complaints of pain and swelling in the right knee. The pain was worse with the movement of the knee joint and at night. The patient also felt a lump on the right knee for 6 months which felt getting bigger (Figure 1). The patient had difficulty walking without aids and doing daily activities.

Radiographs of the knee showed cortex destruction of the distal femur and described aggressive tumor tissue

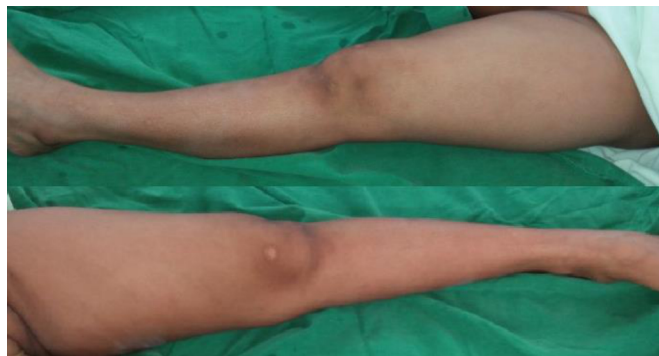


Figure 1. Preoperative patient's clinical picture

(Figure 2). A diagnostic procedure with open biopsy was performed and discussed at a clinical pathological conference forum, the results were consistent with osteosarcoma (Figure 3). The patient underwent neoadjuvant chemotherapy and showed a good response. The tumor size and general clinical condition improved compared to before undergoing neoadjuvant chemotherapy.



Figure 2. X-Ray photograph of the femur

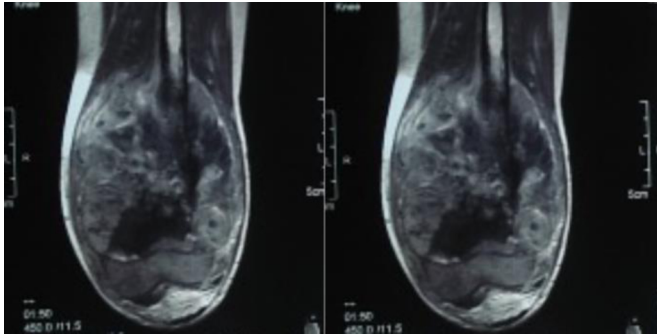


Figure 3. MRI of the patient

This was followed by limb salvage surgery in the form of biological reconstruction. Durante surgery revealed tumor tissue on the metaphysiodiaphyseal femur (Figure 4). Resection of the tumor tissue to the healthy margin was performed. The bone tissue was soaked in hydrogen peroxide liquid, and then the bone tissue was replanted with plate and screw fixation (Figure 5). Histopathological examination showed that the microscopic features of the tumor were consistent with osteosarcoma. Postoperatively, the patient reported improvement in pain at the site of surgery. On follow-up at the polyclinic, the patient stated that there were nosymptoms or signs of recurrence.

Postoperatively, periodic wound care and rehabilitative physiotherapy exercises were performed. The patient regularly visits the polyclinic for postoperative evaluation. No signs of infection were found, and the patient could walk with assistive devices and continue the rehabilitation regimen at the medical rehabilitation polyclinic of Soeharso Hospital.

One year after surgery, an evaluation was conducted. From the physical examination, the postoperative wound is good and there are no signs of infection or recurrence, the LLD is 4 cm and the Range of motion (ROM) examination results are 0-140°. The results of the supporting examination also showed good results, there was no increase in ALP, CRT, or LED 1-2. At the 1- year evaluation, a Musculoskeletal Tumor Rating Scale (MSTS) assessment was also carried out, with a score of 25 out of a total score of 35 (71%) which is a good result, the patient is satisfied with the surgery performed.

DISCUSSION

Medicamentous therapy in the distal femur and proximal tibia, especially when the tumor size is so large

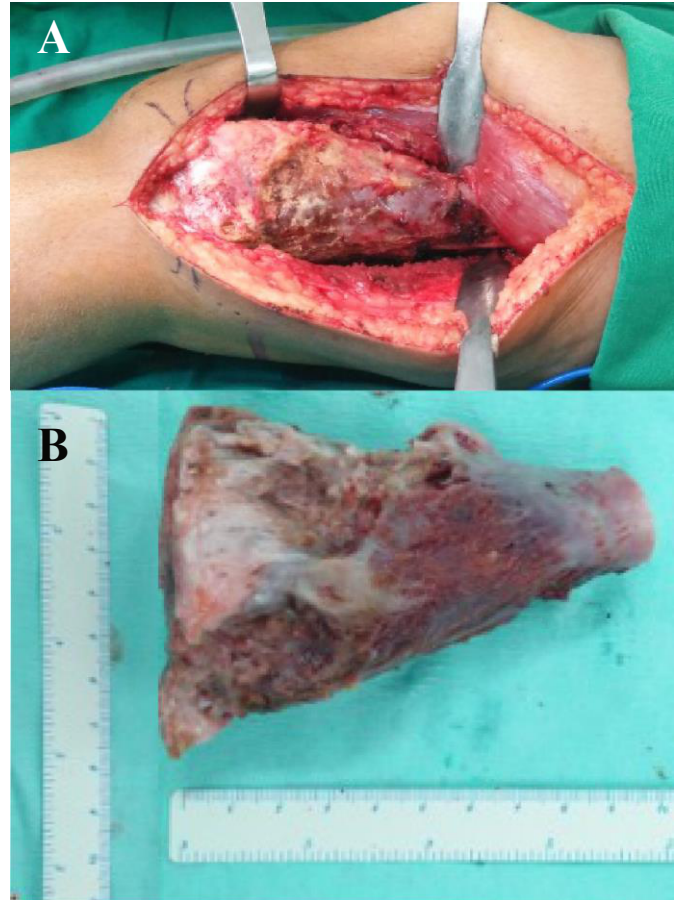


Figure 4. (A) Tumor tissue in the distal femur before resection. (B) Clinical appearance of tumor tissue after resection.

that the only surgical alternative is amputation. Very young or athletic patients have the advantage of performing this procedure from a functional point of view as well as the procedure can minimize the need for further surgery in the future.

Recent studies have demonstrated hydrogen peroxide's capacity to cause apoptosis in a variety of cell types. Despite being a simplistic chemical, hydrogen peroxide is crucial for intracellular signal transduction pathways. Gene expression, protein phosphorylation, and calcium mobilization are some of the factors that contribute to hydrogen peroxide production. Exogenous hydrogen peroxide in excess is regarded to have potentially disastrous effects on the cell's capacity to eliminate ROS (Reactive Oxygen Species).

For osteosarcoma that recurs as one or more lesions in the lung within just over one year of discharge, surgical resection alone can play a curative role, as the likelihood of metastases to other sites is very low. Chemotherapy is

considered if recurrence occurs early, as the risk of micrometastases is high.

Hearing loss is a side effect of cisplatin. There may also be fever and neutropenia, requiring hospitalization for monitoring and intravenous antibiotic therapy. Patients may also need to be hospitalized for various other health issues during the chemotherapy phase including varicella infection, mucositis, dehydration, meningitis, constipation, fungal pneumonia, and cystitis. Before the use of chemotherapy, Osteosarcoma was treated with surgery. Despite good local control, more than 80% of patients had recurrences that appeared as pulmonary metastases. This high rate indicates that most osteosarcoma patients have already undergone a micrometastatic process at the time of diagnosis. Therefore, the use of adjuvant (postoperative) systemic chemotherapy is very important in the management.

Neoadjuvant chemotherapy has been shown to not only facilitate the surgical procedure in terms of helping to shrink the tumor but also serve as a risk parameter. Patients who have a good histopathological response to neoadjuvant chemotherapy (>95% tumor cell death or necrosis) have a better prognosis than patients whose tumor cells do not respond significantly. Hydrogen peroxide is one of the agents that can cause oxidative stress potential and has been demonstrated in many cells, where it is effective to induce the apoptosis of HS-Os-1 osteosarcoma cells.

The primary goal of resection is patient safety. Resection should be to the tumor-free margin. All patients with osteosarcoma should undergo surgery if resection of the primary tumor is possible. The type of surgery required depends on several factors that should be evaluated on an individual patient basis. Radical extent, defined as the removal of the entire involved compartment (bone, joint, muscle) is usually not required. The outcome of combined chemotherapy with resection is better than radical amputation without adjuvant therapy, with 5-year survival rates of 50-70% and 20% for radical amputation only. Pathological fractures, with contamination of all compartments, may exclude the use of limb salvage surgery therapy, but if surgery can be performed with tumor-free border resection then limb salvage surgery can be performed. In some circumstances, amputation may be an option, but more than 80% of patients with osteosarcoma of the extremities can be treated with limb salvage surgery and do not require amputation. If possible, limb salvage

reconstruction should be selected based on individualized considerations, as follows:^{9,10}

- Autologous bone graft: This can be with or without vascularization. Rejection is not present with this type of graft and infection rates are low. Patients with immature growth plates have limited options for stable bone fixation.
- Allograft: graft healing and infection can be a problem, especially during chemotherapy. There may also be graft rejection.
- Prosthesis: joint reconstruction using a prosthesis can be solitary or expandable, but this is costly. Durability is an issue with implants for adolescent patients.

CONCLUSION

A case of a female patient with distal osteosarcoma of the femur who was treated with neo-adjuvant chemotherapy and limb salvage surgery in the form of biological reconstruction has been reported. Neoadjuvant chemotherapy had a satisfactory impact. The patient's general condition improved and the tumor size significantly decreased compared to before. Biological reconstruction can be an option for management in patients with osteosarcoma. So it is hoped that it will be able to maintain the extremities that the patient has. From the results of the action, it was found that the surgical wound was good.

REFERENCES

1. Menendez LR, OKU (Orthopaedic Knowledge Update): Musculoskeletal Tumors, American Academy of Orthopaedic Surgeon, Illionis, 2007, 113-8.
2. Salter RB, Textbook of Disorders and Injuries of the Musculoskeletal System, 3th edition, Lipponcott Williams & Wilkins, Maryland, 1999, 408-9.
3. Solomon L, Appley's System of Orthopaedics and Fractures, 8th edition, Arnold, New York, 2009, 181-2.
4. Miller MD, Review of Orthopaedics, 5th edition, Saunders Elsevier, Philadelphia, 2008, 535.
5. Canale ST, Campbell's Operative Orthopaedics, 10th edition, Mosby, Philadelphia, 2003, 813-7.
6. Skinner HB, Lange Current Diagnosis and Treatment Orthopedics, 4th edition, Mc Graw Hill, California, 2007, 322-3.
7. Wiesel SW, Essentials of Orthopedics Surgery, 3th edition, Springer, Washington, 2007, 131-4.
8. Greenspan A, Orthopedic Radiology: A Practical Approach, 3th edition, Lippincott Williams & Wilkins,

- Philadelphia, 2008, 631-5.
9. Greene WB, Netter's Orthopaedics, 1st edition, Saunders Elsevier, Philadelphia, 2006, 177.
 10. Misaghi, A., Goldin, A., Awad, M. & Kulidjian, A. A. Osteosarcoma : a comprehensive review. (2018).
 11. Stitzlein, R. N., Wojcik, J., Sebro, R. A., Balamuth, N. J. & Weber, K. L. Team Approach: Osteosarcoma of the Distal Part of the Femur in Adolescents. JBJS Rev. 5, e5 (2017).