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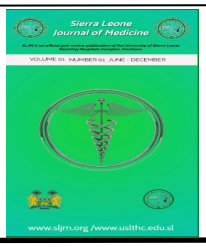

Six Years of Malignant Melanoma Management: A Review of Diagnosis and the Challenges of Treatment and Follow-Up

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ABSTRACT

Background: Melanoma refers to the malignant transformation of melanocytes. There has been a steady rise in the incidence and mortality from malignant melanoma. Malignant melanoma accounts for about 4% of all skin cancers. The mortality resulting from malignant melanoma is about 80-85% of all skin-cancer related deaths. This study is aimed at documenting our experience with malignant melanoma over 6 years; including the diagnosis, treatment options, and challenges with treatment and follows up.

Methods: This is a retrospective study to evaluate the incidence, management options, and treatment challenges in patients treated for malignant melanoma in Benin City, Nigeria. Patients' data were obtained from the patients' chart which included doctors' notes, nurses' charts and investigation reports. These included the biodata, clinical findings, investigations, treatment options and outcome. These data were presented in graphs and charts.

Results: Twelve patients were treated for malignant melanoma over 6 years. The commonest site of the primary lesion was on the lower limb (84.6%). Other sites were the arm and back with one patient (7.7%) respectively. The commonest procedure carried out was excision biopsy (91.7%). Other procedures done were primary wound closure, skin grafting, and sentinel node biopsy and groin dissection. One patient had an excision and split-thickness skin grafting, groin dissection, excision of chest nodular mass and fasciocutaneous flap closure.

Conclusion: The commonest site of melanoma was the lower limb. Nodular foot lesions may result from repeated trauma to the sole. Late presentation and non-compliance to treatment modalities are some of the challenges encountered in our setting

Key words: Melanoma, Excision Biopsy, Groin Dissection, Sentinel, Skin Graft.

1. INTRODUCTION

Melanoma refers to the malignant transformation of melanocytes. It occurs in melanocytes containing regions like the skin, mucosa, eyes, gastrointestinal tract and central nervous system[1]. In the United States, melanoma is the 5th and 6th commonest cancer in males and females respectively[2, 3]. In 2018, nearly 300,000 new cases were diagnosed[4]. The annual age-standardized rate of melanoma incidence is reported to be 19.7 per 100,000 cases[5]. Over the years there has been a steady rise in the incidence and mortality from malignant melanoma[6]. In 2006 United States recorded about 62,190 new cases of melanomas [2, 3].

Historically, Hippocrates first reported his observation of a skin tumour which is believed to be a melanoma[7]. In 1820, Norris reported a case of a rapidly growing tumour which resulted in the patient's death[7]. Autopsy done on the patient revealed "black specks" in every organ except the spleen. The patient had a strong family history of similar illness[7].

Malignant melanoma accounts for about 4% of all skin cancers. The incidence of melanoma among all skin cancers is about 4% in females and 5% in males[8]. There are cases with rapid growth and systemic spread[9]. The mortality resulting from malignant melanoma is about 80-85% of all skin-

cancer related deaths. Globally, the new cases and mortality from malignant melanoma yearly are approximately 160,000 and 48,000 respectively[10].

Malignant melanoma affects mostly young people with the average age at diagnosis of 57 years. Most of the patients (up to 75%) are less than 70 years of age[11, 12]. Females are more commonly affected than males[13]. The lower extremities and the trunk are the commonly affected sites in females and males respectively. Early presentation and diagnosis increases the chances of survival[14].

The Risk factors for development of malignant melanoma include Sun exposure (most important environmental risk factor), skin type (fair skin), genetic basis (CDKN2A gene mutation), large number of previous melanocytic nevi, dysplastic nevus, previous family history of melanoma, history of non-melanoma skin cancer and immunodeficiency[10,15]. Tobacco smoking is considered a risk factor for the development oral mucosal melanoma as the incidence has been found to be more common among smokers[16]. In the African population with a predominant nodular lesion on the sole of the foot and occurrence among farming population working often bare footed with repetitive trauma has been suggested as a possible aetiological factor.

Morphologically, Melanoma can be classified based on clinical and pathological features into; superficial spreading melanoma (60–70%), nodular melanomas (15–30%), lentigo melanoma (2% to 8%), and acral lentiginous melanoma (5–10%)[10]. Other rare subtypes include; Desmoplastic melanoma, Amelanotic melanoma, Ocular melanoma [17,18]. Early detection of cutaneous melanoma can be enhanced by screening using the ABCDE acronym for congenital naevi (Asymmetry, Border irregularity, Colour variegation, Diameter > 6 mm, Evolving /Elevated)[19]. Also, clinical evaluation of lesions using dermoscopic patterns has become a useful non-invasive tool for diagnosis. Definitive diagnosis of malignant melanoma is made by biopsy which can be incisional or excisional biopsy of the lesion[20]. This demonstrates the tumour type, level of invasion into the dermis and the aggressiveness of the lesion. Complete excision of the lesion improve the overall cure rates, 5-year survival rates and the overall outcome when compared to those treated without complete excision[20]. Because of the relative rarities of cases there is paucity of individual hospital data from which larger databases can be extrapolated. There is paucity of literatures on the pattern of presentation of malignant melanoma among the Nigerian population as well as the challenges peculiar to our setting. In our centre even though cases have been managed, these cases have not been reported. This study is aimed at documenting our experience with malignant melanoma over 6 years. This includes the diagnosis, treatment options, and challenges with treatment and follows up. The objective of this study is to highlight the presentation pattern of malignant melanoma among the Nigerian population, the treatment offered within our limited resources as well as the challenges encountered.

2. PATIENTS AND METHODS

This is a retrospective study of all the patients managed for malignant melanoma from January 2017 to December 2022. These consist of patients who presented with lesions suggestive of malignant melanoma that were confirmed by histology in the plastic and reconstructive surgery unit. This also included referrals from the Dermatology clinic of University of Benin teaching hospital, Benin City.

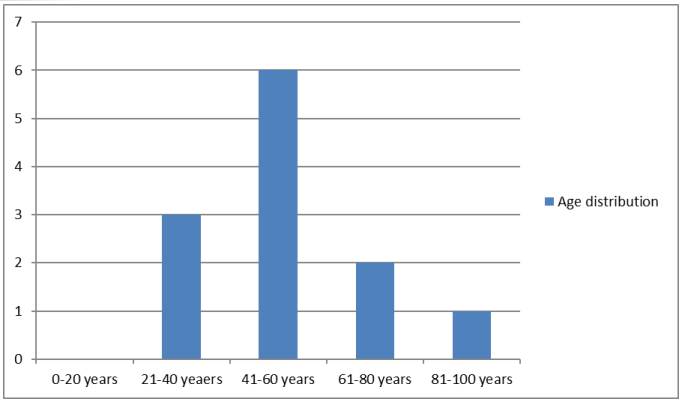

Figure 1: Age Distribution of Patients Treated for Malignant Melanoma.

The University of Benin Teaching Hospital (U.B.T.H.) is located in Benin City, Edo State, Nigeria. It is a 700 bedded hospital located in the southern region of Nigeria. Patients' data were obtained from the patients' records which include doctors' notes, nurses' charts and investigation reports. The data collated included the biodata, clinical findings, investigations, treatment options and outcome. These data were presented in graphs and charts.

2.1 Sampling Method:

All consecutive patients that presented in our centre were recruited for the study. Patients' records were obtained from documentations made in patients' file in the clinic, wards and theatre. Patients' data included both the doctors' notes and nurses' documentations in the nurses' chart. Continuous variables were summarized in mean. The age distribution was grouped into categories of 20 years. These data were presented in graphs and charts.

2.2 Treatment Modality:

These patients were worked up for excision biopsies after informed consent was obtained. The margin of excision was determined by the depth of the tumour. A normal skin margin of 0.5 cm was used for in situ melanomas and 1 cm for tumours with thickness up to 2 mm and 2 cm for thicker tumours. Following excision samples are tagged to identify possible areas of incomplete tumour clearance if any. The patients were sent to the oncology unit for further treatment after histological confirmation of diagnosis and complete loco-regional tumour clearance.

3. RESULT

3.1 Socio-Demographic Features:

A total of 12 patients were treated for malignant melanoma during the period under review. This accounted for 16.2% of all the patients managed for skin cancers in U.B.T.H. This consisted of 5 (38%) males and 7 (62%) females with a male with a male to female ratio of 1:1.4.

The age of the patients ranged between 25 years to 85 years. The mean age was 51.2 ± 18.5 years. Three patients (25.0%) were between the ages of 21-40 years as shown in figure 1. Patients between ages 41-60 years accounted for 50.0% of the study population. The time frame from when the patients noticed their first symptom to their first presentation in the hospital range between 5 months to 1 year. The mean presentation time was 8.3 months.

Seven of the patients were strictly farmers (58.3%). Three (25.0%) patients were civil servants who were also farmers and had significant sun exposure. The others were traders. The patients all had significant sun exposure of over 6 hours daily. None of the patients

Table 1: Tumour Stage at Presentation

Tumour Stage	Frequency (n = 11)	Percentage (%)
I	3	25
II	2	16.7
III	4	33.3
IV	3	25

had a family history of malignant melanoma.

3.2 Clinical Presentation:

The commonest site of the primary lesion was on the lower limb (84.6%). Most of these lesions were nodular and ulcerated (figure 2 and 3). Other sites were the arm and back occurring in one patient each (7.7% each). A patient presented with primary foot lesion and had huge nodular swellings in the groin (enlarged groin lymph nodes) and the anterior chest wall (figure 4, 5 and 6).

Ultrasonographic finding in four patients showed feature of enlarge groin nodes. Two patients had enlarged iliac nodes. One patient had both sonographic features of enlarged groin node and soft tissue chest mass which was confirmed to be metastatic deposits on histology. Two patients had deranged liver enzymes.

Majority (4, 33.3%) of the patients presented with stage III disease of which one did not consent to groin dissection (table 1).

3.3 Surgical Treatment and Outcome:

Patients that presenting presented with grade I and II disease had excision biopsy with sentinel lymph node biopsy. Patients with stage III and IV disease had incisional/ excisional biopsies, groin node dissection plus chemotherapy and radiotherapy. Incisional biopsies were done to confirm the diagnosis in patients with large ulcers. The commonest procedure carried out was wide local excision accounting for 91.7% of the treated patient as shown in figure 7. Nine patients (75%) had split thickness skin grafting after excision of tumour. Three patients (25%) had primary wound closure. Three patients had sentinel node biopsy and three patients had groin dissension for groin metastasis. One patient had excision and split thickness skin grafting, groin dissension and excision of chest nodular mass and closure with a fasciocutaneous flap (figure 8). One patient had re-excision for positive margins and the defect was re-grafted. Following surgery patients were referred to the oncologist for chemotherapy and radiation therapy. These patients were followed up in the plastic surgery outpatient clinic. Only two patients complied with the treatment of the oncologist.

Outcome: Two (16.7%) of patients complied with treatment and had no recurrence after 2 years of follow up. One of these two had a stage I tumour and the other was stage II with no nodal involvement. The other ten patients were lost to follow-up; hence their outcome could not be determined post-surgery and chemotherapy.

4. DISCUSSION

Malignant melanoma is an aggressive pigmented skin lesion with propensity for metastasis[21]. It is commoner in females with median age at diagnosis ranging 54- 57 years in previous studies[8, 2]. This study has a female preponderance with male: female ratio of 1:1.4. The median age at diagnosis was 51.4± 18.5 years, with age range of 25-85 years. This suggests that younger patients are affected more in native Africans when compared to other studies done in other continents of the world. This study had the extremities as the commonest site of the primary lesion with the lower limb accounting for 84.6% of all the cases. This corroborated studies done in Turkey that had the limbs as the commonest primary

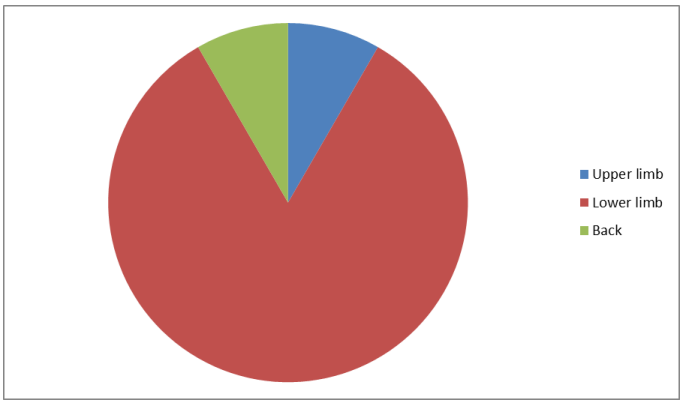

Figure 2: Primary Site of Lesion

site lesion[23]. The lower limbs of native Africans are exposed all year round exposure to the sun as seen in actinic skin damages observable in African albinos but this does not explain the high incidence on the non-pigmented sole where earlier workers have proposed repetitive trauma as a putative cause. Sun exposure over a lifetime has been recognized as the commonest aetiological factor in the development of malignant melanoma[10]. Prolonged exposure to sunlight puts such an individual at risk of Ultraviolet A and ultraviolet B radiation exposure.

Two patients had the tumour resulting from a mole. However, patients with melanoma occurring at the sole could not tell if there was a pre-existing mole. However, moles have not been frequently encountered in this location. Dysplastic moles, large numbers of moles and giant congenital melanocytic naevi are recognized risk factors for the development of melanoma[24]. Family history and previous history of melanoma put a patient at significant risk of malignant melanoma[24, 25]. None of the patients had a family history of melanoma. This could be due to poor health seeking behavior

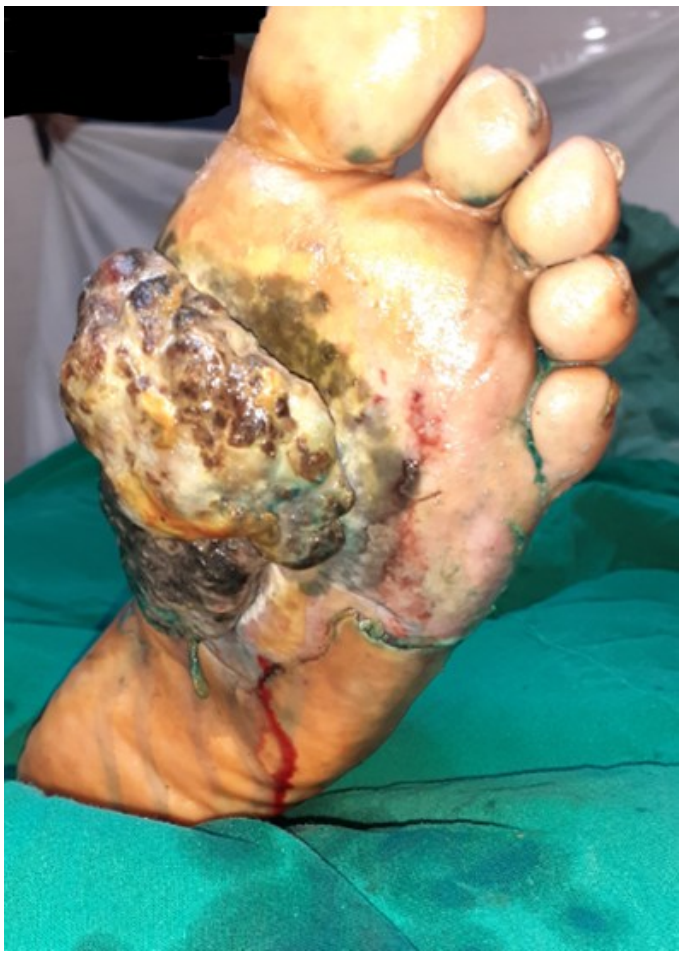

Figure 3: Foot Lesion in a Patient with Late Presentation

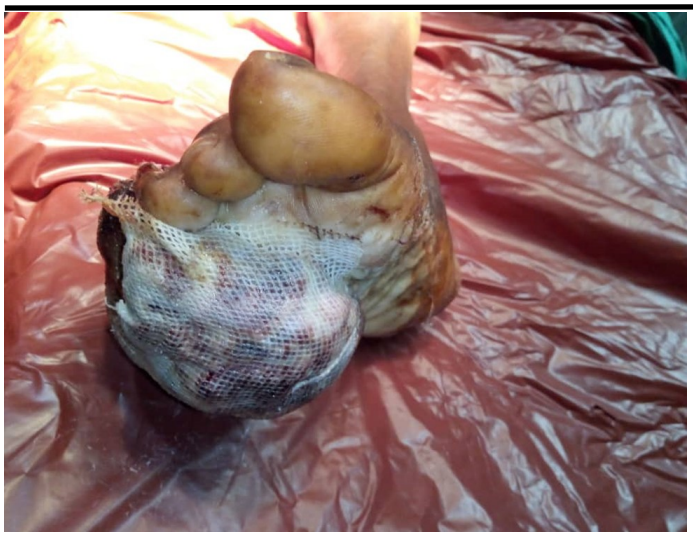

Figure 4: Huge Nodular Foot Mass in a Patient with Groin and Chest Metastasis.

as most patients initially got care from traditional homes where histological confirmation of disease is not done .

The incidence of melanoma globally has been on the increase[26]. However, malignant melanoma is under diagnosed in our environment due to the poor health-seeking behavior of Nigerians living in the southern region. Patients usually present late with fungating lesions and clinical evidence of metastasis as shown in figures 5 - 8. Myths and fetish beliefs act as a limitation to early presentation and compliance to care. Hence getting comprehensive data on this condition is limited by these factors.

The commonest procedure done was wide local excision. This included surgical excision of the tumour with a 1- 2 cm margin of normal surrounding tissue excised along the tumour. The tumour was excised down to the fascia. This was done to achieve complete tumour clearance. Stage 1 tumours were excisesed using 1cm margin of excision. Stage 11 and above were excised with a 2cm margin. Tagging with different colours of sutures helps to identify areas in which there may be residual tumour cells. The

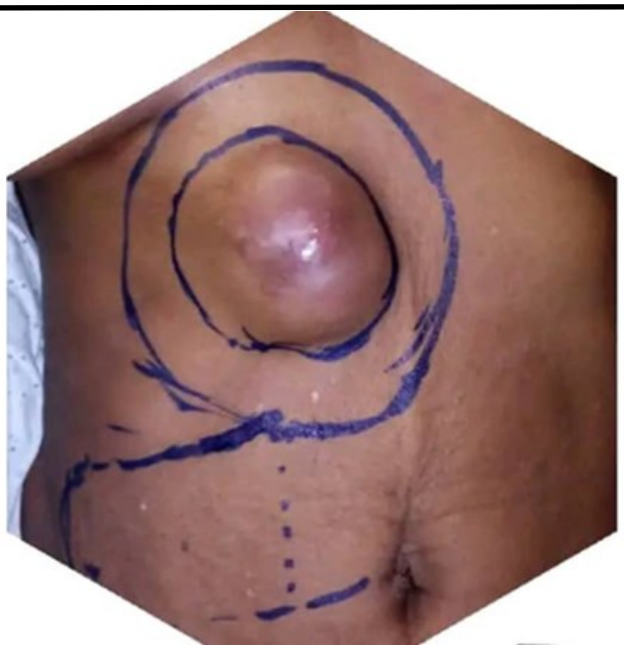

Figure 5: Picture Showing Chest Nodules Plus Marking for Excision and Fasciocutaneous Flap Cover

goal of surgical treatment of melanoma is the removal of the primary tumour with free surgical margins, evaluation of regional spread as well as giving adjuvant treatment that will increase the life expectancy of the patient[27]. Wide excision of primary tumors with a normal skin margin of 0.5 cm for in situ melanomas, of 1 cm for tumors with a Breslow thickness up to 2 mm and 2 cm for thicker tumors is recommended[28, 29].

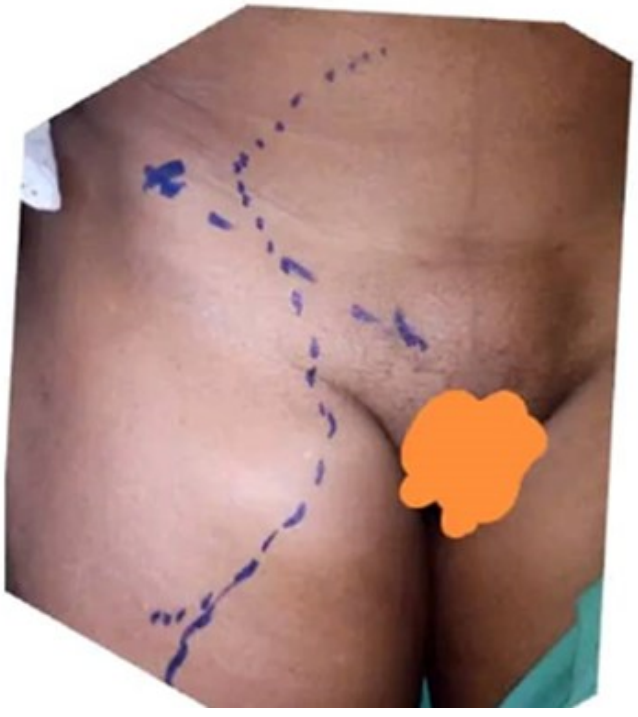

Figure 6: Showing Groin Metastasis Plus Markings for Groin Exploration

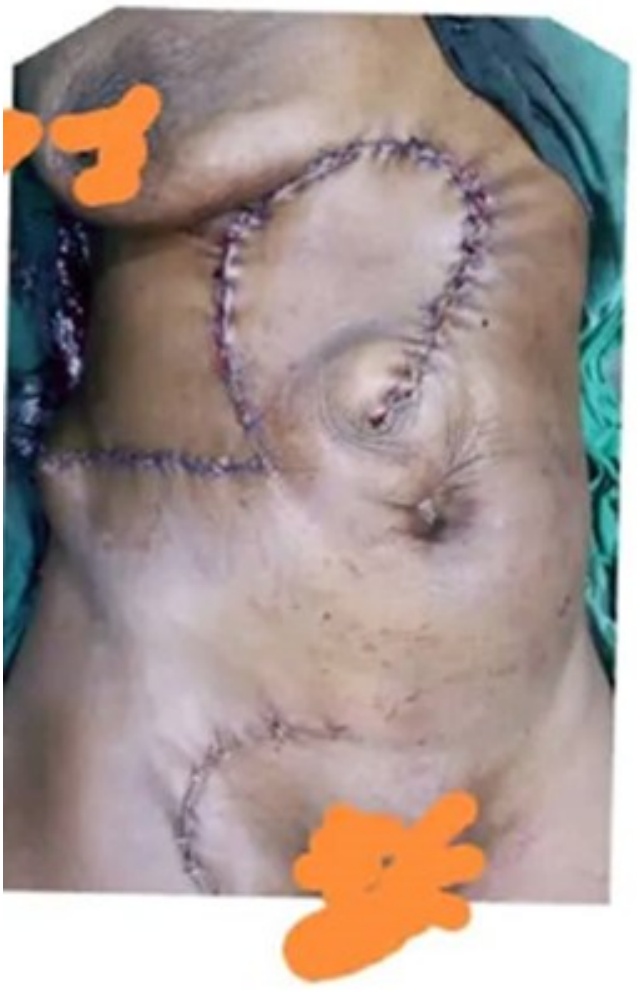

Figure 8: Immediate Postoperative Photograph of Flap Cover of Chest Defect.

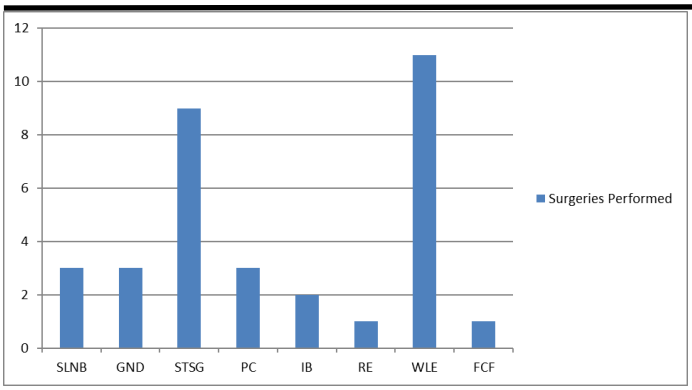

Figure 7: Surgical Procedures Performed

SLNB (sentinel lymph node biopsy), GND (groin node dissection), PC (primary closure), IB (incisional biopsy), RE (re- excision of positive margins) FCF (fasciocutaneous flap), WLE (wide local excision).

Following tumour excision, closure of the resulting defect may posed a significant challenge. Primary closure where possible is the simplest mode of closure in the reconstructive toolbox. Skin grafts, locoregional flaps as well as distant flaps may be necessary depending on the defect, the patient's desire and possible aesthetic outcome[30, 31]. In this study primary closure was done for patients who had small defects, of less than 5cm. The edges of the wounds were undermined and closed in layers. Three patients (25%) had primary closure for tumour involving the upper limb, back and the leg. The margin of excision of these tumours was 1cm. Most of the patients (75%) had split thickness skin grafting after the excision of the tumour, due to the large post excision defect. This gave room for easy re-examination of the site for possible recurrence. The graft healed adequately with one patient having re-excision for positive margins.

Sentinel lymph node biopsy is a surgical technique that involves the intraoperative injection of a radioisotope or blue dye (in our cases methylene blue), in the tumour bed. The first node ("sentinel node") to pick up the dye is examined in the groin nodal basin histologically for melanoma. This is considered the most important prognostic factor for disease-specific survival of patients with melanoma greater than 1 mm in thickness[32]. Groin dissection was done for patients with lymph nodes positive for melanoma and nodular groin swelling as shown in figure 7. Studies have demonstrated overall survival advantage of groin dissection in patients with histological positive nodes for melanoma[33]. Following histological diagnosis and surgical clearance of tumour, patients were sent to radio-oncologist for radiotherapy and chemotherapy depending on tumour stage and grade.

However, the challenges noticed in this series were the noncompliance of patient with chemotherapy, follow up treatment as well as monitoring for recurrence after excision. This may be due to financial constraint and poor coverage of the national health insurance scheme. Only 2 patients were on follow up for 2 years. Others were lost to follow up. The two patients who complied with chemotherapy had good outcomes, with no tumor recurrence even after two years of follow-up. This finding suggests that chemotherapy may have a positive effect on overall treatment outcomes. However, previous studies have shown that chemotherapy does not significantly prolong survival but rather helps to palliate symptoms in patients with advanced disease[34, 35]. The results of this study therefore suggest that compliance with adjuvant therapy after surgery may improve overall patient outcomes. Further studies are needed in our setting to confirm these potential benefits, especially given the small sample size of the present study

4.1 Conclusion

The commonest site of melanoma was the lower limb. Nodular foot lesions may result from repeated trauma to the sole of the foot. Excision biopsies and skin grafting were the commonly performed procedures. Late presentation and non-compliance to treatment modalities are some of the challenges encountered in our setting.

Conflict of interest:

We declare that we have no financial or personal relationship(s) which may have inappropriately influenced us in writing this paper.

Data Availability Statement:

Data used for this work can be made available by the author or co-authors on request.

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