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Platelets Levels before and after Surgical Intervention in Patients with Oral and Maxillofacial Tumors at MNH, Tanzania

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Abstract

Background: There are documented effects of platelets on the solid tumors which need further study. The elevated platelet counts have been described for majority of cancers. There is inadequate information of effect of benign and malignant oral and maxillofacial tumors on the regulation of platelets. The aim of this study was to investigate the changes in platelet counts among patients with oral and maxillofacial benign and malignant tumors following surgical interventions. Methods: A descriptive postoperative study was done whereby patients with benign and malignant oral and maxillofacial tumors who met the inclusion criteria were included. The included patients were those who had no history of blood transfusion prior, during or after surgery, not on haemoglobin-boosting or bone marrow suppressing medications, not seropositive to human immunodeficiency virus also without clinical findings suggestive of lymphadenopathy, splenomegaly, ecchymosis and petechiae. Demographic data, Platelet counts and haemoglobin levels before and after surgery were documented and analysed by chi-square test and values were considered to be significant if $p < 0.05$. Results: A total of 61 patients were included in the study. The mean age of participants was 37.03 ± 16.6 years with range of 7 to 77 years. Majority 82.5% (n = 52) had benign tumors with a leading diagnosis of ameloblastoma followed by ossifying fibroma. In general there was an increase of platelet counts following surgery from the mean of 276.38 ± 109.40 K/uL to 308.51 ± 117.24 K/uL. Looking at benign and malignant separately, following surgery there was an increase of platelet counts for benign tumors (278.87 ± 106.37 to 305.96 ± 123.12) but a decrease for malignant tumors group (282.33 ± 147.03 to 232 ± 78.48). The haemoglobin level changed from the mean of 12.60 ± 1.71 g/dl before surgery to 11.69 ± 1.70 g/dl after surgery. Conclusion: The mean postoperative increase in platelet counts in benign and malignant tumors was due to healing process of the wound following surgery while the postoperative decrease in platelets counts in malignant tumors was due to effect of tumor removal which diminished the production of platelets activating factors. Malignant tumors produce platelets activating factors which are

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necessary for them to grow. Also, the difference in postoperative platelets counts in benign and malignant oral and maxillofacial tumors could be attributed by different biological behavior of benign and malignant tumors and hence different interactions of platelets to these tumors.

Keywords

Oral Maxillofacial Tumors, Pre-Operative Platelets Levels, Post-Operative Platelets Levels

1. Introduction

The primary regulator of the platelet count in human is thrombopoietin, a glycoprotein that is produced primarily in the liver and cleared primarily by platelets and their precursors [1]. Solid tumors generate a prothrombotic environment capable of platelet activation. Activated platelets are crucial regulators of tumor vascular homeostasis in that they prevent tumor hemorrhage [2]. Thus, tumors are capable of activating platelets, and it has been suggested that platelets in turn promote tumor growth [3] [4]. Elevated platelets counts in patients diagnosed with malignant tumors were first described more than 100 years ago [1]. In 1872, a "massive increase of platelets" in patients with carcinoma was described by Leopold Riess [5]. These findings were confirmed and extended by Theodor Bilroth, the first to link platelets not only with tumor growth but also with metastatic spread [6]. The increase in platelet counts may be an epiphenomenon of tumor growth, as tumor secreted cytokines can induce thrombopoiesis [1]. Elevated platelet counts have been described for the majority of all cancer entities including breast, lung, colon, esophageal, gastric to mention the few but has not described or documented in patients with Oral and Maxillofacial tumors. Neither of association has been established on whether platelets decreased or increased following surgical intervention of these tumors. The aim of this study is to correlate the platelet levels before and after surgical intervention in patients with oral and maxillofacial tumors.

2. Material and Methods

This descriptive prospective study was conducted at Muhimbili National Hospital (MNH) from May 2009 to May 2013. The study population included patients with histologically diagnosed oral and maxillofacial tumors admitted for surgical procedure, and had given a written informed consent. In all patients enrolled there was no history of prior blood transfusion or during and after the surgical procedure, recent medication, human immunodeficiency virus risk factors. Also negative findings on physical examination which included no evidence of lymphadenopathy, splenomegally, ecchymosis or petechieae were criteria for inclusion to the study. Data on socio-demographic characteristics and platelet levels before surgical procedure and during postoperative period were collected entered into computer, and were analyzed by chi-square test and values were considered to be significant if $P < 0.05$, using statistical package for social sciences (SPSS) version 19.0.

3. Results

A total of 61 patients were included in this study. The age range of the participants ranged from 7 years to77 years, with the mean age being 37.03 ± 16.6, with 24.6% (n = 15) of the patient falling in the age group of 30-39. Of the 61 patients who were included in this study, 50.8% (n = 31) were male, with the male to female ratio being 1:1 (**Table 1**).

Of the 61 patients who were included in the study, 85.2% (n = 52) had been diagnosed to have benign tumour while 14.8% (n = 9) had malignant lesions. The most frequent diagnosis was ameloblastoma (42.6%, n = 26) followed by ossifying fibroma (18%, n = 11) (**Table 2**).

The pre-op haemoglobin level ranged from 9.35 g/dl to 15.60 g/dl with the mean of 12.60 ± 1.71 g/dl. On the other hand post-op haemoglobin levels ranged from 7.47 g/dl to 14.90 g/dl, mean being 11.69 ± 1.70 g/dl. The difference in the means was statistically significant p = 0.004.

The overall pre-op platelet count ranged from 83.4 K/uL to 667 K/uL, mean of which was 279.38 ±109.40 K/uL, while the post-op platelet count ranged from 112 K/uL to 611 K/uL, with the mean being 308.51 ± 117.24 K/uL. The difference in mean was statistically significant p = 0.00.

The mean platelet count for the benign tumour were 278.87 ± 103.37 and 305.96 ± 123.12 for pre-op and post-op respectively the difference being statistically significant p = 0.001.

The mean platelet count for the malignant tumour was 282.33 ± 147.03 and 232.22 ± 78.48 for pre-op and post-op respectively the difference being statistically significant p = 0.00 (**Table 3**).

4. Discussion

The overall results of this study showed increase of platelets counts in the pre-operative and post-operative period in both malignant and benign tumors. Following resection of tumor, it is expected to have a reduction in-platelets counts, since increase of platelets is induced by the presence of the tumor. Contrarily to this expectations, the levels of platelets counts increase in the pre-operative and post-operative periods. This increase of platelets counts post-operatively could be due to wound healing process and not due to tumor factors since the tumor which produce platelet activating factors has already been removed. It has been documented that increased platelets counts are induced by tumor growth in patient with cancer [7]. This has been demonstrated by

Table 1. Distribution of the patient by age group and gender.

Age Group	Gender		Total (%)
	Male (%)	Female (%)	
0 - 9	1 (1.6%)	1 (1.6%)	2 (3.3%)
10 - 19	3 (4.9%)	6 (9.8%)	9 (14.8%)
20 - 29	7 (11.5%)	4 (6.6%)	11 (18.0%)
30 - 39	8 (13.1%)	7 (11.5%)	15 (24.6%)
40 - 49	5 (8.2%)	4 (6.6%)	9 (14.8%)
50 - 59	6 (9.8%)	4 (6.6%)	10 (16.4%)
60+	1 (1.6%)	4 (6.6%)	5 (8.2%)
Total	**31 (50.8%)**	**30 (49.2%)**	**61 (100%)**

Table 2. Distribution of the patients by the diagnosis.

Histological Diagnosis	Frequency	Percentage
Ameloblastoma	26	42.6
Ossifying. Fibroma	11	18.0
Fibrous Dysplasia	6	9.8
Odontogenic Myxoma	3	4.9
Pleomorphic Adenoma	3	4.9
Squamous Cell Carcinoma	3	4.9
Others	9	14.8
Total	**61**	**85.2**

NB: other tumours were: adenocarcinoma, adenoid cystic carcinoma, chondrosarcoma, basal cell carcinoma, hemangioma, lymphangioma, malignant pleomorphic adenoma.

Table 3. Difference in Mean platelet count for benign, malignant and overall tumours (pre-op and post-op).

Nature of tumour	Mean Pre-Op platelet count	Mean Post-Op platelet count	p-value
Benign	278.87 ± 103.37	305.96 ± 123.12	0.001
Malignant	282.33 ± 147.03	232.22 ± 78.48	0.00
Overall	279.38 ± 109.40 K/uL	308.51 ± 117.24 K/uL	0.00

this study in that the level of platelet counts increased in the pre-operative period. Cancer is frequently accompanied by increasing platelets counts, which most probably is thought to be related to the release of thrombopoietic cytokines from the tumor cells. Complex interactions between tumor cells and circulating platelets play an important role in cancer growth and dissemination, and a growing body of evidence supports a role for physiologic platelet receptors and platelet agonist in cancer metastasis and angiogenesis [8]. Tumors generate a prothrombic environment capable of platelets activation and platelets in turn promote tumor growth.

The study also demonstrated that the levels of platelets increased after the operation in benign and decrease in malignant oral and maxillofacial tumors. There is a growing evidence to suggest that the interplay between platelets and tumors is neither passive nor unidirectional [9]. The postoperative increased in platelets counts in benign tumors could be associated with other factors such as wound healing rather than the tumor itself. A relationship between platelets and tumor angiogenesis is suggested by the fact that platelets appear to be the main physiologic transporters of vascular endothelial growth epithelial factor (VEGEF) [10] [11]. However, angiogenesis, the formation of new blood vessels, is critical in wound healing because of the need to supply nutrients and oxygen to the injured area. Therefore it seems that the increased postoperative platelets in benign tumors were important in assisting wound healing. Under normal physiologic conditions, platelets have been suggested to release angiogenic proteins to promote wound healing. These pro-angiogenic proteins are later counterbalanced by the release of angiogenic inhibitor from stromal cells and platelets, to stop uncontrolled growth in late stages of healing in non-malignant wounds [9]. On the other hand, the mean decrease in platelets counts in malignant tumours post-operative period was due to effect of tumor removal which diminishes the production of platelets activating factors.

Thehaemoglobin (Hb)-level in post operative period was low compared to pre-operative period. There are two factors which could be linked to this. During surgery there could be bleeding which might lead to postoperative low level of haemoglobin. The second reason is loss of megakaryocytes activation by tumor. The presence of tumor activates the megakaryocytes which lead to increase production of platelets and red blood cells. Therefore low postoperative Hb-level could be attributed to the removal of the tumor which normally activates the production of red blood cells and hence low post operative haemoglobin level.

Importantly, a clear understanding of the contribution of the platelets specifically to tumor-associated angiogenesis remains unclear. For example, while platelets enhance angiogenesis in some tumors platelets-endothelial interaction in tumor micro-vessel have been found to be reduced in other tumors [12].

Findings of this study might need some caution in interpretation because of some inherent limitations. The study recruited a group of patients with both benign and malignant pathological conditions; however there were more patients with benign conditions than those with malignant conditions.

5. Conclusion

The mean postoperative increase in platelet counts in benign and malignant tumors was due to healing process of the wound following surgery while the postoperative decrease in platelets counts in malignant tumors was due to effect of tumor removal which diminished the production of platelets activating factors. Malignant tumors produce platelets activating factors which are necessary for them to grow. Also, the difference in postoperative platelets counts in benign and malignant oral and maxillofacial tumors could be attributed by different biological behavior of benign and malignant tumors and hence different interactions of platelets to these tumors.

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