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Original Research Article

Histopathological spectrum of chronic skin ulcers in a tertiary care hospital

Imza Feroz[1]*, Abdul Haseeb Wani[2], Mir Wajahat Un Nazir[1], Mohammad Iqbal Lone[1], Arshed Hussain Parry[2]

[1]Department of Pathology, [2]Department of Radiology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India

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***Correspondence:**
Dr. Imza Feroz,
E-mail: drimzaferoz@gmail.com

ABSTRACT

Background: The skin is the largest organ of the body, comprising of epidermis, dermis and hypodermis. Thus, a wide range of diseases can develop from the skin ranging from infectious diseases to malignancy, some of which may present as non-healing ulcers. Skin biopsy forms the fundamental basis for differentiation of similar looking lesions, thus helping the pathologists to make a definitive diagnosis and more so to the clinician for better management of patients. The objective was to study the histopathological spectrum of chronic non healing ulcers of skin for proper management and treatment.
Methods: This was a hospital-based study which was conducted in SKIMS, Soura, a tertiary care hospital of Kashmir valley for a period of 1 year extending from January 2018 to December 2018. All the patients who presented with the complaint of non-healing ulcer for more than 4 to 6 weeks were subjected to skin biopsy and histopathological examination.
Results: A total of 260 biopsies were examined. Out of 260 patients 146 were males and 114 were females. Ninety out of 260 cases (34.61%) and 170 (65.39%) were diagnosed as malignant and benign ulcers respectively. Diabetic ulcer was the second most common cause of non-healing ulcers followed by bacterial infections and tuberculosis. Squamous cell carcinoma was the most common neoplastic pathology.
Conclusions: It was concluded from the study that non-healing skin ulcers can be encountered at any age in daily medical practice.

Keywords: Diabetic neuropathic ulcer, Skin biopsy, Non-healing ulcer, Squamous cell carcinoma, Malignant melanoma, Xeroderma pigmentosum

INTRODUCTION

The skin is the largest organ of the body, comprising of Epidermis, dermis and hypodermis. Skin has important functions to perform like protection, temperature regulation and also metabolic.[1] Because of its complexity a wide range of diseases can develop from the skin ranging from infectious diseases to malignancy, some of which may present as non-healing ulcers.[2]

Chronic ulcers or non-healing ulcers are defined as spontaneous or traumatic lesions, typically in lower extremities that are unresponsive to initial therapy or that persist despite appropriate care and do not proceed towards healing in a defined time period with an underlying aetiology that may be related to systemic disease or local disorders.[3,4] There are many types of non-healing ulcers that may include venous, arterial, diabetic, pressure and traumatic ulcers. The normal wound healing

process is dynamic and complex having three phases: inflammation, tissue formation and tissue remodelling. However, if the normal healing process is interrupted, an ulcer can become chronic in nature due to lack of growth factors and cytokines which delay the healing process.[5] These non healing ulcers form a diagnostic challenge, and the biopsy and histopathological examination form the gold standard of diagnosis for them.

The presence of a chronic wound can result in significant morbidity or mortality. Chronic cutaneous ulcers are common in the developing countries like India, especially in rural areas with poor living conditions. Thus, the diagnosis of these diseases is very important for proper treatment of these ulcers to reduce morbidity and mortality.

Skin biopsy forms the fundamental basis for differentiation of similarly looking lesions, thereby giving valuable information to the pathologists to make a definitive diagnosis and more so to the clinician for better management of patients.[1] Cytopathology is a good option in the outpatient dermatological practice, but has many shortcomings.[6,7] Clinical diagnosis alone may not be conclusive many a times and histopathology becomes a prime requisite for the definite diagnosis.

METHODS

This was a hospital-based study which was conducted in SKIMS, Soura, a tertiary care hospital of Kashmir valley for a period of 1 year extending from January 2018 to December 2018. All the patients who presented with the complaint of non-healing ulcer for more than 4 to 6 weeks after a conventional therapy were included in this study. The detailed history and examination of patients was done, biopsy was done and sent to department of pathology. The tissue was sent in 10% formalin. The tissue was processed and slides were made which then were examined.

RESULTS

During the two years period department received biopsies from 260 patients with non-healing skin ulcers. Out of 260 patients 146 were males and 114 were females. Ninety out of 260 cases (34.61%) and 170 (65.39%) were diagnosed as malignant and benign ulcers respectively (Table 1). The age of our patients ranged from 35 years to 82 years with most patients in 6th and 7th decade of life. Diabetic ulcer was most common benign ulcer in 73 (28.07%) patients followed by infections in 62 (23.84%) patients. Tubercular ulcer was seen in 6 (2.30%) patients who responded to antitubercular therapy. Among malignant cases, Squamous cell carcinoma (Figure 1 and 4) was the most common malignancy encountered accounting for 74.66% of cases followed by basal cell carcinoma in 18.44% and malignant melanoma (Figure 2 and 3) in 6.9% of cases (Table 2).

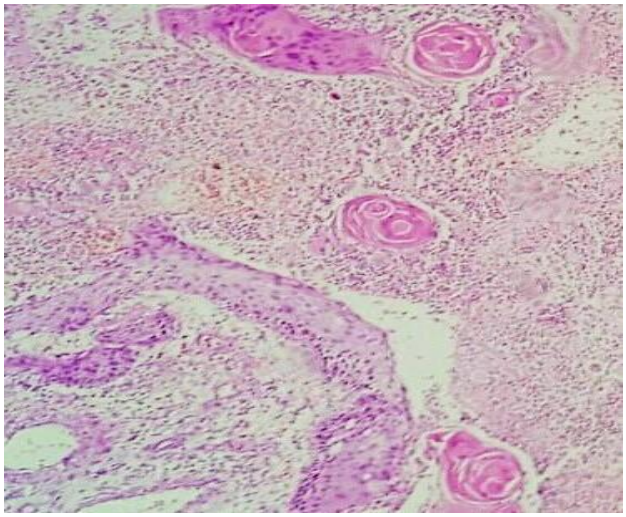

Figure 1: Low power (10X) view photomicrograph of skin biopsy showing tumour cells arranged in nests and irregularly at places with formation of keratin pearls. Individual tumour cells are pleomorphic with irregular vesicular nuclei. Features are suggestive of well differentiated squamous cell carcinoma.

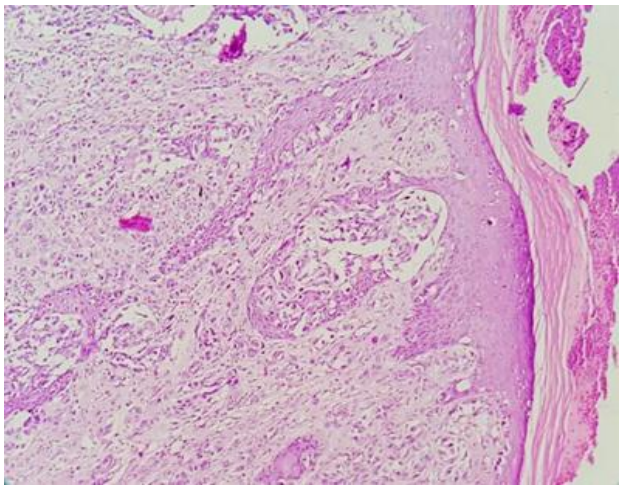

Figure 2: Low power (10X) view photomicrograph of skin showing junctional activity with trans epidermal migration of tumour cells forming nests at places. Individual cells are big with pleomorphic nuclei and abundant cytoplasm and prominent nucleoli. There is deposition of brown pigment. Features are that of malignant melanoma.

Table 1: Etiological factors of skin ulcers.

Etiology	No. of patients	Percentage (%)
Malignancy	90	34.61
Diabetic ulcer	73	28.07
Infections	62	23.84
Tuberculosis	6	2.30
Leprosy	3	1.15
Others	26	10
Total	260	100

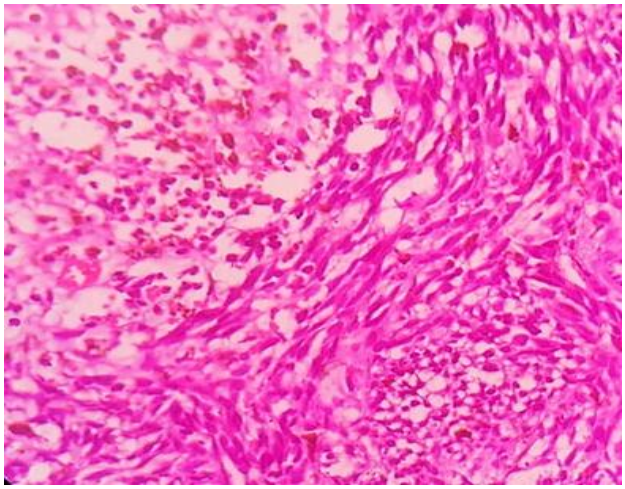

Figure 3: High power (40X) view of malignant melanoma showing brown pigment deposition.

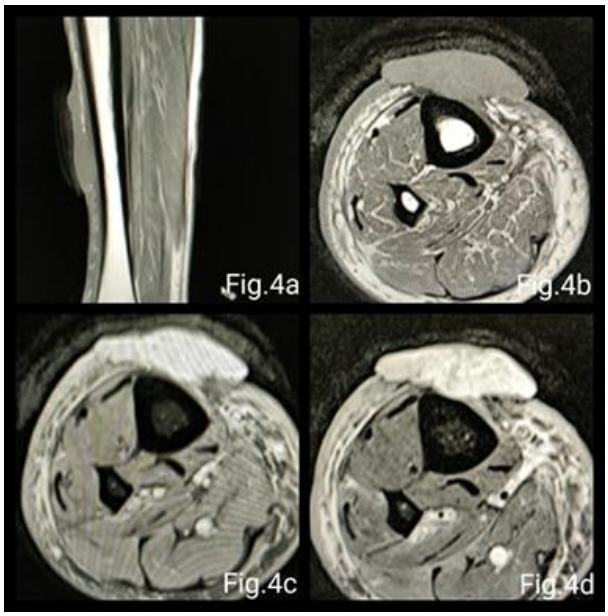

Figure 4: (a) Coronal TIW, (b) axial T1W, (c) axial T2W and (d) post-contrast T1W axial MRI images in a 60-year old patient at the junction of mid and lower third of right leg show enhancing cutaneous lesion extending up to the anterior cortex of tibia which proved to be squamous cell carcinoma on histopathology.

Table 2: Type of malignancy.

Malignancy	Percentage of patients (%)
Squamous cell carcinoma	74.66
Basal cell carcinoma	18.44
Malignant melanoma	6.9

Swabs from wound of 62 patients diagnosed as infectious ulcers were sent for culture and sensitivity tests, Staphylococcus was the most common pathogen accounting for 62% of the cases. Other organisms found were streptococcus, klebsiella, pseudomonas. Leprosy was seen in 3 patients, rest of the 26 cases were benign ulcers with no specific features to be categorised.

DISCUSSION

Non healing skin ulcers are an important cause of morbidity in developing countries.[8,9] Poor health services in remote areas and lack of public awareness may be the factors responsible for their development. The causes of non-healing skin ulcers are vascular insufficiencies including venous and arterial insufficiency, metabolic diseases like gout and diabetes, connective tissue diseases, hemoglobinopathies, neoplasia, traumatic, iatrogenic which includes drugs, panniculitis and cutaneous micro thrombotic ulcers.[10] Cutaneous leishmaniasis and cutaneous diphtheria are important cause of chronic skin ulcers in many tropical countries.[11] Zeegelar et al reported that venous ulcers and diabetic ulcers are common in developed countries.[12] However much is not known about the cause of ulcers in developing world which may be due to the poor availabilty of records.

In this study we found that the most common cause of non- healing skin ulcers is malignancy in 90 patients (34.61%) followed by diabetic neuropathic ulcers in 73 patients, tuberculosis in 6 patients, bacterial infections were found in 62 patients, leprosy in 3 patients and other causes in 26 patients. Results of our study were similar to studies from India by Saraf et al.[13] However the results were different from the western world data, where vascular ulcers were the common cause of non- healing skin ulcers. infections were leading cause in other study done by Zeegelar.[12,14] The difference may be because of different geographical distribution, racial characteristics, poor healthcare facilities and illiteracy.

It was observed that common age group for malignant ulcer was 6th and 7th decade of life with a male preponderance. Similar conclusions were drawn by Baba et al.[15] Also malignancy below the age of 42 years was seen in only 3 cases Similar to study done by Laishram et al.[16]

On histopathology malignant ulcers were found to be the most common cause of non-healing ulcers of skin accounting for 34.61% cases with squamous cell carcinoma (Figure 1 and 4) being the commonest in 74.66% cases followed by Basal cell carcinoma in 18.44% and Malignant melanomas in 6.9% cases (Figure 2 and 3). This is similar to the study done by Baba et al.[15] 6 patients with squamous cell carcinoma on histopathology presented with Marjolin's ulcer clinically. One patient was a 16-year old male who was a known case of Xeroderma pigmentosum first presented with ulcer on cheek and biopsy revealed squamous cell carcinoma and after 6 months patient developed spine metastasis. An image guided biopsy was done which

revealed metastatic deposits of malignant melanoma. Thus, this patient developed a double malignancy.

Diabetic ulcers were the second common cause for non-healing ulcers in our study in 28.07% patients. The result was similar to study done by Baba et al and Neil et al.[15,17] Neil et al found that approximately 20% of all non-healing skin ulcer related admissions in UK were due to diabetic foot ulcer disease.[17] However, our study results were different from Nyamu et al where the incidence of diabetic ulcer was 4.6%.[18] Diabetes is a fairly common lifestyle disease in Kashmir with high incidence of neuropathic complications. The reason for complications may be the negligence of people about the proper treatment of the disease.

Another cause of chronic ulcers was bacterial infection in 23.84% patients. *Staphylococcus* was the most common causative agent accounting for 62% of the infections similar to Zeegelar et al and Erikson et al.[11,19] Enterococcus was the most common organism in study done by Gaur et al and *Pseudomonas* as the most common organism in study by Bansal et al.[20,21] Giacometti et al also reported *Staphylococcus* as the most common organism.[22] The reason for discrepancy could not be assessed but may be due to the environmental factors and the intrinsic properties of the microorganism as reported by Paltrey et al.[23]

Granulomatous pathology was demonstrated in 9 patients. Tubercular ulcer was seen in 6 (2.30%) cases and leprosy in 3 patients. This result was in contrast to the study done by Baba et al where tuberculosis was seen in 18.46% cases however it is similar to the conclusion drawn by Padmavathy et al and Zafar et al who reported incidence of cutaneous tuberculosis as 1.6% and 3.62% of all skin biopsies respectively.[15,24,25] However, in the recent years, with the emergence of anti-tubercular drug resistant strains and AIDS epidemic, there is a worldwide rise in the incidence of tuberculosis. More so in the poverty struck areas of the world due to poor nutrition, poverty, non-availability of diagnostic aids and treatment, over-crowding, ignorance about the disease, rise in immunosuppressive therapy, decline in Tuberculosis control efforts and emergence of resistant strains of *Mycobacterium tuberculosis* have amplified the situation.[26,27] Tubercular ulcers were common in young people unlike malignancy which was common in elderly patients like the study of Padmavathy et al.[24] In 3 patients we demonstrated acid fast bacilli on Ziehl-Neilson staining. These patients responded well to anti tubercular drugs.

In 26 patients the findings were not consistent with any specific diagnosis and were categorised as other ulcers. These included venous and arterial ulcers, connective tissue diseases, and other aetiologies including trauma. The histopathological findings included skin denudation and non-specific chronic inflammation.

CONCLUSION

The most common cause of non-healing ulcer was malignancy in 90 patients with squamous cell carcinoma being the commonest. Most common benign cause of ulcer was diabetic neuropathic ulcer. It can be concluded from the study that non-healing skin ulcers can be encountered at any age in daily medical practice. Thus, an early biopsy to rule out malignancy and confirm the aetiology is mandatory for proper management of the patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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