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Histopathological Study of Tumours of Epidermis and Epidermal Appendages

Shilpa V. Uplaonkar*, Mandakini Tengli, Syeda Farheen***, Pratima S.******

*Assistant Professor, **Associate Professor, ***Post Graduate, ****Professor, Dept of Pathology, Khaja Banda Nawaz Institute of Medical Sciences, Kalaburagi, Karnataka 585104, India.

Abstract

Introduction: Skin is a complicated protective covering [1]. It is divided into two seemingly separate but functionally interdependent layers, i.e., epidermis and dermis. Adnexae extend from epidermis into the dermis and consist of specialized cells for hair growth, epithelial renewal (stem cells), and temperature regulation [2]. Epidermis has the capacity to develop an array of keratinocyte lesions, the causes of which are not known. Adnexal tumors may be benign or malignant, solitary or multiple [3]. *Aim of the Study:* 1. To study the histomorphological features of tumors of epidermis and epidermal appendages. 2. To analyze the clinicopathological features of these tumors. *Materials and Methods:* This was a 5 years' study on tumours of epidermis and epidermal appendages, studied i.e., from Jan. 2012 to Dec. 2016. Both biopsies and resected specimens were included in the study. *Results:* 69 cases of tumours of epidermis and epidermal appendages were encountered, of which, 51 cases (73.91%) were epidermal neoplasms, and 18(26.08%) cases were neoplasms of epidermal appendages. Out of 69 cases, 36(52.17%) were benign neoplasms and 33(47.83%) were malignant neoplasms. The incidence of keratinocytic tumours was high in the present study. Among adnexal tumours, most common were benign sweat gland tumours followed by tumours of hair follicle and sebaceous gland. Malignant adnexal tumours and hematolymphoid tumours were very rare. *Conclusion:* Skin tumours, at times, may be difficult to diagnose clinically. Hence histopathological examination is a must for definitive diagnosis. Increasing public awareness and surveillance will help in diagnosing the cases early for better management and prognosis.

Keywords: Epidermis; Appendages; Histopathology; Skin and Tumours.

Introduction

Skin is the largest organ in the body. It is a complicated protective covering, in which, precisely regulated cellular and molecular interactions govern many essential processes [1]. It is composed of cells with varied functions like mechanical and photoprotection, immunosurviellance, nutrient metabolism and repair [2].

Histology of the skin is amazingly complex. Skin is divided into two seemingly separate but functionally interdependent layers, i.e., epidermis and dermis. The epidermal layer is composed of 90% of keratinocytes and the remaining 10% includes melanocytes, Langerhans cells and neuroendocrine (Merkel cells). Adnexae extend from epidermis into the dermis and consist of specialized cells for hair growth, epithelial renewal (stem cells), and temperature regulation [2].

Epidermis has the capacity to develop into an array of keratinocyte lesions, the causes of which are not known. Adnexal tumors may be benign or malignant, solitary or multiple. There is considerable clinical and histological overlap, so clinicopathological correlation is a must for their exact identification [3].

The study of familial cancer syndromes has led to the discovery of key genes that are important not only for the understanding of the mechanismsm of genetic susceptibility but also for giving new insights

Corresponding Author: Shilpa V. Uplaonkar, C/o, Dr. Vinod Uplaokar, H.No. 2-415, Jagat, Uppek Lake, Kalaburgi. E-mail: mandakinibt@gmail.com

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into genetic and signaling pathways involved in sporadic cancers [4].

Aims and Objectives

1. To study the histomorphological features of tumors of epidermis and epidermal appendages
2. To analyze the clinicopathological features of these tumours .

Materials and Methods

The present study was conducted in the department of Pathology , Khaja Banda Nawaz Institute Medical Sciences, kalaburagi. This was a histopathological study of tumours of epidermis and epidermal appendages, studied retrospectively (3years) and prospectively (2years) i.e., from Jan. 2012 to Dec.2 016. Both biopsies and resected specimens were included. Tissue was processed for paraffin sections and stained with hematoxylin & eosin. Special stains and immunohistochemistry were carried out wherever necessary.

Inclusion Criteria

Benign and malignant tumors of epidermis and epidermal appendages.

Exclusion Criteria

1. Tumor-like lesions,
2. Tumors of mucosa and genitalia.

Results

There were 69 cases of tumours of epidermis and epidermal appendages, diagnosed during the study period of five years, of which, 51 cases (73.91%) were epidermal neoplasms, and 18 cases were neoplasms of epidermal appendages. Male to female ratio was 1.03:1.

Out of 69 cases, 36(52.17%), were benign neoplasms and 33(47.83%), were malignant neoplasms.

Tumours were commonly found in head and neck (43%), followed by the tumours in upper limb (21%), trunk (19%) and lower limb (17%).

Table 1: Distribution of keratinocytic tumours

Sl. No.	Diagnosis	No. of cases.	Gender	Age range (Yrs)	Site.
1.	**Keratinocytic tumours**				
	A. Benign				
	Squamous Papilloma	6	M-3, F-3	45-65	LL-3,UL-1, HN-1,TRUNK-1
	Acrochordon	2	M-1, F-1	35-50	H&N – 2
	Adenoacanthoma	2	M-2, F-0	35-40	TRUNK-1,UL-1
	Seborrheic Keratosis	5	M-3, F-2	20-60	TRUNK-1 H&N-2, LL -2
	B. Malignant				
	Basal Cell Carcinoma Keratotic	08	M-6,F-2	25-75	H&N-08
	Pigmented	07	M-4,F-3	20-80	H&N-06,LL-01&Back-01
	Adenoid Cystic	02	M-0,F-2	50-60	H&N-02
	Basosquamous	01	M-0,F-1	60-70	UL-01
	Squamous Cell Carcinoma	4	M-0,F-4	45-60	LL-3 UL-1

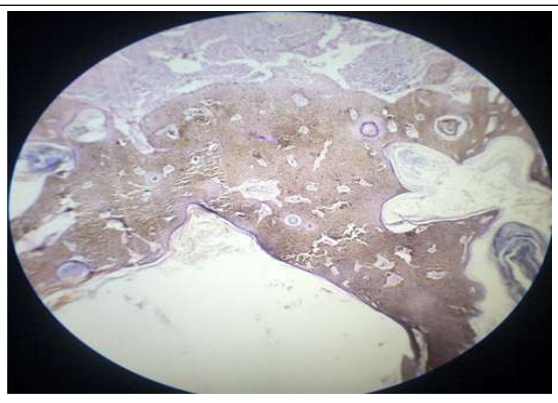

Fig. 1: Seborrheic Keratosis: Photomicrograph showing extensive pigmentation with many horn cysts (H&E x 100).

Five cases of seborrheic keratosis were noted of which two cases showed extensive melanin pigment in both the keratinocytes and basaloid cells and there were multiple horn cysts(Figure 1).

There was a single case of Spitz nevus (Figure 2). It was compound and composed of spindle-shaped cells aligned parellely in nests, separated by clefts. The cells were large, with abundant amphophilic cytoplasm and scanty melanin pigment. The nuclei were large, pale, with dispersed chromatin; regular, smooth nuclear membranes, and prominent eosinophilic nucleoli. Mitoses were absent. There was diminution in size (maturation) of the lesional cells with increasing depth. Single cells were dispersed between collagen bundles of reticular dermis at the base of lesion.

Table 2: Distribution of melanocytic tumours

2.	Melanocytic	No. of Cases	Gender	Age Range (yrs)	Site
	A. Benign				
	Intradermal Nevus	3	M-2,F-1	10-60	UL-2 LL-2
	Compound Nevus	1	M-0,F-1	10-20	UL-2
	Spitz Nevus	1	M-1,F-0	10-20	LL-1
	Cellular blue Nevus.	1	M-1,F-0	10-30(27)	UL-1
	Giant Congenital melanocytic Nevus.	1	M-1,F-0	7days	TRUNK-1
	B. Malignant				
	Amelanotic Melanoma	3	M-2,F-1	15-45	H&N-2 UL-1
	Malignant Melanoma	2	M-1 F-1	60-70	UL-1 LL-1

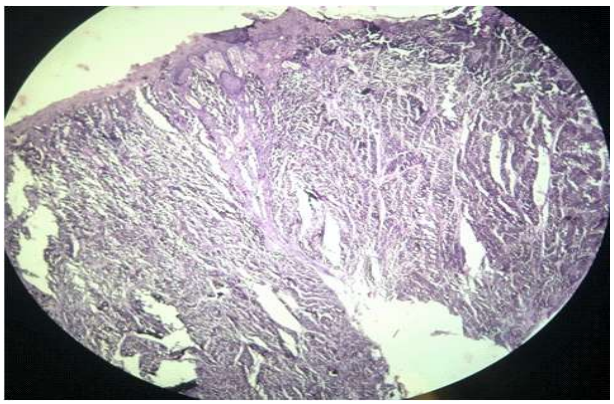

Fig. 2: Spitz Nevus: Spindle shaped cells arranged in parallel nests in between the collagen bundles. There is maturation of the cells in the deeper dermis(H&E x 100)

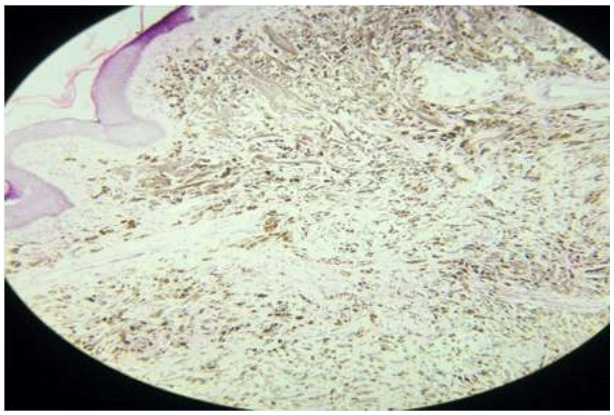

Fig. 3: Cellular blue-nevus Photomicrograph showing acanthotic epidermis with extensive pigmentation in the dermis and spindle cells (H&E x 100)

A 27 yrs. old male presented with a small, blue nodule on the upper limb since the age of five years. Microscopy showed elongated melanocytes in the interstices of dermal collagen of the upper and mid dermis admixed with spindle cells. The diagnosis was Cellular blue nevus (Figure 3).

A newborn male baby, presented with pigmented lesion involving the chest and back similar to garment, which extended upto upper thigh bilaterally. The lesion was broad and deep. Microscopy revealed hyperkeratotic epidermis with pigmented basal cell layer. No junctional activity was seen. Dermis showed proliferation of spindle cells. The diagnosis was Giant congenital melanocytic nevus.

There were three cases of amelanotic melanoma. The patients were middle aged and two were males with lesion in the head and neck region and one was a female patient with a lesion on the upper limb. Microscopy of the lesions showed trabecule of large cells with cytologic atypia, large, eosinophilic nucleoli and junctional activity, but no melanin pigment. The tumour cells were positive for S-100 protein.

There were two cases of malignant melanoma.

Among 18 appendageal tumors, 14 were benign and four were malignant. Predominantly the lesions were found in females and in head and neck region.

Syringocystadenoma papilliferum (Figure 4, Figure 5 & Figure 6) was seen in a patient of 60yrs., with lesion over head and neck region. Microscopy showed

epidermis with several cystic invaginations having papillary projections lined by two rows of cells. The luminal row consisted of columnar cells and outer row consisted of cuboidal cells. Dense plasma cell infiltrate was seen in the papillary core.

Table 3: Distribution of Appendageal tumours

3.	Appendageal tumours.	No. of cases	Gender	Age Range (yrs.)	Site
	A. Benign				
	Cylindroma	2	M-1,F-1	30-40	H&N-2
	Nodular hidradenoma	2	M-0,F-2	20-30	TRUNK-2
	Syringoma	1	M-0,F-1	20-30	H&N-1
	Trichoepithelioma	2	M-0,F-2	30-50	H&N-2
	Pilomatricoma	2	M-2,F-0	30-40	H&N-2
	Eccrine Spiradenoma	1	M-0,F-1	10-20	TRUNK -1
	Chondroid Syringoma.	1	M-0,F-1	10-30	H&N-1
	Clear Cell Hidradenoma	1	M-1,F-0	50-60	H&N-1
	Eccrine Poroma	1	M-0,F-1	40-50	UL-1
	Syringocystadenoma Papilliferum	1	M-1,F-0	50-60	H&N -1
	B. Malignant				
	Papillary Eccrine carcinoma	1	M-0,F-1	40-50	H&N-1
	Malignant Eccrine Spiradenoma.	1	M-1,F-0	30-40	H&N-1
	Malignant Chondroid Syringoma	1	M-0,F-1	30-40	H&N-1
	Sebaceous Carcinoma.	1	M-0,F-1	50-60	TRUNK-1

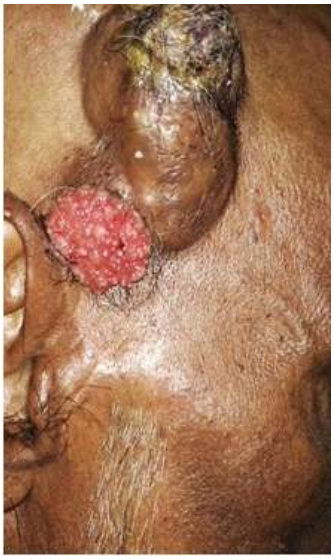

Fig. 4: Syringocystadenoma Papilliferum (ulcerated cystic lesion)

Fig. 5: Syringocystadenoma papilliferum Photomicrograph showing lesion ms.4.8x3.2cms with granular external surface and C/S showing cysts filled with serosanguinous fluid.

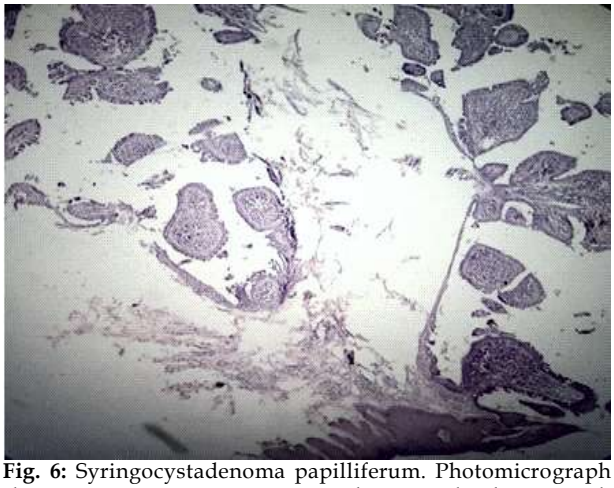

Fig. 6: Syringocystadenoma papilliferum. Photomicrograph showing cystic invagination extending into the dermis, with numerous papillary projections (H&E x 100).

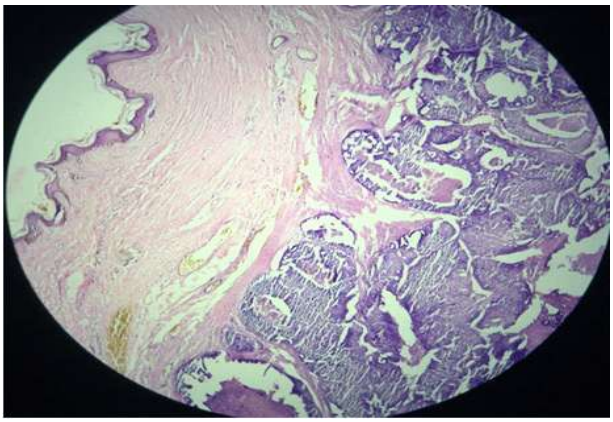

Fig. 7: Papillary Eccrine Carcinoma. Tubular and ductal structures associated with papillary projections protruding into cystically dilated lumina. Macropapillae are lined by atypical epithelial cells.

There was a rare case of sebaceous carcinoma (Figure 8) found over the trunk in a 54 yrs. female. There was infiltrative growth into the dermis consisting of irregular epithelial lobules. Lesional cells showed marked cytological atypia, mitotic activity and focal sebaceous differentiation.

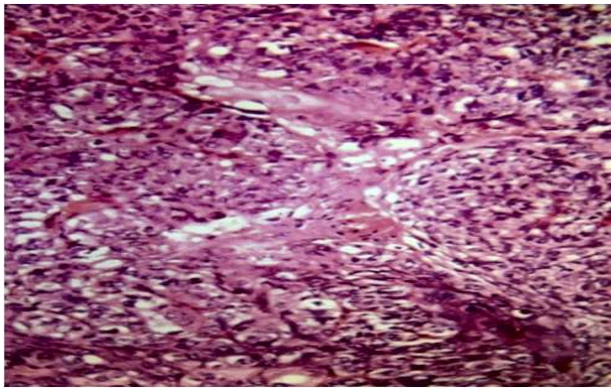

Fig. 8: Sebaceous carcinoma. Photomicrograph showing lobules and sheets of malignant cells with variable sebaceous differentiation (H&E x100).

Two cases of hematolymphoid tumors were found in males of older age group.

One case of cutaneous lymphoma was seen in 73yrs old male and showed patchy, band-like lymphocytic infiltrate within the papillary dermis, with coarse fibrosis. The lesional cells were small to medium sized lymphocytes with hyperchromatic, indented nuclei (Figure 9). Immunophenotyping for CD2, CD3, CD4, CD5 were positive and CD8 negative.

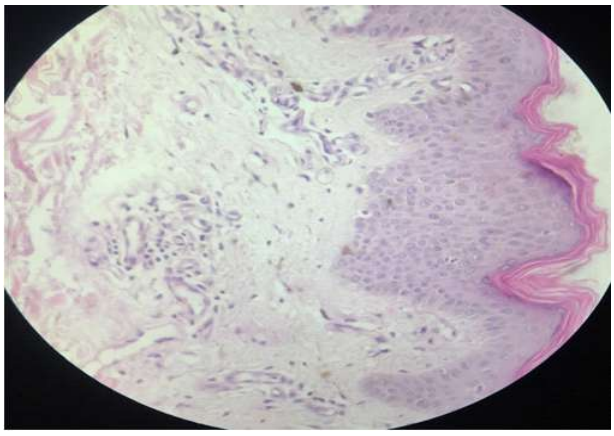

Fig. 9: Cutaneous lymphoma. Photomicrograph showing band-like perivascular lymphocytic infiltration (H&E x 400).

The case of mycosis fungoides was in 68 yrs male who presented with papules and nodules over trunk. Routine peripheral smear and Bone marrow showed presence of atypical cells. Biopsy from the nodule showed flat epidermis and dense infiltration by cells of varied sizes showing pleomorphic nuclei in the dermis. Few mitosis and coarse fibrosis were noted and confirmed with CD4.

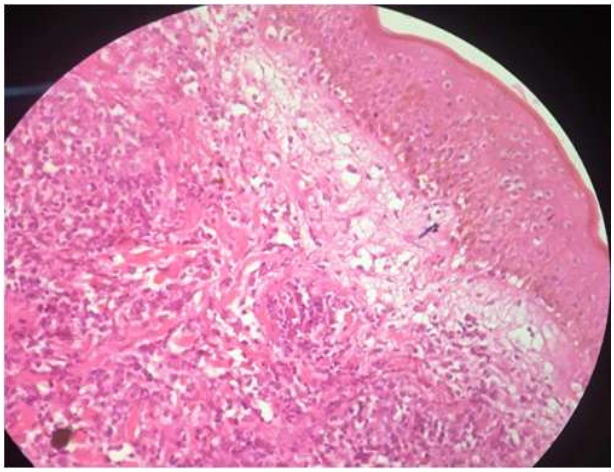

Fig. 10: Mycosis fungoides. Photomicrograph showing papillary dermal interstitial lymphoid infiltration with coarse fibrosis (H&E x 400).

Discussion

Contrary to the ubiquitous simplistic concept, skin is a remarkably heterogeneous organ. The tumours of skin are more numerous than those produced by any other organ. This diversity, combined with clinical, histologic, immunohistochemical and ultrastructural data, will aid in arriving at a definitive diagnosis [5].

In comparison with other studies, benign to malignant ratio was slightly high in the present study.

The incidence of keratinocytic tumours was high in the present study, compared to other studies.

Keratinocytic tumours are derived from epidermal and adnexal keratinocytes and there is a large spectrum of lesions ranging from benign acanthomas to malignant squamous cell carcinomas and basal cell carcinomas. There were 18 cases of basal cell carcinomas and four cases of squamous cell carcinomas. Bari V, Mukaram P, Gosavi A et. al. in

Table 4: Comparative study of benign and malignant epidermal and epidermal appendages

Sl. No	Authors	No of cases	Benign	Malignant	B.M Ratio
1	Sharma A. et.al.[6]	56	45(80.4%)	11(19.6%)	4.1: 1
2	Narhire V.[7]	36	25(69.4%)	11(30.6%)	2.3:1
3	Present study	69	36(52.17)	33(47.8%)	1.1:1

Table 5: comparative analysis of distribution of various benign neoplasms of epidermis and epidermal appendages

Tumor type	Gundalli. S[8]	Narhire. V[7]	Present study
Keratinocytic	20.8%	20%	44.4%(16)
Melanocytic	24.5%	16%	16.6%(6)
Appendageal	54.7%	28%	38.8%(14)

their histopathological review of 125 cases of skin tumours, concluded that squamous cell carcinoma was the commonest malignant tumour (45.9%) followed by basal cell carcinoma (34.4%) [9]. In the present study the incidence of basal cell carcinoma was 26% and that of squamous cell carcinoma was 6%, a deviation from other studies and the exact cause from this is unclear.

Melanocytic tumours include a large variety of benign and malignant neoplasms with distinct clinical and morphological profiles. In the present study there were seven benign tumours and five malignant tumours. When compared with other studies, Deo S V etal (2005) showed 26.1% and Reema Harwal etal (2012) found 2.7% cases of melanoma [10]. Whereas the present study showed it to be 7.2%.

Appendageal tumours are neoplasms whose differentiation is toward one or more of the adnexal structures of the skin.

Table 6: Comparison of frequency of tumours of epidermal appendages

Sl. No.	Studies	Benign (%)	Malignant (%)	Total No. of Cases
1.	Vaishnav and Dharkar et al (1982)[8].	43 (89.6%)	05(10.4%)	48
2.	Reddy et al(1982)[8]	59 (69.4%)	26(30.6%)	85
3.	Present Study (2017)	14 (77.7%)	04 (22.2%)	18

The incidence of benign and malignant appendageal tumours, was compared with other studies and was found to be similar.

Ramya G and Soumya, in their study of 20 adnexal tumours found that benign tumours of eccrine glands are more common [11]. Sharma A, Paricharak D, Nigam J et.al., in their histopathological study of 56 cases of adnexal tumors concluded that, the incidence of benign skin adnexal tumors was more as compared to the malignant tumors. Malignant tumors were seen in older age group, usually over 50 years of age [6].

Table 7: Comparison of frequency of benign tumours of epidermal appendages

Sl. No.	Authors' Name	Nair. S P[8]	Solanki. R.L[8]	Radhika[12]	Present Study
	Tumors				
1.	Hair follicle tumors	12(36.36%)	22(23.4%)	05(14.2%)	04(28.5%)
2.	Sweat gland tumors	19(57.56)	50(53.2%)	13(37.14%)	10(71.42%)
3.	Sebaceous gland tumor	02(6.06%)	22(23.4%)	05(14.2%)	---
	Total no of cases.	33	94	23	14

The frequency of benign tumours of epidermal appendages was compared with other studies, but there were no benign tumours of sebaceous gland in the present study.

There were two cases of hematolymphoid tumours in the present study. One case was cutaneous lymphoma and another was mycosis fungoides, both seen in patients of older age group, and both were confirmed by immunohistochemistry. Lymphoma may involve the skin as the primary and only site of involvement, or may spread to the skin as a secondary site of the disease. Some cutaneous lymphomas morphologically resemble their counterparts in lymph node, but differ in terms of phenotype, genotype, and clinical behaviour, suggesting that they represent an independent entity.

Conclusion

Skin and adnexal neoplasms account for a small percentage among all the histopathological lesions reported. Incidence of these tumours is increasing dramatically.

They affect people of all age groups.

In the present study, most common benign, keratinocytic tumour was squamous papilloma, followed by seborrheic keratosis and malignant keratinocytic tumours were basal cell carcinoma and

squamous cell carcinoma. Among melanocytic tumours intradermal nevus was the common benign tumour and malignant tumours were amelanotic melanoma and malignant melanoma.

Among adnexal tumours, most common were benign sweat gland tumours followed by tumours of hair follicle and sebaceous gland. Malignant adnexal tumours were papillary eccrine carcinoma, eccrine spiradenoma, chondroid syringoma and sebaceous carcinoma noted. Two cases of hematolymphoid tumours were encountered in the study.

Skin tumours, at times, may be difficult to diagnose clinically. Hence histopathological examination is a must for definitive diagnosis. Increasing public awareness and surveillance will help in diagnosing the cases early for better management.

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