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A Histomorphological Study of Dermal Lesions

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Abstract

Context: The plethora of pathologies makes diagnosis of dermal lesions challenging. Though, benign lesions are common, malignant conditions need to be ruled out. Clinical and radiological modalities result in inconclusive diagnosis due to overlapping features. *Aims:* The objectives of the present study are to collocate and organize dermal lesions based on anatomical location and distribution. We also highlight light microscopic features of these dermal lesions. *Methods and Material:* All cases clinically presenting with a dermal lesions were collected from histopathology archives. Relevant clinical details and histopathological slides were retrieved. The diagnosis was confirmed by review of the slides. *Results:* Out of 125 cases, only eight cases constituted pathologies with intermediate and/or malignant behavior. Non-neoplastic pathologies such as calcinosis cutis, ganglion cyst, keloid too were encountered. Lipoma accounting for 49.6% cases was the most common pathology. Most malignant lesions were located on extremities and were seen in elderly. *Conclusions:* It is prudent to consider even non-neoplastic lesions in differentials of dermal lesions. Age and location among other clinical details help in listing the differentials. Adequate sampling and recognisition of characteristic histological pattern helps in accurate pathological diagnosis.

Keywords: Dermal Lesions; Soft Tissue Tumors; Histopathology.

Introduction

Although superficial dermal lesions are commonly encountered by clinicians, most of them are benign and not life threatening. They have never been regarded as significant health problem to necessitate focused public health measures. These lesions pose diagnostic dilemmas as they share common clinical features. Many investigators have evaluated the role of radiological modalities in diagnosis of dermal lesions.[1] Only few pathological studies exist describing the spectrum of dermal diseases. The present study is aimed to describe anatomical location, clinical details and distribution of such lesions. The other objective of the present study is to highlight histopathological features of dermal lesions we encountered.

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Materials and Methods

The present study is a retrospective study of 2 years duration. All the cases clinically presenting as dermal nodule/papular lesion and referred to histopathology between Jan 2014 to Dec 2015 were collected from archives. Relative frequency of age and sex distribution, location, relevant clinical details was analyzed. The H and E sections were reviewed to confirm the diagnosis. All epidermal lesions, mucosal lesions and adenexal tumors were excluded from the study. Lesions originating from tissues deeper to fascia were excluded.

Results

A total of 125 cases were included in the study, out of which 48.8% were males. Adults formed 87.2% of the study group. In males, the commonest lesion was lipoma (n=29, 47.5%) followed by inflammatory

lesions and keloid. In females too the commonest lesion was lipoma (n=33, 51.5%) followed by calcinosis cutis, keloid and ganglion cysts. Eight cases with intermediate and malignant behavior were seen. Inflammatory lesions were distributed through all decades. Lipoma was most commonly distributed in extremities, while hemagiomas were common to head and neck location. The sex, age distribution and natural history are depicted in Tables 1 to 3.

Discussion

Superficial pathologies are generally categorized as mesenchymal tumors, metastatic tumors, skin appendage tumors or inflammatory lesions and tumor like lesions. Based on location such lesions, are either cutaneous (epidermis and dermis), subcutaneous or fascial [2].

The following discussion reviews the frequency, location, presentation and unique histological features of the dermal lesions that were included in the present study.

Benign soft tissue tumors outnumber malignant by a ratio of 100:1 [1]. Average size of superficial benign soft tissue tumors is less than two centimeters [3]. In the present series, all benign and non-neoplastic lesions were of less than five centimeters, with exceptions of lipoma, angiomyxoma, calcinosis cutis and nerve sheath tumors.

Most of soft tissue tumors are seen in males with exception of few such as angiolipomas, well differentiated liposarcoma, leiomyomas, hemangioma, glomus tumors, lymphangioma, neurofibroma etc. [3]. Table 3 depicts the higher distribution of benign soft tissue tumors in extremities. Most benign tumors are distributed in the extremities with the exceptions of rhabdomyomas, angiofibromas, chondromas, granular cell tumors which are commonly located in head and neck region [3].

Certain lesions show a striking predilection for a specific location. For example, the case of elastofibroma in our collection was located in characteristic location - upper back. Aggressive angiomyxoma in the present series was located in labia majora, conforming to pelviperitoneal site being the commonest location [4].

Non-Neoplastic Lesions

We encountered seven cases of ganglion cyst. Of these four were located around wrist, one near finger and two in lower leg. Around seventy percent of ganglion cysts are found near wrist joint. Several theories have been proposed for pathogenesis of ganglion cyst. Displacement of synovial tissue, degeneration of connective tissue and migration of synovial fluid into soft tissue are few of these [5]. Microscopy often reveals dense fibrous wall lined by macrophages and myxoid material [Figure 1b].

Keloid is result of an aberrant healing process with excuberant scar formation. The term keloid is derived from "chele", a greek word which means crab claw. Extensions beyond the original borders of keloid help to differentiate from hypertrophic tumor. The sections of keloid show characteristic abundance of thick glassy collagen bundles [Figure 1a]. Eight of ten keloid cases were situated on external ear lobe. This predilection is attributed to the social practice of ear piercing. The other sites of predilection are anterior chest, upper arms and cheeks [6].

Non-neoplastic inflammatory pathology was seen in twelve cases. Special stains were applied to demonstrate pathogens in all cases. Four of such cases highlighted the presence of branching fungal elements [Figure 2c]. Arteriovenous malformation consists of abnormal connections between arteries and veins without an intervening normal capillary bed [7]. On light microscopy, AVM is recognized by presence of variable number of thin and thick walled vessels without an intervening capillary bed [Figure 2d] [7,8].

Calcinosis cutis is a group of disorders characterized by accumulation of calcium salts in dermis. Several forms namely, dystrophic, metastatic, iatrogenic and idiopathic types have been described [9].Dystrophic form follows inflammatory or neoplastic diseases such as pilomatricoma, pilar cyst, acne, scar, dermoid cyst etc.[9,10]. Noaimi et al described eight cases of idiopathic calcinosis cutis which included a case of was scrotal calcinosis [10]. All the eight cases in our study showed diagnostic circumscribed dermal basophilic calcification [Figure 2a].A lone case of scrotal calcinosis was included into the group. Idiopathic scrotal calcinosis is presumed to follow rupture and inflammation of epidermoid cysts. Tumoral calcinosis is a distinct type of peri-articular calcification described chiefly around hip, knee, shoulder and elbow joints. The pathogenetic classification lists primary normo-phosphatemic, primary hyperphosphatemic and secondary types [9,10]. All of the four cases of tumoral calcinosis described herein showed distinct common features such as age more than 70 years, female sex and localization to hip joint. In absence of history of trauma, previous disease, biochemical abnormalities all the cases fit into primary normo-phosphatemic type.

Benign Adipocytic Lesions

Lipoma is a capsulated superficial tumor. 46.7% of Lipoma was seen in males. With the exception of few such as lipoblastoma, juvenile angiofibroma, hemangioblastoma most benign soft tissue tumors are seen in young adults [3]. Most are common in fifth to seventh with the exception of lipoblastoma, angiolipoma and angiomyolipoma [1,2]. Pleomorphic lipoma and hibernoma are commonly located on the shoulder, back and posterior neck [3]. Lipoma are most common mesenchymal tumors, represent about 50% of all soft tissue tumors [1,2,11]. Most measure less than 5 cm and are located in the trunk, shoulder, neck and upper arm [1,7,11]. They are composed of mature adipocytes with surrounding capsule and intervening connective tissue stroma [Figure 3a]. Surgical resection is indicated for cosmesis, compression of adjacent structures or if the diagnosis is uncertain [11].

Benign Vascular Lesions

Benign vascular tumors occur predominantly in females with the exception of angiofibroma. They are seen distributed equally in adults and children. Angiomatous lesions can be congenital and have a familial tendency [3,7].

Hemangiomas are the most common vascular tumor, accounting for 7% of all benign soft tissue tumors [1,2]. There are two types of classification systems, Weiss and colleagues and the Mulliken/ Glowacki classification [1]. Microscopically, the hemagiomas showed multiple endothelial lined thin capillaries [Figure 4a].

Glomus tumors constitute about 1.6% of all benign soft tissue tumors. It develops from neuromyoarterial glomus apparatus. Subungual location of the fingers is the most common location (65%). Other sites include palm, wrist, forearm and foot. The classical clinical triad of pain, tenderness and cold sensitivity is seen in 30% of the cases [1]. Solid glomus tumors, glomangiomyoma, glomangioma, glomangiopericytoma, glomangiomatosis and malignant glomus tumors are included under the rubric "Glomus tumors" [4]. Our case had vascular channels encased by sheath of monomorphic rounded cells, befitting the diagnosis of Glomangioma [Figure 4d].

Several variants of Angioleiomyoma have recognized: solid (with slit like channels), cavernous (large lumen) and venous (medium sized lumen) [12]. Histologically, the case in our series was composed of thick walled vessels with gaping lumen and smooth muscle cells arranged around them [Figure 4c]. Thus, it was labeled as of venous type. Admixture of adipocytes can be seen as in our case [Figure 4c], which can be incorrectly designated superficial angiomyolipoma [4,12].

Aggresssive angiomyxoma is a benign mesenchymal neoplasm usually affecting females of third to seventh decade. It tends to grow around pelvic floor structures [4]. This lesion of uniform low cellularity generally shows stellate cells embedded in loose myxoedematous stroma, frequently zonated around blood vessels [Figure 6b].

Benign Nerve Sheath Lesions

Schwannoma and neurofibroma are included in the rubric "benign peripheral nerve sheath tumors". Schwannoma is a non collagenous benign nerve tumor, mostly seen at head, neck and flexor surface of extremities [1,3,13]. The characteristic features include encapsulation, Verocay bodies surrounded by nuclear palisades [Figure 5b] and Schwann cells distributed in Antoni A and Antoni B tissue patterns. The parent nerve is seen adhering to the capsule [Figure 5b]. It comprises 5% of all benign soft tissue tumors. It is seen in patient aged 20 – 50 years [1].

Neurofibroma is slightly more common than schwannoma. These benign peripheral nerve sheath tumors consist of Schwann cells and fibroblasts within a collagenous network [7,13]. Histologically, neurofibroma showed all the cellular elements of a nerve namely Schwann cells, fibroblasts, perineurial cells and axons [Figure 5c]. Neurofibromas are not capsulated and the nerve of parental origin is seen traversing throughout the lesion. Hence, they are difficult to dissect and likely to recur. Three types of neurofibroma – localized, diffuse and plexiform types are described [3,13]. Neurofibroma is commonly seen in patients aged between 20 years and 30 years [3].

Benign Fibrous/Fibrohistiocytic Lesions

Benign fibrous histiocytoma are derived from mesodermal cells. They commonly occur on anterior surface of lower limbs [11]. Several histological variants such as cellular, epitheloid, aneurysmal, hemosiderotic, clear cell and pseudosarcomatous types have been described [14]. The case here described was located near ankle. Lipidized Fibrous histiocytoma occur commonly in and around ankle, hence the old terminology "ankle type fibrous histiocytoma". Histologically, foamy cells are seen distributed between wiry collagen [Figure 1c]. The histological diagnosis is established by the presence of spindle cells in stroiform pattern at least focally [14].

Elastofibroma is a slowly growing fibroelastic reactive pseudotumor frequently seen in sixth and seventh decade with slightly female predominance. The presence of characteristic thick fragmented eosinophilic elastic fibers embedded in fibro-collagenous stroma clinched microscopic diagnosis in our case [Figure 5a] [4].

Pleomorphic hyalinizing angiectatic tumor of soft parts is a recently described locally aggressive soft tissue entity by Smith et al. The localization of our case on left leg conforms to the common site being lower extremity [15,16]. On light microscopy, our case showed characteristic clusters of hyalinized vessels filled with fibrin and surrounded by spindled stroma. The spindled stromal cells displayed pleomorphic nucleus with intranuclear inclusion [Figure 1d].

Myxoid Tumors

Superficial myxoid tumors are benign and deep ones are malignant. The exceptions are intramuscular myxoma which is deep and myxofibrosarcoma is superficial [17].

Myxoma is an undifferentiated tumor composed of spindled cells in a myxoid background. Myxomas are commonly seen in age between 40 and 70 years with a female predilection. Myxomas are well defining homogenous lobulated tumors [1]. Carney et al in 1985 described familial syndrome consisting of myxomatous tumors, spotty pigmentation and endocrine activity. Superficial myxomas associated with Carney complex are most common on eyelid. Myxomas unassociated with syndrome are more common. Myxomas commonly arise on the trunk, lower extremity, head and neck region and arm. Myxoma presents as soft lobulated pendunculated lesions measuring less than 5 cm [17]. Fifteen percent of myxoma arise in cutaneous tissue and 22% in the subcutaneous apneurosis.[2] Histologically, the lesion shows variably demarcated hypocellular angiomyxoid nodules composed of bland spindled and satellite cells [Figure 6a]. Thin wavy collagenous fibers course through the lesion [2,17]. It should be differentiated from other myxoid lesions such as myxoid liposarcoma, myxofibrosarcoma, myxoid chondrosarcoma, ganglion, synovial cyst and schwannoma [1].

Malignancy

The incidence of soft tissue tumors increases with age. All of our malignant lesions were seen in aged more than 40 years. The common sarcomas seen in elderly are liposarcoma, pleomorphic sarcoma, myxofibrosarcoma and leiomyosarcoma. The lesions with intermediate and malignant behavior included four cases of spindle cell sarcoma diagnosed on biopsy, a case each of myxofibrosarcoma, liposarcoma, dermatofibrosarcoma and non-hodgkin lymphoma. Most of these are seen in limbs consistent with findings of epidemiological review that state extremity as the commonest site [4].

Following the reappraisal of malignant fibrous histocytoma (MFH) subtypes, myxoid MFH has been now termed Myxofibrosarcoma [18]. Myxofibrosarcoma of our collective was located in forearm. Grossly, it resembled the classical description of superficial multiple myxoid and firm nodules [4]. The histology section showed diagnostic features of infiltrating lobulated tumor composed of plump spindle cells with enlarged hyperchromatic nuclei [Figure 6d]. The characteristic finding is presence of curvilinear thin blood vessels traversing the tumor [Figure 6c].

Liposarcoma accounts for 20% of soft tissue sarcoma [2,4,19]. The WHO recognizes four subtypes of liposarcoma namely, atypical lipomatous tumour/ well differentiated liposarcoma, dedifferentiated liposarcoma, myxoid liposarcoma and pleomorphic liposarcoma [4,19]. Atypical lipomatous tumour represents the largest group accounting for 40% of all liposarcoma. Our case on histology showed varying sized adipocytes and the diagnostic hyperchromatic scalloped nuclei. Numerous multivacuolated lipoblasts were seen aggregated focally [Figure 3b]. Repeated pre-operative needle aspiration had resulted

Table 1: Sex distribution of dermal lesions

Dermal lesion	Males	Females
Inflammatory lesions	8	4
Ganglion cyst	2	5
Keloid	5	5
Calcinosis cutis	3	5
Scar endometriosis	0	1
Lipoma	29	33
Benign vascular lesions	4	5
Benign nerve sheath lesions	4	0
Benign fibrous/fibrohistiocytic lesions	2	1
Myxoma	0	1
Malignancy	4	4

Table 2: Age distribution of dermal lesions

Dermal lesions	0-10 yrs	11-20 yrs	21-30 yrs	31-40 yrs	>41 yrs
Inflammatory lesions	1	1	3	0	7
Ganglion cyst	0	1	3	0	3
Keloid	0	1	5	3	1
Calcinosis cutis	0	0	0	1	7
Scar endometriosis	0	0	0	1	0
Lipoma	1	5	9	14	33
Benign vascular lesions	1	4	1	1	2
Benign nerve sheath lesions	0	1	2	1	0
Benign fibrous/fibrohistiocytic lesions	0	0	0	2	1
Myxoma	0	0	0	0	1
Malignancy	0	0	0	2	6

Table 3: Natural History of Dermal Lesion

Histological Diagnosis	Number of case	Most common site	Average size (cm)	Histology
		Non-neoplastic lesions		
Inflammation	12	Extremities	4	Fungal hyphae in four cases
Ganglion cyst	7	Extremities	4	Fibrous wall, myxoid material
Keloid	10	Pinna	5	Thick eosinophilic collagen
Calcinosis cutis	8	Iliac crest	10	Dermal calcification
Scar endometriosis	1	Abdominal wall	4	Endometrial glands, fibrous stroma
		Adipocytic lesions		
Lipoma	62	Extremities	8	Capsulated lesion of mature adipocytes
Liposarcoma	1	Thigh	11	Varying sized adipocytes, bizarre stromal nucleus, lipoblasts
		Vascular tumors		
AV malformation	1	Head & neck	3	Thick vessels, absent capillary bed
Hemangioma	3	Head & neck	2	Aggregates of vessels
Glomangioma	1	Forearm	2	Monomorphic glomus around vessels
Lymphangioma	2	Axilla	5	Lymph filled vessels
Angioleiomyoma	1	Face	3	Smooth muscle proliferation around vessels
Aggressive angiomyxoma	1	Labia majora	8	Paucicellular, myxoid stroma, zonation around vessels
		Nerve sheath tumors		
Neurofibroma	2	Neck, extremity	6	Unencapsulated, polymorphic cells
Schwannoma	2	Chest, back	9	Capsule, Vercuay body
		Fibrous/fibro-histiocytic lesions		
Lipidized BFH	1	Extremity	3	Foam cells, storiform pattern
Elastofibroma	1	Back	4	Thick fragmented elastin fibers
PHAT	1	Knee	3	Cluster of vessels, fibrin, intranuclear vacuole
DFSP	1	Extremity	5	Spindle cells, storiform patter,
		Myxoid tumors		
Myxoma	1	Eyelid	2	Lobulation, paucicellular, bland stellate cells
Myxofibrosarcoma	1	Axilla	8	Lobulation, myxoid stroma, thin capillaries, pleomorphic nuclei
		Other malignancies		
Spindle cell sarcoma	4	Extremity	1	Undifferentiated pleomorphic spindle cells
Non Hodgkin lymphoma	1	Shoulder	4	Monomorphic neoplastic lymphoid cells

Note: BFH - Benign fibrous histiocytoma, PHAT - Pleomorphic hyalinizing angiectatic tumour of soft parts, DFSP - Dermatofibrosarcoma protuberans

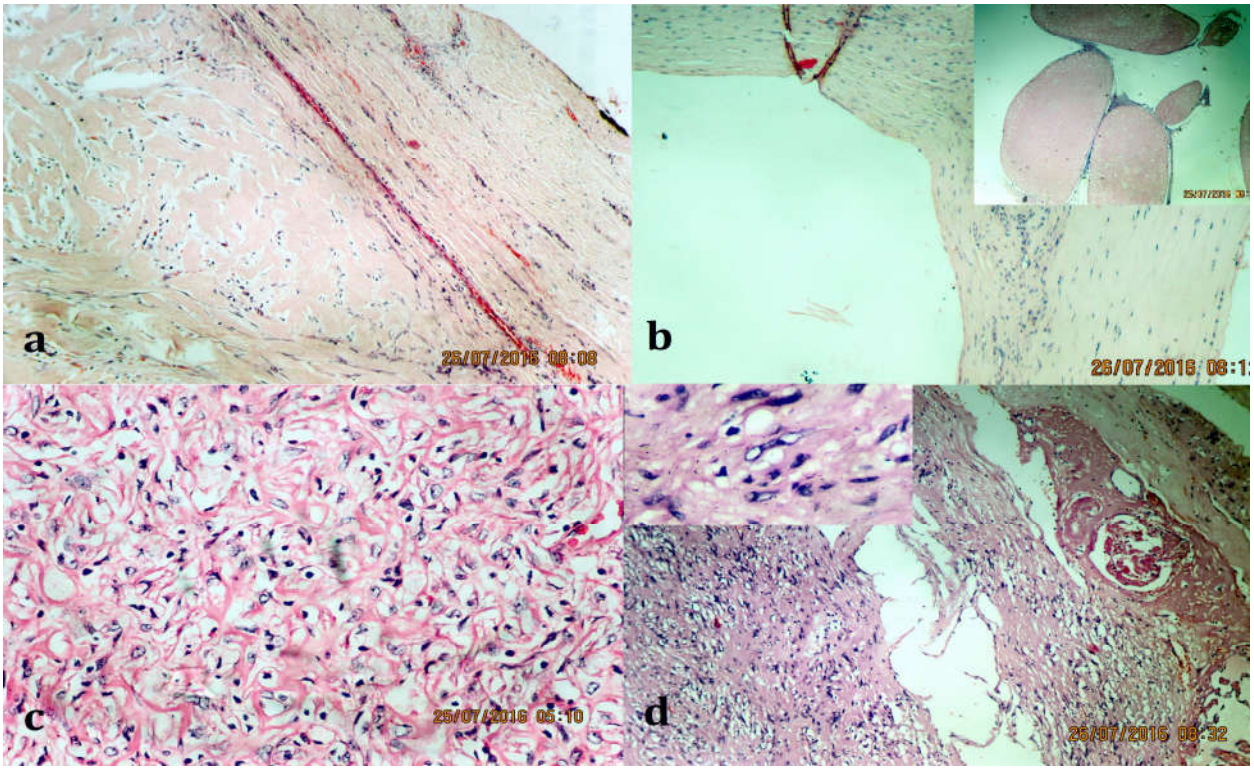

Fig. 1: Light microscopy a, Keloid with thick glassy homogenous collagen fibers. b, Ganglion cyst shows fibrous wall and myxoid material (inset). c, Lipidized Fibrous Histiocytoma shows foamy cell with vague storiform pattern. d, Pleomorphic hyalinizing angiectatic tumor of soft parts with fibrin filled blood vessels and intranuclear vacuole (inset) (H&E, X400).

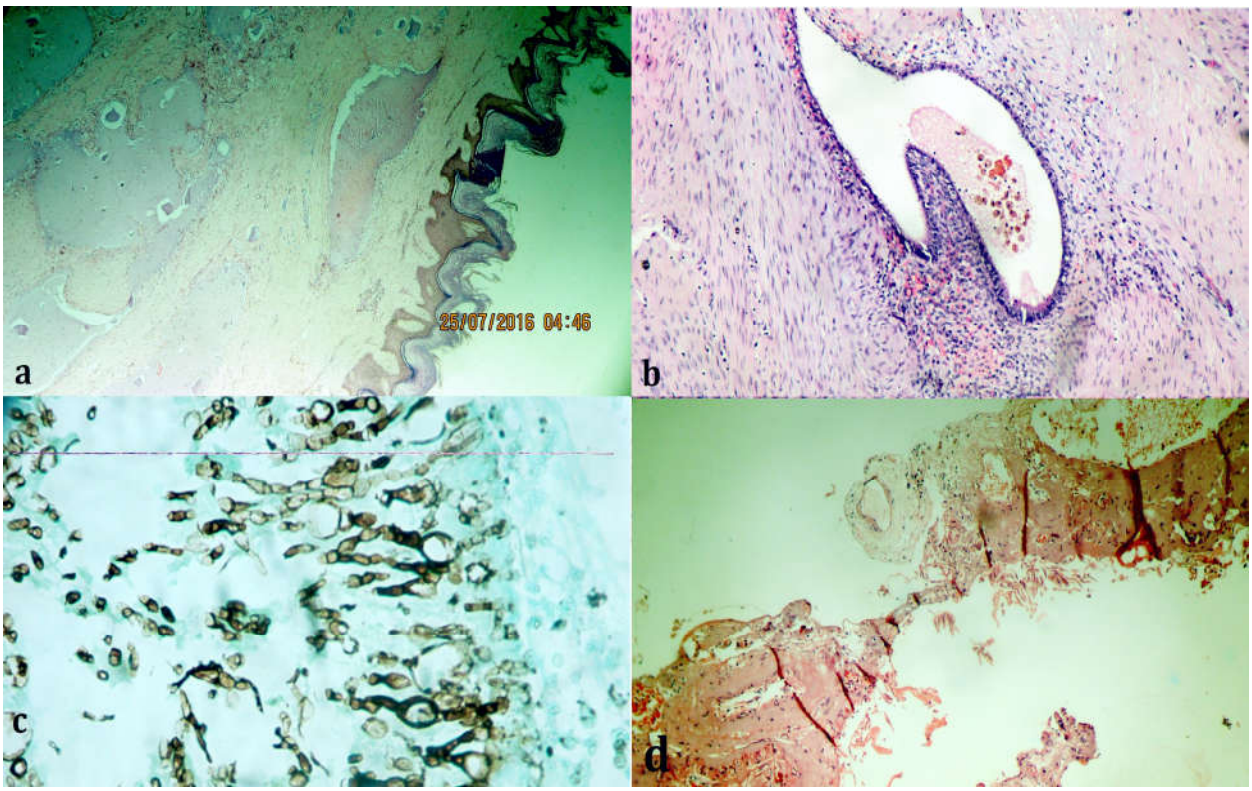

Fig. 2: Microscopy of non-neoplastic lesions a, Dermal circumscribed calcification of Calcinosis cutis (H & E,X100). b, Endometriotic glands and stroma embedded in fibrous stroma (H & E,X400). c, Branching hyphae of fungal elements (GMS, X400). d, Thick walled vessels without capillaries in between (H&E, X400).

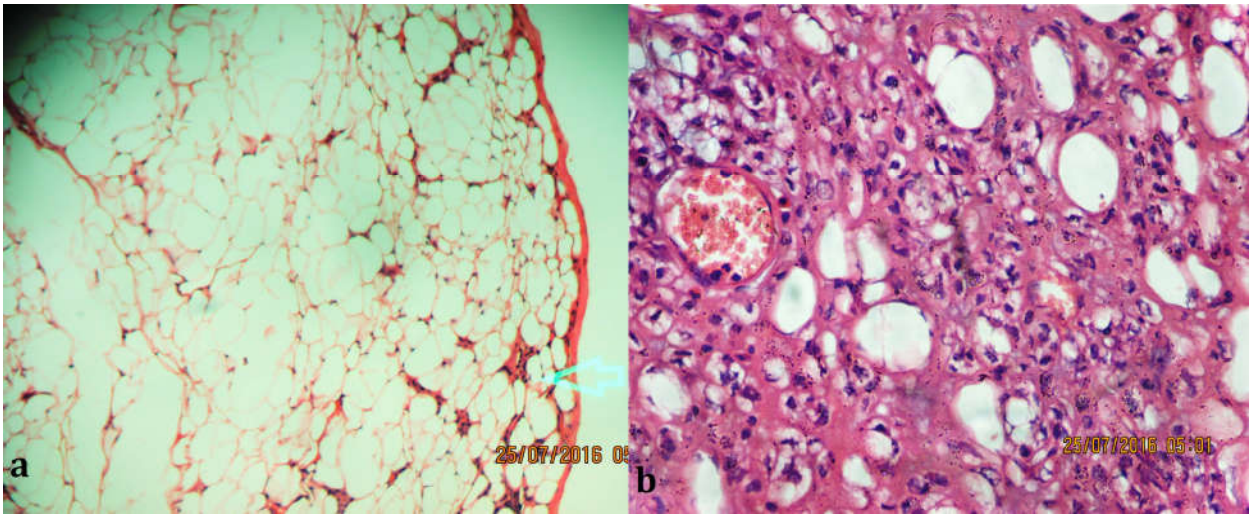

Fig. 3: Microscopy of adipocytic lesions a, Encapsulated mature adipocytes of Lipoma (H&E, X100) . b, Variable sized adipocytes and lipoblasts having scalloped nucleus in Well differentiated liposarcoma (H&E, X400).

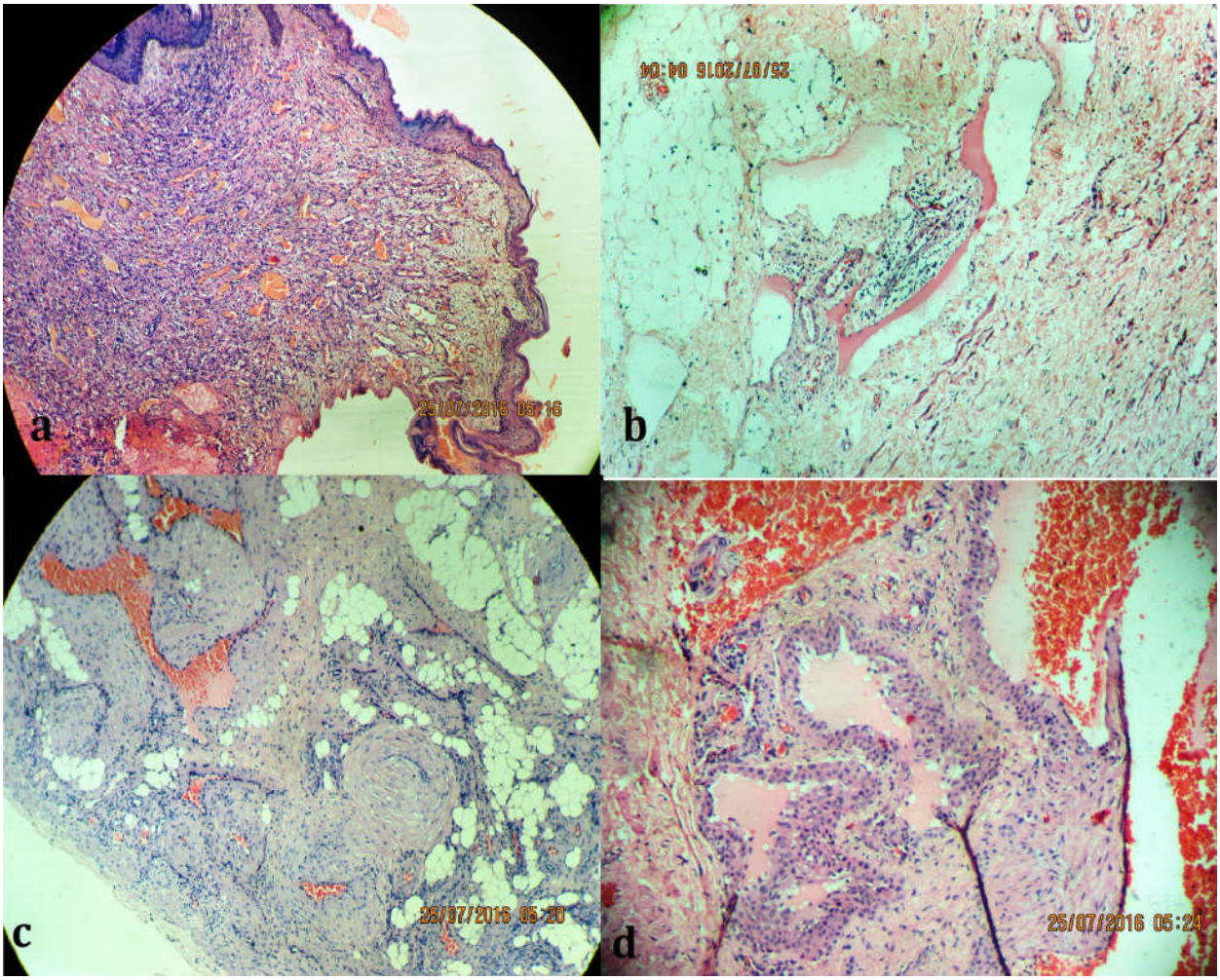

Fig. 4: Microscopy of vascular lesions a, Compactly arranged endothelial lined capillaries in Hemangioma (H&E, X100). b, Collection of lymph filled vessels surrounded by lymphocytes suggestive of lymphangioma (H&E, X100). c, Smooth muscle proliferation around muscular vessels in Angioleiomyoma (H&E, X400). d, Monomorphic glomus cells having rounded nucleus and eosinophilic cytoplasm arranged around vessels, diagnostic of Glomangioma. (H&E, X400).

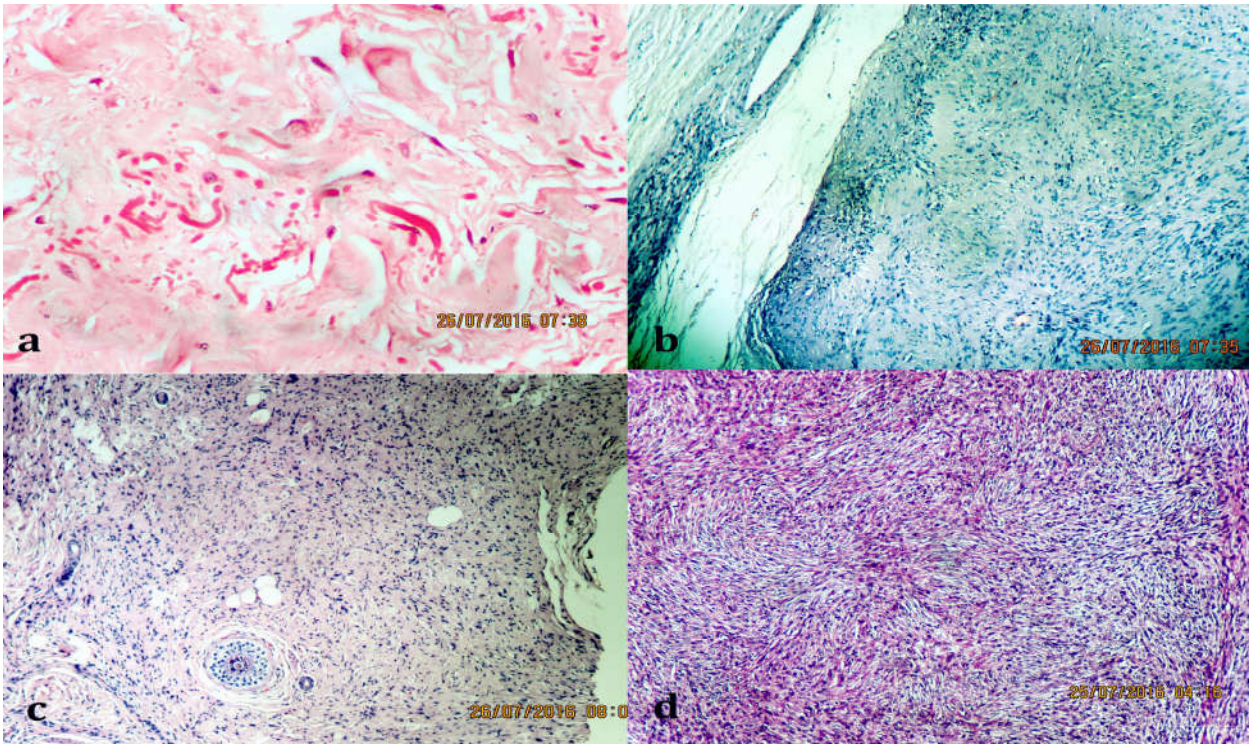

Fig. 5: Light microscopy a, Fragmented thick glassy elastin fibers of Elastofibroma (H&E, X400). b, Encapsulated spindle cell lesion showing Verocay body in Schwannoma. Parental nerve is seen beside capsule (H&E, X100). c, Polymorphic population of wavy spindle cells entrapping adnexal structures in Neurofibroma (H&E, X100). d, DFSP showing classic storiform arrangement of spindle cells (H&E, X100).

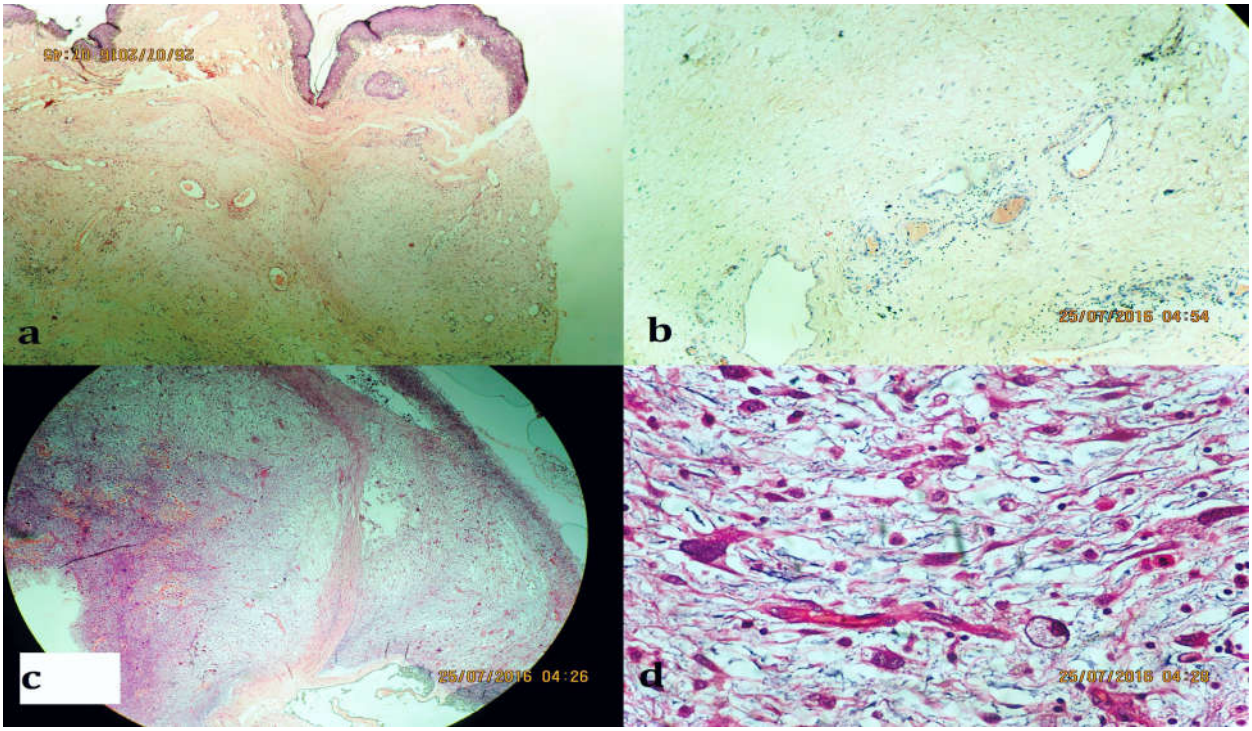

Fig. 6: Microscopy of myxoid lesions a, Dermal circumscribed paucicellular myxomatous lesion suggestive of myxoma (H & E,X100). b, Angiomyxoma showing spindle cells in paucicellular stroma and aggregation around vessels (H & E,X100). c, Lobulation and the characteristic thin elongated curvilinear vessels of Myxofibrosarcoma (H & E, X100). d, Pleomorphic spindle cells of Myxofibrosarcoma set in myxoid stroma (H&E, X400).

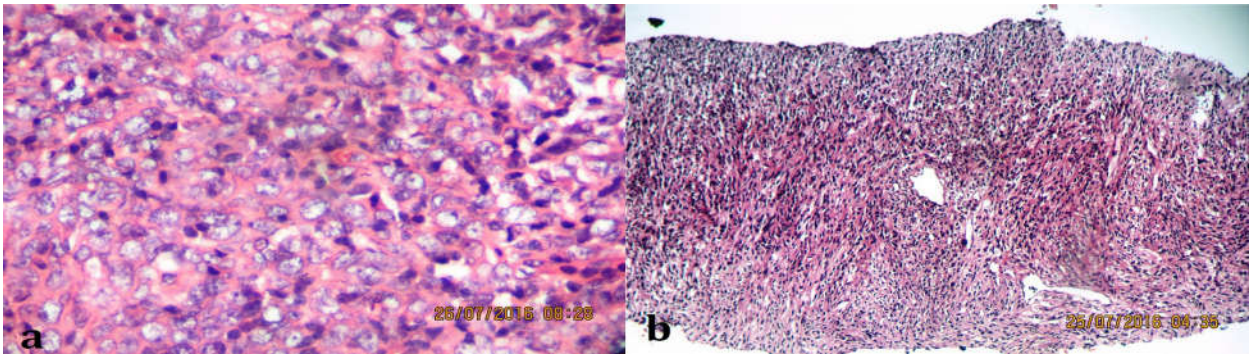

Fig. 7: a, Microscopy of Non-Hodgkin lymphoma showing sheets of large lymphoid cells (H&E, X400). b, Malignant spindle cells having pleomorphic nucleus on biopsy labeled as Spindle cell sarcoma (H&E, X100).

in central hemorrhagic necrosis of the mass. Thus, the diagnosis required extensive sampling to differentiate from benign lipoma.

Dermatofibrosarcomas protuberans is a locally aggressive tumor with high risk of recurrence. It is most commonly seen between 20-50 years. In 40%-50% of cases, the tumor is locate on the trunk and in 30%-40% affects limbs. Histologically, several variants have been documented which include myxoid, granular cell, sclerotic, pigmented (Bednar tumor), myoid, giant cell fibroblastoma and atrophic DFSP [16]. Conventionally, it displays a poorly circumscribed dermal tumor that invades surrounding tissues. The tumor is composed of fibroblast like proliferation arranged in a characteristic storiform pattern [Figure 5d].

A lone case of cutaneous lymphoma was included. Cutaneous lymphoma is subclassified as B cell, T cell/NK cell, Histiocytic and others [2]. The lone case of Non-Hodgkin lymphoma was diagnosed by the presence of infiltrating tumor showing sheets of monomorphic malignant lymphoid cells having pleomorphic vesicular nuclei admixed along with mature lymphocytes [Figure 7b].

Although soft tissue accounts for 40% of body weight, it is relatively resistant to metastasis. No metastatic deposits were seen in our collective.

Histological typing could not be done in four cases with pre-treatment biopsy. They were thus labeled as Spindle cell sarcoma [Figure 7a]. Even though biopsy is appropriate to establish malignancy and assess histological grade, additional sampling and/or adjuvant tests are often required for accurate histological typing [4].

Multitude of pre-operative radiological investigations such as ultrasonography, conventional radiography and MRI are available. However, none of these can differentiate benign from malignant lesions with accuracy. Most soft tissue tumors are diagnosed on histological evaluation after surgical excision [2]. Most of these superficial tumors are not amenable for radiological evaluation [1]. When the diagnosis is uncertain based on history and clinical features, the lesion is biopsied for histopathological evaluation [11].

Benign can be soft tissue tumors histologically heterogenous. Pleomorphic hyalinizing angiectatic tumor of soft parts and lipidised fibrous histiocytoma in our collective had bizarre, pleomorphic and atypical nuclei. Benign soft tissue tumors displaying mitotic figures include Benign fibrous histiocytoma, lipoblastoma, pleomorphic lipoma, hypertrophic hemangioma, hemangioblastoma and glomus tumors. Thus, core biopsy and needle aspirate can be misleading and are not sufficient for classification of benign soft tissue tumors [3].

Conclusion

We describe here our experience with superficial dermal soft tissue lesions. We emphasize that most common dermal lesion is lipoma. The study highlights low prevalence of malignancy in superficial lesions. Accurate diagnosis of these lesions requires adequate sampling of specimen as demonstrated in the case of liposarcoma. Non-neoplastic lesions such as calcinosis cutis, keloid and ganglion cyst should also be included in differentials of dermal lesions. A systematic approach towards dermal lesions incorporating clinical and histological features can achieve a definitive diagnosis.

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