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Pattern, Presentation and Management of Marjolin's ulcer in OmdurmanTeaching Hospital

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Abstract:

Background: Marjolin's ulcer is a rare but highly aggressive squamous cell cancer that is most often associatedwith chronic burn wounds.It is the worst complication that victims surviving burn injuries suffer from, but it can be prevented by proper initial management of burn injuries. There was no enough data about this condition in Sudan.

Objectives: This study was conducted to study the presentation, causes, latency period, frequency, and management of Marjolin's ulcer in our local setting in Omdurman teaching hospital.

Patients and Methods: This is a prospective cross sectional hospital based study that has been investigating the patients of Marjolin's ulcer seen at plastic and reconstructive surgery in Omdurman teaching hospital. The study was conducted during the period from May 2010 to January 2013. A special patient data sheet was designed for data collection. Data was analyzed and presented graphically using Statistical Package for Social Sciences (SPSS) software.

Results: During this period, 65 cases of Marjolin's ulcer were included in this study, 44 (67.7%) of them were males and 21 (32.3 %) were females. Male to female ratio is 2.1:1. The mean age was 48 years ± 14.7. With regard to the distribution of the study population by geographical areas, 37 (56.9 %) of them were residing in rural areas and 28 (43.1 %) in urban areas. 25 (38.5 %) of them were farmers and 17 (26.2 %) were house wifes. Chronic un-healed ulcer was the presentation of all patients.

Burn was the cause of ulcer in 43 (66.2 %) of the patients, followed by trauma 15 (23.1 %), and infection 7 (10.8 %). Flame burn represented 34 (52.3 %) of cases (p = .000). Concerning the management of the primary cause of the ulcer 44 (67.7 %) were managed in a hospital either by dressing or surgery, while 21 (32.3 %) were managed at home by dressing. The lower limbs were the common site of Marjolin's ulcer 47 (73.3 %), followed by the upper limbs 10 (15.4 %).The mean ulcer duration (latency period) was 25.96 years ± 8.59. 8 (12.3 %) of the patients has regional lymph nodes involvement all of them were offered lymph nodes dissection.All patients underwent surgery, 43 (66.2 %) underwent excision of the ulcer and split thickness skin grafting, 14 (21.5 %) excision and flap, and 8 (12.3 %) underwent limb amputation. The commonest histological type was squamous cell carcinoma (SCC) 63 (96.9 %).

Conclusion: Marjolin's ulcers are not uncommon in our setting and commonly occur in burn scars due to deep burn that were not skin grafted and were left to heal secondarily;

In general this disorder is rarely diagnosed although its etiology is well known; and most of the patients presents late when the disease is already in advanced stages.

ملخص الدراسة:

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مقدمة: قرحة مارجولين هى سرطان جلدى يصيب الخلايا الحرشفية يحدث غالباً بعد الحروق فى مواضع التليف وبعد الجروح المزمنة. المرضى الذين يتعافون من الحروق معرضون للإصابة بمضاعفات كثيرة أخطرها قرحة مارجولين والتى يمكن منع حدوثها بالعلاج الأولى الفعال للحروق. لاتوجد دراسات كثيرة عن هذا المرض فى السودان.

أهداف الدراسة: هذه الدراسة الغرض منها دراسة طريقة حدوث قرحة مارجولين و الأسباب المؤدية لها وفترة الحضانة منذ الإصابة الأولى حتى التحول لقرحة مارجولين وطريقة علاجها فى مستشفى أمدرمان التعليمى.

طرق البحث: لقد تم تصميم إستبيان خاص لجمع المعلومات عن مرضى قرحة مارجولين الذين تم علاجهم فى وحدة جراحة التجميل والترميم بمستشفى أمدرمان التعليمى فى الفترة من مايو 2010 حتى يناير 2013. تم ملء الإستبيان و بعد ذلك تم تصنيف المعلومات وإدخالها الكمبيوتر وتحليلها بواسطة البرنامج الإحصائى الحزمة الإحصائية للعلوم الإجتماعية.

النتائج:خلال الفترة المذكورة 65 حالة قرحة مارجولين شملتهم الدراسة 44 منهم (67.7%) رجال و21 (32.3%) نساء نسبة الرجال إلى النساء 2.1:1 .متوسط الأعمار 14.7±48 سنة. فيما يتعلق بالتوزيع الجغرافى للمرضى وجدنا أن 37 (56.9%) منهم يعيشون فى الريف بينما 28 (43.1%) يعيشون فى الحضر. 25 من المرضى (38.5%)مزارعون و17 (26.2%) ربات منازل.القرحة المزمنة التى لم تلتئم هو السبب الرئيسى لحضور المرضى للعلاج. الحروق هو سبب القرحة فى 43 مريض(66.2%) يليه الإصابات15 (23.1%) ثم الخمج 7 (10.8%).

الحروق بواسطة اللهب سبب القرحة فى 34 (52.3%) من المرضى. فيما يخص علاج السبب الأولى للقرحة 44 (67.7%) منهم تم علاجهم فى المستشفى إما بواسطة غيار فقط أوجراحة فى حين 21 (32.3%) تم علاجهم فى المنزل عن طريق غيار الجروح. فى 47 (73.3%) حالة كانت القرحة فى الأطراف السفلية يليها الأطراف العلوية 10 (15.4%). متوسط فترة الحضانة من حدوث القرحة إلى إكتشافها كقرحة مارجولين 25.96 ± 8.59 سنة . 8 مرضى (12.3%) كانت لديهم نقائل فى الغدد اللمفاوية المجاورة كلهم أجريت لهم عملية إزالة للغدد اللمفاوية. كل المرضى أجريت لهم عمليات جراحية تفاصيلها كما يلى:

43 (66.2%) تم إزالة القرحة وعمل رقعة جلدية جزئية السمك.
14 (21.5%) إزالة القرحة ورقعة سميكة

8 (12.3%) بتر الطرف المصاب بسبب تقدم المرض.

بفحص العينات للنسيج الإمراضى 63 حالة (96.9%) كانت سرطان الخلايا الحرشفية

خاتمة: قرحة مارجولين ليست نادرة فى مجتمعنا وغالباً تحدث بعد الحروق فى حال عدم علاجها برقعة جلدية عندما يؤثر على كل سمك الجلد وتركها لتلتئم لوحدها. بصورة عامة هذا المرض نادراً ما يتم تشخيصه بالرغم ان سببه معروف و معظم مرضى قرحة مارجولين فى مجتمعنا يأتون متأخرين ويكون المرض فى مرحلة متقدمة.

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Introduction:

Background: Marjolin's ulcer is a cutaneous malignancy usually squamous cell carcinoma that arises in previously traumatized or chronically inflamed skin, particularly after burns [1].

The term "Marjolin'sulcer" was named after French surgeon, Jean Nicolas Marjolin, who first described the condition in 1828 [1,3]. But it was Dupuytren who noted it was a malignancy. [4]

In 1923, DaCosta first coined the expression "Marjolin's ulcer" to describe malignant tumors forming over burn injuries [5]. Marjolin's ulcer is commonly mistaken for an infected ulceration occurring at the scar tissue sites.

Marjolin's ulcers present histopathologically as squamous cell carcinoma in 75% to 96% of cases [6]. Other neoplasms, such as basal cell carcinomas, melanoma, sarcomas (fibrosarcoma, liposarcoma, dermatofibrosarcoma protuberans, mesenchymal tumors), and osteogenic sarcoma, have also been reported [7,8].

Risk factors: Marjolin's ulcer no longer refers only to carcinomas secondary to burns, it has been reported in relation to osteomyelitis, venous stasis ulcer, tropical ulcers, chronic decubitus ulcer, frostbite, pilonidal sinus, vaccination site, urinary fistula, hidradenitis suppurativa, skin graft donor site, gunshot wounds, puncture wounds, dog bites, and lupus rash.[9]

Incidence and Latency period: Marjolin's ulcers have a 1% to 2% incidence in all burn scars. Men are three times more frequently affected than women [10].

The latency period from the time of injury to the onset of malignant transformation averages 36 years [11].The age of the scar is more important than the age of the patient, the longer the duration of the chronic ulcer, the more likely for a malignant transformation to occur, however, early arising Marjolin's ulcers have been described in the literature [7,11]. Studies from western countries have shown that the average age at diagnosis is in the fifth decade of life with a range of 18-84 years.

In Sub-Saharan Africa, Marjolin's ulcer appears to be affecting younger patients and the transition time is getting shorter over the years. [12]

Anatomical distribution: Most of the Marjolin's ulcers occur on the extremities (60%), with ulcers on the head and face occurring less frequently (30%) and the lowest frequency (10%) on the trunk [4].Marjolin's ulcers in unusual sites such as the genitalia as a complication of Fournier's gangrene [13] and breast skin developing in a post burn scar [14] have also been reported.

Of 93 cases studied and collected from the literature, Lawrence [15] found that 35 (37.6%) involved the lower extremities; in 21 cases (22.6%) the upper extremities was affected; in 20 (21.5%) the face and neck, in nine (9.6%o) the trunk, and in eight (8.6%o) the scalp was involved. This distribution is in marked contrast to that recorded by Elliott and Welton [16] for spontaneous carcinomas of the skin; in 1,742 patients treated, more than 90 percent of the lesions were located on the face and neck.

Mechanism and pathogenesis: The exact mechanism of malignant transformation of Marjolin's ulcer remains unclear and controversial [11,17,18]. Several theories including the toxin, chronic irritation, traumatic epithelial elements implantation, heredity, immunologic privileged site, co-carcinogen, ultraviolet rays, initiation and promotion and environmental and genetic interaction

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theories have been reported to explain the malignant transformation [12].

Hill et al (1990) proposed that chronic irritation leading to a continual circle of repeated damage and repair of the cells could be a contributing factor in the initiation of carcinogenesis. Trauma to the skin results in the implantation of epidermal cells into the dermis. The dermal tissue responds to this with a foreign body type reaction which, in turn, alters the normal regenerative process of the dermis. The dermis will fail to behave normally in response to further insults and the healing process will be altered leading to malignancy (Arons et al, 1966; Fleming et al, 1990).

Clinical presentation and diagnosis: Early diagnosis and prompt surgical intervention is mandatory in Marjolin's ulcers as they may invade vital structures. However, in developing countries, most patients are treated as chronic ulcers or infections and present late to hospitals, leading to a delayed diagnosis and resulting in the need for more extensive surgery and an increased risk of metastasis. The typical clinical presentation is that of a chronic scar or non-healing ulcer that becomes painful and is acutely associated with change in size, appearance, and odor [34, 35].The changes include enlarging in circumference, with elevated and indurated borders, foul smelling discharge in 68% of cases and hemorrhage in 58% of cases [34].

A retrospective review of 56 cases in Tanzania by Chalya et al showed that the majority of patients presented with increasing pain (92.9%) and foul smelling pus discharge (89.3%) and most of them (51.8%) had exophytic proliferative ulcers [39].

Surgical biopsy performed in multiple sites is recommended to confirm the neoplasmatic conversion [37, 38, 39]. Quite often, additional X-ray may show bone destruction. Unfortunately diagnosis is often delayed. As a result approximately 30% of the cases have enlarged lymph nodes with possible metastasis [40]. 449 cases reviewed confirmed the highly metastatic potential of Marjolin's ulcer. Available data showed lymph node invasion in 19% of the cases and 13% had distant metastases. [40, 41, 42, 43]

Novick et al reported a 54% incidence of metastasis from lower extremity lesions. Metastasis to the brain, liver, lung, kidney, and distant lymph nodes have been reported [44].

Grading: Lifeso and Bull used a three-grade histopathological classification: grade I (well differentiated), grade II (moderately differentiated), and grade III (poorly differentiated). [35]

Treatment: Treatment of Marjolin's ulcer should be multidisciplinary. Although there has not yet been a consensus reached over the management protocol, there is agreement among most of the researchers that surgery is the primary treatment.

First of all, excision should be performed with cautery (which is believed to be safer as it may prevent metastasis by preventing tumor cells from being washed into the blood and lymph systems) with the addition of a small margin, for the skin, performed with a surgical scalpel for better healing. [38, 39]

Excision of ulcers should include a 3–4cm margin of normal skin with muscle and fascia due to the high metastatic potential and recurrence tendency [38, 39,40].

Defects are usually skin grafted either with split-thickness skin grafts (STSG) or free flaps [38, 39].

If there is a clinically palpable lymphadenopathy, lymph node dissection is recommended [38, 39, 40,34] with an exception for malignant melanoma, where the sentinel lymph node biopsy should be

performed regardless of the presence of enlarged lymph nodes.

Controversies Surrounding Radiation and Chemotherapy: The role of radiation and chemotherapy is controversial and, frankly, unknown.Coburn questioned the rationale for using radiation in poorly vascularized scar tissue and indicated that surgery is a better therapeutic option [45]. Dupree and colleagues found that radiation and 5-fluorouracil therapy were ineffective in the treatment of Marjolin ulcer [21]. Novick and colleagues wrote that, because of the nature of this carcinoma, radiation treatment is not recommended [44]. In contrast, Ryan and colleagues concluded that 5-fluorouracil induced round-cell infiltrate, creating immunologic benefit and actually eliminating cancer in 3 cases [56]. Overall, a literature review supports adjuvant radiation and/or chemotherapy when resection is not logical or when a patient refuses surgery. [43].

Objectives:

General: To study the presentation, frequency and management of Marjolin's ulcer in Omdurman teaching hospital

Specific:

1. To study the age distribution pattern of Marjolin's ulcer.
2. To determine predisposing factors and causes among those patients.
3. To assess the average time for the carcinomatous changes to occur in a chronic ulcer.
4. To study the types of management of Marjolin's ulcer in plastic and reconstructive surgery unit in Omdurman teaching hospital.
5. To study the histological types of Marjolin's ulcer.
6. To compare the results with literature.

Methodology:

This is a prospective cross sectional hospital based study that has been investigating the patients of Marjolin's ulcer seen at plastic and reconstructive surgery in Omdurman teaching hospital. The study was conducted during the period from May 2010 to January 2013. A special patient data sheet was designed for data collection and it was filled pre- and postoperatively. Data was coded and fed in a computer to handle statistical procedure, to display the analyzed data and present them graphically using Statistical Package for Social Sciences (SPSS) software.

Results:

Demographic data: During the period from May 2010 to January 2013, 65 cases of Marjolin's ulcer were included in this study, 44 (67.7%) of them were males and 21 (32.3 %) were females. Male to female ratio is 2.1:1.The mean age was 48 years ± 14.7; .With regard to the distribution of the study population by geographical areas, 37 (56.9 %) of them were residing in rural areas and 28 (43.1 %) in urban areas. 25 (38.5 %) of them were farmers and 17 (26.2 %) were house wives (Figure 1).

Causative previous lesions: Chronic un-healed ulcer was the presentation of all patients. Burn was the cause of ulcer in 43 (66.2 %) of the patients, followed by trauma 15 (23.1%), and infection

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7 (10.8 %) (Table1). Flame burn represent 34 (52.3 %) of casesof burn (p = .000) (Table 2).

Management that was received for the primary cause of ulcer: Concerning the management of the primary cause of the ulcer 44 (67.7 %) were managed in a hospital either by dressing or surgery, while 21 (32.3 %) were managed at home by dressing (Table 3).

Latency period: The mean ulcer duration (latency period) was 25.96 years ± 8.59.

Anatomical distribution and regional lymph nodes involvement: The lower limbs were the commonest site of Marjolin's ulcer 47 (73.3 %), followed by the upper limbs 10 (15.4 %) (Figure 2).8 (12.3 %) of the patients had regional lymph nodes involvement.

Treatment modalities and histopathological type: All patients underwent surgery, 43 (66.2 %), they underwent excision of the ulcer and split-thickness skin grafting (SSG), 14 (21.5 %) excision and flap for reconstruction, and 8 (12.3 %) underwent limb amputation (Figure 3). Squamous cell carcinoma (SCC) represented 63 (96.9 %) of patients, and 2 patients (3.1%) were soft tissue sarcomas.We had not encountered the other variants of skin cancer. All lymph node positive patients were offered lymph nodes dissection and confirmed by histopathology to have metastases

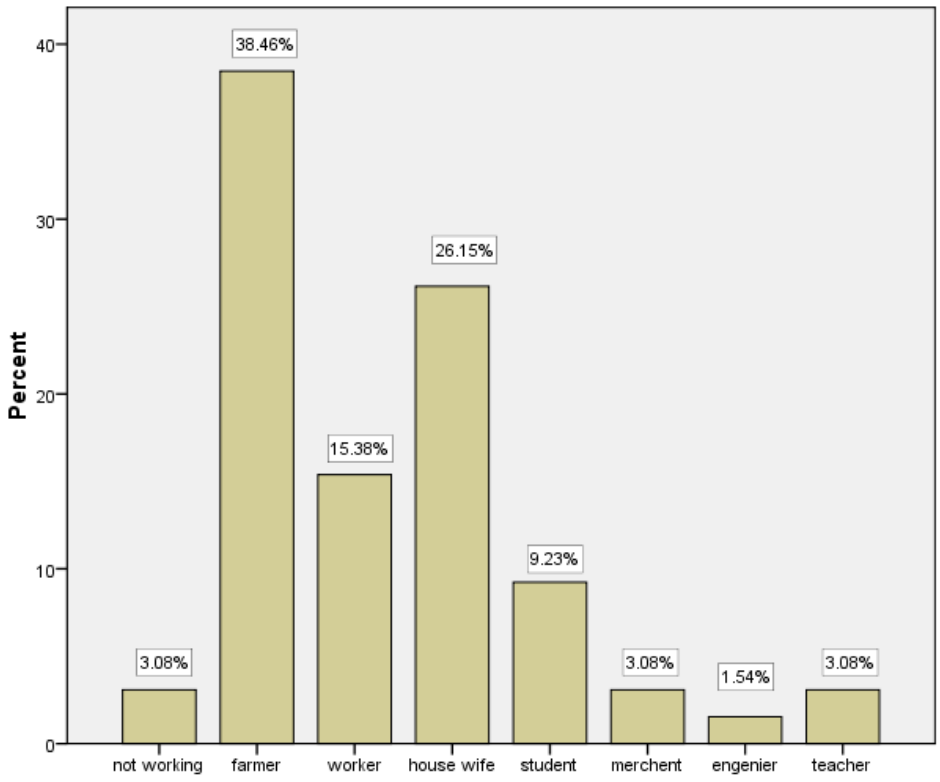

Figure (1):

Patient's occupation

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Table (1): Causes of the ulcer

Cause	Frequency	Percent %
Burn	43	66.1
Trauma	15	23.1
Infection	7	10.8
Total	65	100.0

Table (2): Causes of burn*

Cause	Frequency	Percent %
Flame	34	52.3
hot fluid	5	7.7
Electrical	3	4.6
Chemical	1	1.5
Total	43	66.1

***The reminder of cases 22 (33.9 %) were trauma and infection**

Table (3): The management for the initial cause of ulcer

Management	Frequency	Percent %
Dressing	48	73.8
Surgery	17	26.2
Total	65	100.0

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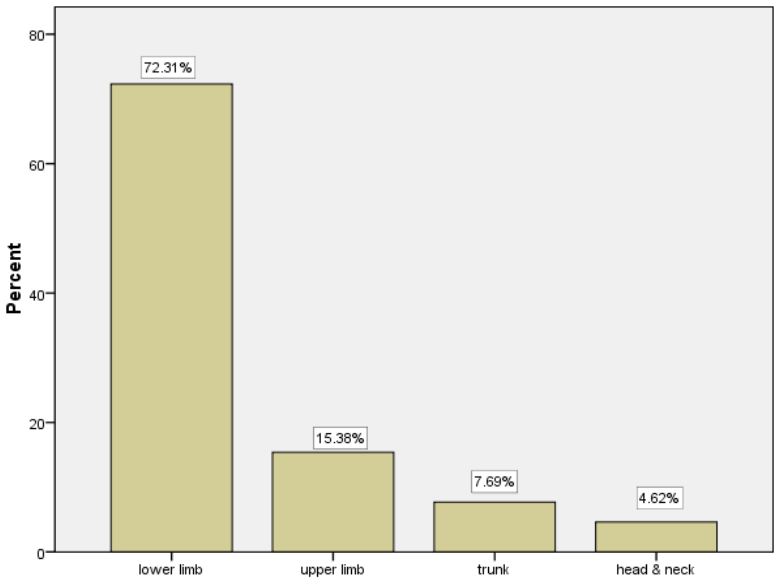

Figure (2): Site of ulcer

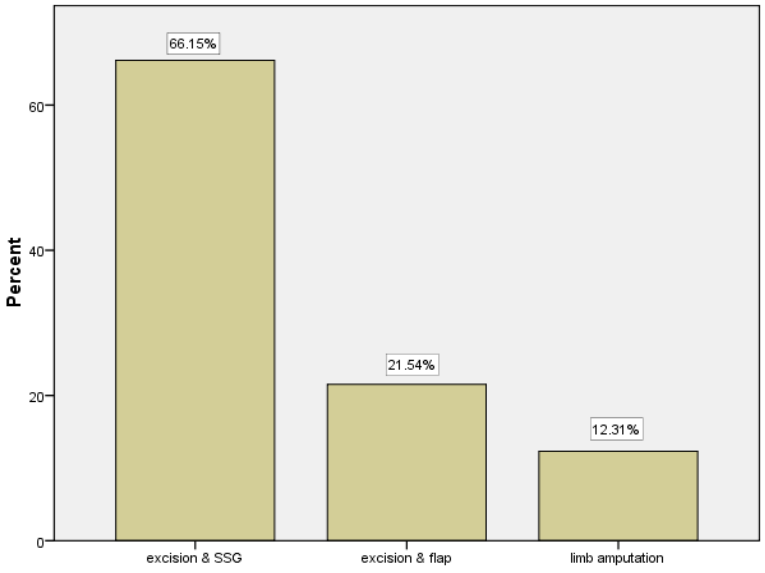

Figure (3): Type of surgery

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Figure (4): example of Marjolin's ulcer in the lower limb

A

B

Figure (5): (A) Marjolin's ulcer in the non-weight bearing area of the sole of left foot; (B) after excision and split-thickness skin grafting (SSG).

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Figure (6): Anterior neck Marjolin's ulcer excised and reconstructed using pectoralis major miocutaneous flap.

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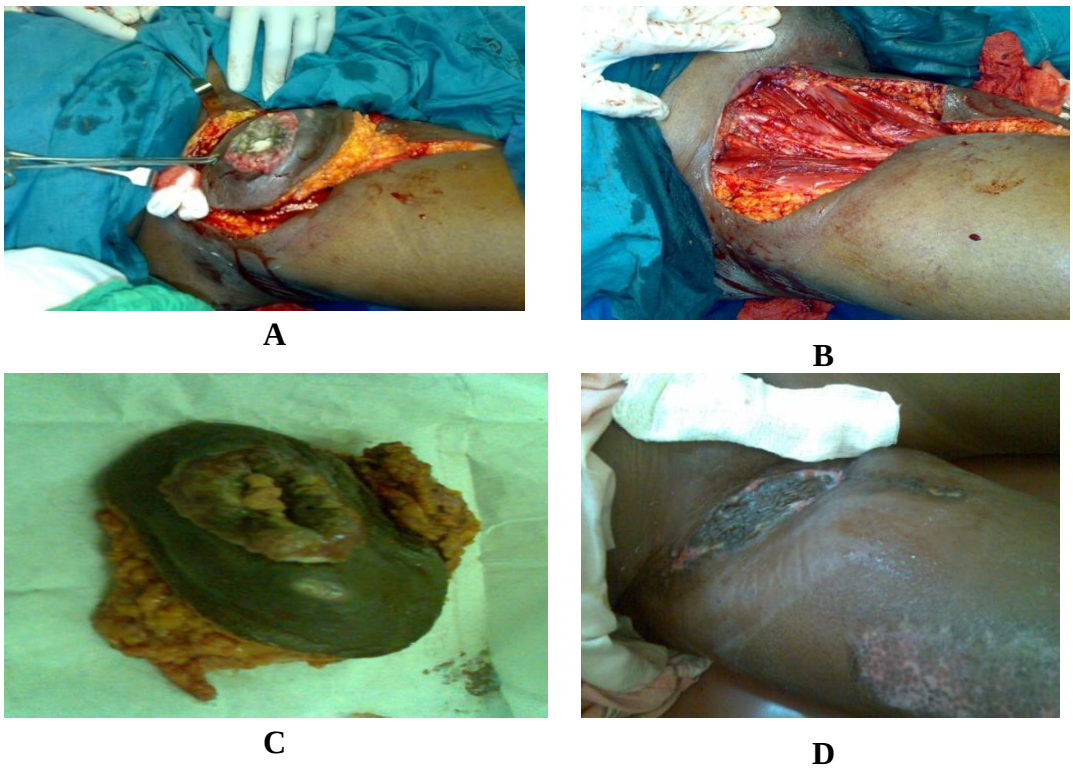

Figure (7): Inguinal lymph nodes dissection, A: en bloc dissection of the fungating lymph nodes, B: the bed with visible femoral vessels which was covered with gracilis muscle and skin graft, C: the specimen, D: the patient after wound healing.

Discussion:

Marjolin's ulcer is defined as a tumor arising from a chronic wound, scar or chronic inflammation [(1)]. Jean Nicholas Marjolin first described the malignant transformation of cutaneous scars in 1828 [(1,3)]. Since then, several reports of post-burn scar ulcers have been reported .Various studies indicate that Marjolin's ulcers make up 1% to 2% of all skin cancers. [(10)]

In this study, the mean age of patients was 48 ± 14.7 years which is close to the age reported in western countries as they state that the average age at diagnosis is in the fifth decade of life [(10,19)] , but it is higher than what has been reported in Tanzania, where the mean age was 38.2 years [(36)] . Male to female ratio was 2.1:1, the same ratio reported by Chalya et al from Tanzania in his retrospective review of 56 cases of Marjolin's ulcer [(36)]. We have two patients (3.1 %) below 18 years, and this is going with what has been mentioned by Nthumba PM [(12)] that in Sub-Saharan Africa, Marjolin's ulcer appears to be affecting younger patients and the transition time is getting shorter over the years, therefore, patients presenting with chronic ulcers should be investigated during the initial evaluation for this possibility. Further research is needed in our region to explain and confirm this observation.

The two-fold increase in the number of males with Marjolin's ulcer compared to females in this study is similar to what has been reported in other studies [(18,34,36)]. Male preponderance in this

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study may be due to their increased susceptibility to trauma (38.5 % were farmers) which, if poorly managed, has been reported to undergo malignant transformation.

In agreement with other studies [4,8,10,14,18], the most frequent predisposing lesion of Marjolin's ulcers in this study was post burn scars (66.2 %). Marjolin's ulcer has also been reported following other traumatic injuries 23.1 %, infection, mainly osteomyelitis 10.8 %. Marjolin's ulcer generally occurs in regions of previous deep burn that healed slowly without skin grafting. This observation is reflected in our study where 56.9 % of patients were residing in rural areas, and 32.3 % of them were reported to manage their previous causative lesions at home only by dressing. There is strong association between burn scar due to flame burn and the development of Marjolin's ulcer (P = .000). This could be due to the full thickness burn caused by flame burn and subsequent scar formation if untreated properly.

In keeping with other studies [4, 20, 32, 43] the lower limbs were the most frequent site of Marjolin's ulcer 73.3 %, followed by the upper limbs 15.4 %, trunk 7.7 % and head & neck 4.6 %. The anatomical locations reported by Lawrence [15], Arons [25], and Novak [44] show that average distribution of Marjolin's ulcers is 40 % in the lower extremity, 30 % in the head & face, 20 % in the upper extremity and 10 % in the trunk area. The reason for this anatomical site predilection is not well understood.

The mean latent period between original injury and diagnosis of Marjolin's ulcer in this study was 25.96 ± 8.59 years, a little bit higher than what has been reported by Chalya et al from Tanzania 11.34 ± 6.14 years. [36]

The treatment of Marjolin's ulcers requires multidisciplinary approach. Treatment modalities include wide local excision, block dissection of the regional nodes when they are involved, amputation in advanced lesions of limbs. Radiotherapy and chemotherapy given either as neo or adjuvant therapy [11]. Wide local excision (surgical margin of at least 2 cm), together with skin grafting primarily or primarily delayed, is usually considered appropriate in the treatment of Marjolin's ulcers [11,39].Adequate surgical resection is most important to prevent local recurrence and a margin of 2-5 cm has been advocated [12,39]. Frozen sections have been reported to be used for intraoperative diagnosis and evaluation of surgical excision safety margins [49]. However, like in most developing countries, frozen sections are not performed in our center partly because of few available pathologists and lack of facilities for performing frozen sections. Amputation is indicated when wide local excision is not possible due to deep invasion, bone or joint involvement, infection, or hemorrhage, or when excision would cause major functional disability. In this study, all patients underwent surgery. In agreement with other studies, wide local excision with either skin grafting (66.2 %), or flap coverage (21.5 %), was the most frequent surgical procedure performed in this study. Limb amputation was performed in 12.3 % of cases. Regional lymph node dissection is indicated when nodes are clinically palpable with an exception for malignant melanoma, where the sentinel lymph node biopsy should be performed regardless of the presence of enlarged lymph nodes [39].All patients who have lymph nodes involvement (12.3 %) underwent lymph node dissection, and confirmed by histopathology to have metastases. The commonest histopathological type of carcinoma in Marjolin's ulcer is squamous cell carcinoma, followed by

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basal cell carcinoma as the second commonest carcinoma [7,8,11,18,34]. This finding is in agreement with the present study in which more than 96.9% of Marjorie's ulcers were squamous cell carcinoma but the difference is we have two patients of soft tissue sarcoma. One of them was proved to be fibrosarcoma and the other was malignant mesenchymal tumor.

Conclusion:

1. Marjolin's ulcers are not uncommon in our setting and commonly occur in burn scars that were not skin grafted and were left to heal secondarily;
2. Burn scar cancers have a predilection for the extremities and trunk, contrasted to cutaneous carcinomas which arise in the face.
3. The age of the burn scar is of greater importance than the age of the patient.
4. Marjolin's ulcers have a variable latent period and sometimes occurred in younger patients.
5. Although Marjolin's ulcers are usually of low pathologic grade, metastases can occur and the prognosis may be poor;
6. In general this disorder is rarely diagnosed although its etiology is well known
7. Most of the patients in our society present late when the disease is already in advanced stages.

Recommendations:

1. Most researchers agree that the best prevention of these scar malignancies is primary skin grafting of the burn sites, so early excision and grafting of all full thickness burns is crucial.
2. Chronic non healed ulcers should be adequately evaluated.
3. Sinuses, osteomyelitis should be treated properly, and any suspicious lesions that arise within affected areas should biopsied as a gold standard.
4. Further research is needed in our region to explain the development of Marjolin's ulcers in younger ages.
5. Health education is highly needed to convince patients to accept doing surgery for full thickness burns, and to discourage patients with cutaneous ulcers from presenting late to hospital.
6. Multidisciplinary approach should be adopted in the management of patients with Marjolin's ulcer.

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