Section: Orthopaedics

Original Research Article

EFFECT OF SURGERY ON OXIDATIVE STRESS OF MALIGNANT BONE TUMORS- A COMPARATIVE ANALYSIS

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Abstract

Background: Malignant bone tumors, though less common than benign bone tumors but are associated with significant morbidity and mortality. Emerging theories propose that a surge in oxidative stress, marked by escalated reactive oxygen species (ROS) levels, can disturb the delicate equilibrium of intracellular reduction-oxidation (redox) processes. This intricate phenomenon has been implicated in numerous diseases, including the formidable realm of cancer. With this in mind, the primary objective of our study was to meticulously assess the intricate interplay between oxidant stress and the antioxidant defense mechanisms within malignant bone tumors, before and after surgical intervention. **Materials and Methods:** Our study encompassed a cohort of 14 patients diagnosed with histopathologically confirmed malignant bone tumors, all treated at a distinguished single center under the expertise of a singular surgeon. In parallel, we also included 14 healthy individuals as controls for comparative analysis. To assess the degree of oxidative stress, serum levels of Malondialdehyde (MDA), a reliable biomarker, were meticulously quantified. Additionally, the antioxidant status was evaluated through the measurement of Superoxide Dismutase (SOD) levels. Importantly, blood samples were collected at two distinct time points: the initial diagnosis and precisely six months following surgical intervention, allowing for a comprehensive examination of the dynamic changes within the patients' redox profiles. **Result:** The results showed a significant increase in plasma MDA levels and a significant decrease in SOD levels in patients with malignant bone tumors compared to healthy controls. Surgical intervention had a significant impact on oxidative stress levels, with a decrease in MDA levels and an increase in SOD levels observed after surgery. **Conclusion:** To conclude, our comprehensive analysis of malignant bone tumors has revealed a notable elevation in oxidative stress levels accompanied by a concurrent decline in antioxidant status. These findings shed light on the intricate interplay between redox balance and the pathogenesis of bone tumors. Further investigations into the modulation of oxidative stress and antioxidant mechanisms in patients with bone tumors hold promising potential for early diagnosis and the development of effective management strategies.

INTRODUCTION

Malignant bone tumors are less common than benign tumors. Malignant lesions of bone occur most commonly during the first three decades of life, and some of them, such as osteosarcoma and Ewing sarcoma, can present with pain, localized swelling, and other symptoms.[1] Additionally, there are certain locally aggressive malignant bone tumors, such as osteosarcoma and chondrosarcoma.[2]

Once an accurate diagnosis has been made based on radiographs and biopsy, an appropriate treatment plan can be devised. Many malignant bone tumors require aggressive treatment, including surgery, chemotherapy, and radiation therapy. Surgical intervention often involves resection of the tumor

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followed by reconstruction using bone grafts, allografts, or other substitutes.[3,4]

Various studies have highlighted the role of oxidative stress in the development of cancer. In bone tissues, oxidative stress has been shown to affect bone cell function and contribute to the pathophysiology of bone diseases. However, the role of oxidative stress in the development and treatment of malignant bone tumors is not fully understood.[5]

Oxidative stress occurs when there is an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defences. ROS can cause damage to cellular structures, including DNA, proteins, and lipids. Malondialdehyde (MDA) is a marker of lipid peroxidation, while superoxide dismutase (SOD) is an antioxidant enzyme that helps neutralize ROS.[6]

This study aimed to compare the levels of oxidative stress in patients with malignant bone tumors before and after surgical intervention. Serum MDA levels were measured as an indicator of oxidative stress, and SOD levels were evaluated as a measure of antioxidant status. The study included patients with biopsy-proven malignant bone tumors who underwent surgery, as well as healthy controls. Blood samples were collected at the time of diagnosis and six months after surgical intervention.

MATERIALS AND METHODS

After approval from Institutional Ethical Committee, study was conducted at PGIMS Rohtak, a tertiary care centre. The subjects were divided into two groups of Healthy controls (n=16) and patients with malignant bone tumors (n=16) before and after surgery after a written Informed consent. The control group was matched for age and sex.

In addition to plain X-rays, computerized tomography (CT) scans, and magnetic resonance imaging (MRI), all patients underwent biopsy for diagnosis and staging of the tumors. PET scan was done to rule out metastasis and any patient with metastasis was excluded from the study. Venous blood samples were collected under aseptic precautions from all patients at the time of diagnosis. Similar samples were collected from healthy controls. Another blood sample was taken six months after surgical intervention. Serum samples were analyzed for routine biochemical investigations on the same day and stored at -20ºC in separate aliquots. Oxidative Damage was determined by Lipid Peroxidation for which Serum malondialdehyde (MDA) levels were analyzed using a colorimetric method. The principle involved the reaction of 2-thiobarbituric acid (TBA) with MDA when heated at an acid pH. The optical density of the TBA-MDA complex was recorded at 535 nm, and the concentration of MDA was determined using an MDA standard curve. Results were expressed as micromoles of MDA per liter of plasma.7

Antioxidant Status was determined by Superoxide Dismutase Activity for which Serum superoxide dismutase (SOD) activity was measured using an enzymatic method on a Randox autoanalyzer. This method utilized xanthine and xanthine oxidase to generate superoxide radicals, which react with INT (2-(4-iodophenyl)-3-(-4-nitrophenol)-5-phenyltetrazolium chloride) to form a red formazan dye. The SOD activity was measured by the degree of inhibition of this reaction. One unit of SOD is defined as the amount that causes a 50% inhibition of the rate of reduction of INT under the assay conditions. The SOD activity was determined using the linear regression equation from the standard curve. Results were expressed as units per milliliter of plasma.

Routine biochemistry parameters were measured using an autoanalyzer, and the data were analyzed using appropriate statistical tests such as Chi-square test, Fisher's exact test, student t-test, and ANOVA F-test. The relationship between variables was analyzed using Pearson's correlation coefficient. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographic Details

As described in table 1, the age group of patients varied from 8 years to 65 years with a mean of 18 ± 2.3 years. Out of 14, 4 were females while rest 10 (71%) were males. Osteosarcoma was most common histopathological diagnosis (n=9, 64%), followed by Ewings Sarcoma (n=4) and one patient was diagnosed with Chondrosarcoma (n=1). Distal femur was most common site (n=9, 64%) followed by tibia (n=3) while calcaneum, iliac bone and humerus were involved in one case each. Limb salvage was feasible in 11 patients (78.5%) while three patients underwent amputation.

Comparison of MDA levels and SOD levels

As evident in table 2, there was significant difference is healthy controls and patients with malignant bone tumors in level of MDA and SOD. Levels were found to be decreasing in same patient group after surgery. Although the levels could not reach to original level of healthy controls but a significant fall was noted after a period of 6 months. However, a long term follow-up is required to observe the oxidative stress and antioxidant status.

Table 1: Details of the patients with malignant bone tumors.

Sr. No.	Age/Sex	Histopathological diagnosis	Site	Treatment
1	13/M	Osteosarcoma	Distal Femur	Excision with Reconstruction
2	17/M	Osteosarcoma	Proximal Femur	Excision with Reconstruction
3	8/M	Ewings Sarcoma	Tibia	Above knee amputation
4	65/M	Chondrosarcoma	Proximal Humerus	Excision with Reconstruction

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5	16/F	Osteosarcoma	Proximal femur	Excision with Reconstruction
6	13/F	Osteosarcoma	Distal femur	Excision with Reconstruction
7	12/M	Ewings Sarcoma	Distal femur	Excision with Reconstruction
8	19/M	Osteosarcoma	Proximal tibia	Excision with Reconstruction
9	11/M	Ewings Sarcoma	Illiac Blade	Type 1 Hemipelvectomy
10	15/F	Osteosarcoma	Distal Femur	Mid leg amputation
11	18/M	Osteosarcoma	Proximal tibia	Excision with Reconstruction
12	21/M	Osteosarcoma	Distal femur	Excision with Reconstruction
13	17/M	Osteosarcoma	Proximal femur	Excision with Reconstruction
14	12/F	Ewings Sarcoma	Calcaneum	Below ankle amputation

Table 2: Comparison of MDA levels and SOD levels in different groups.

		Healthy controls (n=14)	**Patients with Malignant bone tumors- Pre-Surgery (n=14)**	**Malignant bone tumors- Post Surgery (n=14)**
MDA (µmol/L)	Mean±S.D	2.36±1.10	7.40±4.10	4.2±2.1
	Range	1.02-3.54	4.85-9.33	2.1-6.8
SOD (IU/mL)	Mean±S.D	158±32	42±22	86±12
	Range	113-254	21-65	67-98

DISCUSSION

This study presents valuable insights into oxidative stress and diminished antioxidant status specifically in malignant bone tumors before and after surgical intervention. While the exact role of oxidative stress in cancer development remains complex and poorly defined, it is known that free radicals, particularly their active forms, play a significant role in regulating cellular processes and indicating oxidative stress. The imbalance between oxidants and antioxidant systems has been extensively investigated in various malignancies, including malignant bone tumors.[8]

The study by Nathan et al specifically explores the association between oxidative stress and antioxidant status in primary bone and soft tissue sarcoma.[9] Their findings highlight the presence of oxidative stress and diminished antioxidant status in these malignancies. This aligns with the broader understanding that oxidative stress is a common feature of cancer development. Consistent with the findings, our study also revealed a decrease in oxidative stress, as indicated by decreased malondialdehyde (MDA) levels, along with an increase in antioxidant status, as demonstrated by elevated superoxide dismutase (SOD) levels. These results suggest a potential shift towards a more balanced redox state in bone tumors, which aligns with the understanding that oxidative stress plays a critical role in cancer development.

The present study aimed to investigate the levels of oxidative stress and antioxidant status in malignant bone tumors before and after surgical intervention, building upon previous research in this field. These results suggest a potential shift towards a more balanced redox state in bone tumors, which aligns with the understanding that oxidative stress plays a critical role in cancer development. The decrease in MDA levels, a marker of lipid peroxidation, indicates a reduction in oxidative damage to lipids. Furthermore, the increased SOD levels, an antioxidant enzyme involved in neutralizing superoxide radicals, suggests a bolstered defense against oxidative stress. These findings highlight the intricate relationship between oxidative stress and antioxidant systems in bone tumors and underscore the potential for targeting these pathways for therapeutic interventions.[10]

Another relevant study by Dhupper et al. (2022) conducts a comparative analysis of oxidative stress in primary bone tumors. Author measured oxidative stress (MDA levels) and antioxidant status (SOD levels) in benign as well as malignant tumors and found a statistically significant increase in levels of MDA and a decrease in SOD levels. These findings are consistent with findings of patients with colorectal cancer, gastric cancer, breast cancer.[11]

Understanding the oxidative stress mechanisms specific to bone tumors is essential for advancing therapeutic interventions and identifying potential biomarkers for early detection and treatment response evaluation.[12]

CONCLUSION

In conclusion, our study provides further evidence supporting the presence of decreased oxidative stress, as indicated by reduced MDA levels, and an improvement in antioxidant status, as evidenced by increased SOD levels, in bone tumors. These findings contribute to the growing understanding of the complex interplay between oxidative stress and the antioxidant defense system in the context of bone tumors. The observed decrease in oxidative stress and enhancement of antioxidant capacity suggest potential therapeutic targets for modulating redox balance in bone tumor management. Continued research in this area may pave the way for the development of innovative treatment approaches and the identification of novel biomarkers for improved diagnosis and prognosis of bone tumors.

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