INTRODUCTION

Panniculitis is the inflammation of the subcutaneous fat. It is regarded as the “ugly duckling” in dermatopathology, as it often poses diagnostic difficulties, both clinically as well as histopathologically.\(^1\)\(^-\)\(^3\) There is considerable overlap, not only clinically but also histologically, among various types of panniculitis. The major reasons for the diagnostic difficulties include inadequate biopsy specimen, inadequate clinical details, overlapping histopathological features, and evolving morphology of different types of panniculitides at different stages. In our experience, inadequate skin biopsy specimens are the most common reason for diagnostic struggle in panniculitis followed closely by their overlapping histopathology. In patients with suspected panniculitis, a deep biopsy to include the subcutaneous fat is fundamental.\(^4\)\(^-\)\(^7\) We believe that with satisfactory specimens, adequate clinical history, and comprehensive histopathologic examination, a specific diagnosis may be decreed in most cases of panniculitis. The “gold standard” practice is to examine deeper sections through the block after staining with hematoxylin and eosin (H and E). Sometimes, however, special stains such as elastin stains, polarization of sections, or cultures of the tissue for pathogenic bacteria or fungi are also required for formulating a specific diagnosis.

There are three major components of the subcutis, i.e., lipocytes, blood vessels, and fibrous septa. The fat cells or lipocytes are large and appear as empty cells with signet-ring morphology on H and E stain. This is due to the displacement of the nucleus by a single, large intracytoplasmic, fat containing vacuole. The
thin fibrous septa that divide the subcutaneous fat into lobules are constituted by collagen and reticulin fibers and contain the nerves, blood, and lymphatic channels. Each fat lobule is supplied by an arteriole that branches into capillaries in the lobule. There is a peculiar pattern of blood supply of the lobules. The blood supply is terminal so that there are no capillary communications between adjacent lobules or between dermis and subcutaneous fat. This explains why large-vessel vasculitis involving the septal vessels is commonly attended by little inflammation of the fat lobules, whereas small-vessel vasculitis displays extensive fat necrosis with centrilobular infarction and dense inflammation within the lobule.\[6\]

The subcutaneous fat has a poor repertoire of responses to noxious stimuli, with the most common response being fat necrosis on histopathology, which could in turn be secondary to innumerable conditions.\[9,10\] It is also important to remember that the subcutaneous fat may be involved secondarily in vasculitides, trauma, deep cutaneous fungal infections, and many malignancies.\[11-20\] Histopathologically, panniculitis can predominantly affect lobules or septa, with/without vascular involvement. Accordingly, the panniculitis can be classified into following main classes:
1. Predominantly septal panniculitis without vasculitis
2. Predominantly septal panniculitis with vasculitis
3. Predominantly lobular panniculitis without vasculitis
4. Predominantly lobular panniculitis with vasculitis
5. Others.

The detailed histopathologic classification of panniculitis is given in Table 1.\[3,7-9\]

**SEPTAL PANNICULITIS WITHOUT VASCULITIS**

**Erythema nodosum**

Erythema nodosum (EN) is the prototype of nodular septal panniculitis. It is a clinical syndrome with varied symptoms and etiologies. It typically affects young adults with a predilection for females. There are two clinical forms of EN - acute and chronic, which differ in their clinical manifestations but do not exhibit much histopathological difference. Acute EN also known as migratory panniculitis or subacute nodular migratory panniculitis is typically asymmetrical, unilateral, and predominantly involves legs. It exhibits a female preponderance and tends to affect older age groups, in contrast to classical EN. The chronic form is less recognized, however, shows similar nodular lesions developing over months or even years [Figure 1].\[21-24\]

Histologically, EN shows widening of the septa due to edema and neutrophilic infiltrate admixed with eosinophils. The infiltrate often extends into the periphery of the fat lobules and between the individual fat cells in a lace-like fashion in early stages [Figure 2a]. Vascular changes and hemorrhage are commonly seen but no definite vasculitis is present. In later stages, the infiltrate is replaced by collections of histiocytes, especially around slit-like spaces or blood vessels forming Miescher’s radial nodules, which are considered to be a characteristic feature of EN and can be found in all stages of EN. Further progression of the lesion leads to the development of a granulomatous response with giant cells [Figure 3]. However, fat necrosis is usually not seen. The older lesions of EN show widening of the septa due to fibrosis and inflammation at the edges of the septa and mainly involve the periphery of the fat

| Table 1: Histopathologic classification of panniculitis |
|--------------------------------------------------------|
| **Predominantly septal**                               |
| With vasculitis                                        |
| Leukocytoclastic vasculitis                            |
| Superficial thrombophlebitis                           |
| Cutaneous polyarteritis nodosa                         |
| Without vasculitis                                     |
| Erythema nodosum                                      |
| Necrobiosis lipoidica                                  |
| Scleroderma                                            |
| Rheumatoid nodule                                      |
| Subcutaneous granuloma annulare                        |
| Necrobiosis xanthogranuloma                            |
| **Predominantly lobular**                              |
| With vasculitis                                        |
| Erythema nodosum leprous                               |
| Lucio’s phenomenon                                     |
| Neutrophilic lobular panniculitis associated with rheumatoid arthritis |
| Erythema induratum of Bazin                            |
| Crohn’s disease                                        |
| Without vasculitis                                     |
| Sclerosing panniculitis                                |
| Calciphylaxis                                          |
| Sclerema neonatorum                                    |
| Cold panniculitis                                      |
| Lupus erythematosus profundus                          |
| Pancreatic panniculitis                                |
| Infective panniculitis                                 |
| Traumatic panniculitis                                 |
| Factitious panniculitis                                |
| Subcutaneous fat necrosis of newborn                   |
| Subcutaneous sarcoaidosis                              |
| Post-steroid panniculitis                              |
| Gout panniculitis                                      |
| Postirradiation sclerodermatous panniculitis           |
| Crystal-storing histiocytosis                          |
| **Others**                                             |
| Eosinophilic panniculitis                              |
| Subcutaneous panniculitis-like T-cell lymphoma         |
lobules. The inflammation is rich in macrophages, and neutrophils are usually absent. Macrophages at the edges of the fat lobules show phagocytosis of lipid from the damaged adipocytes. Occasionally, loosely formed residual granulomas can be seen in the septa along with the multinucleated giant cells [Figure 3]. The vascular changes are less prominent. The oldest lesions have septal widening and fibrosis with minimal inflammatory cell infiltrate [Figure 2b]. EN migrans characteristically shows densely scarred and thickened interlobular septa with conspicuous granulomas and giant cells.\footnote{7,25,26}

The differential diagnosis of EN includes erythema induratum of Bazin (EIB), superficial migratory thrombophlebitis, nodular vasculitis (NV), subcutaneous tuberculosis, necrobiosis lipoidica (NL), deep morphea, subcutaneous granuloma annulare (SGA), rheumatoid nodule, and necrobiotic xanthogranuloma.\footnote{27-34} Although EIB and NV predominantly exhibit lobular panniculitis, however, features of septal panniculitis can also be observed, and hence they often sham striking morphologic resemblance to EN. Vasculitis and zones of fat necrosis are absent in EN and frequent in EIB.\footnote{27} NV has mainly lymphocytic infiltration with fibrous thickening and obliteration of vascular lumina.\footnote{28-30} In contrast to EN, superficial migratory thrombophlebitis has a large vein with luminal thrombus. In subcutaneous tuberculosis, the upper portion of the panniculus is spared, whereas it is involved in EN.\footnote{31,32} Furthermore, in subcutaneous tuberculosis, stains for acid-fast organisms and cultures are useful.\footnote{33,34}

As the histopathologic findings of EN can be quite variable, clinical correlation is of paramount importance. However, all biopsies should be accompanied by cultures and special stains for bacteria, fungi, and atypical mycobacteria. In addition, presence of foreign material should also be looked for to rule out other causes of EN.\footnote{25-34}

**Necrobiosis lipoidica**

NL is an idiopathic rare skin disorder mainly affecting the skin of insulin-dependent diabetic females; however, nondiabetic individuals may also be affected. The lesions are usually bilateral, the most common site being lower extremities mainly calves, ankles, thighs, popliteal region, and feet [Figure 4a].

The histopathology is characteristic with variable degree of granulomatous inflammation around degenerated collagen in the dermis with the involvement of subcutaneous fat. The degenerated collagen appears paler with gray hue and more haphazardly arranged on H- and E-stained sections. This alteration in the collagen is known as necrobiosis. Occasionally, there may be few scattered multinucleated or Langhans giant cells and histiocytes with extensive sclerosis. The epidermis is usually normal, may be atrophic or hyperkeratotic [Figure 5].\footnote{35,36} Sometimes, it can be difficult to distinguish NL from granuloma annulare (GA) and rheumatoid nodules though there is...
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no increased mucin in NL and plasma cell collections can be seen in the deeper dermis.\(^7,25,26\)

**Scleroderma**

The word scleroderma is derived from skleros - hard and derma - skin (Greek) is a connective tissue disorder, which leads to thickening and fibrosis of the skin. There are two types of scleroderma, i.e., localized (morphea) and systemic (progressive systemic sclerosis). The thickening and hardening of skin may also be associated with metabolic, genetic, immunologic, or occupational disorders.\(^27\)

In nearly all forms of scleroderma, the inflammatory changes involve both the dermis as well as the subcutaneous fat and cannot be differentiated histologically. In the localized form, early stages show lymphoplasmacytic perivascular infiltrate throughout the dermis, extending into thickened fibrous septa along with hyalinosis and thickened collagen bundles. In the later stages, the inflammatory infiltrate extends from the septa into the periphery of the fat lobules causing reduction in the fat lobules, which is replaced by newly formed pale collagen. In the late sclerotic stage, the inflammation disappears and the collagen bundles in the reticular dermis are thickened, hypocellular and stain more deeply eosinophilic. The eccrine glands too appear atrophic and surrounded by newly formed collagen [Figure 6].\(^7,26\)

**Subcutaneous granuloma annulare**

SGA is an idiopathic condition characterized by palisaded granulomatous infiltration in the dermis commonly occurring in children and young adults with female predilection. The common sites of involvement are hands, arms, legs, and feet. It is a chronic condition with variants including (a) generalized popular form,
(b) perforating, (c) erythematous, and (d) deep GA which involves the subcutis.\cite{38,39}

Histologically, GA shows infiltration of histiocytes palisading the areas of mucin [Figure 7a]. Increased mucin is a hallmark feature of GA and is visible as faint blue finely granular material on H and E stain. Special stains including Alcian blue and colloidal iron are essential to demonstrate increased mucin [Figure 7b]. In addition, there is perivascular lymphocytic infiltrate seen in the dermis and within the septa. The differential diagnosis includes NL where there is no or less mucin and rheumatoid nodules, which contain more of fibrin.\cite{7,25,26}

**Rheumatoid nodule**

Rheumatoid nodules occur in about 20%–25% patients with rheumatoid arthritis with high rheumatoid factor titer. They are usually situated near bony structures close to a joint over extensor prominences. The lesions are deep-seated masses in the subcutaneous tissue and vary in size from few mm to 5 cm.\cite{40-42}

Histologically, there is fibrinoid degeneration of collagen in the deep dermis and subcutis surrounded by a palisading of histiocytes [Figure 8]. This degenerated collagen stains deep red on H and E stain accompanied with nuclear fragments and basophilic material. The mucin is always minimal or absent. The stroma surrounding the nodules shows foreign body giant cells and perivascular lymphocytic infiltrate including plasma cells. Acute or chronic thrombotic endarteritis is observed in some cases along with vascular proliferation.

Old lesions show dense fibrosis, clefts, and cystic degeneration.\cite{7,8}

Accelerated rheumatoid nodulosis is an entity characterized by rapid development of multiple periarticular subcutaneous nodules after institution of methotrexate therapy for rheumatoid arthritis. Regression of nodules is noted after stopping methotrexate. Pseudorheumatoid nodule mimics RN and the term is often used interchangeably with SGA. It is seen commonly in children and patients without a history of joint pains, RA, or systemic lupus erythematosus (SLE).\cite{43}

**SEPTAL PANNICULITIS WITH VASCULITIS**

**Cutaneous polyarteritis nodosa**

Cutaneous polyarteritis nodosa is a variant of polyarteritis nodosa (PAN), which classically involves deep dermis and subcutaneous fat with a classical feature of arteritis. It is more common in men and presents with skin nodules, which are associated with livedo reticularis, fever, and arthralgia. Renal involvement occurs in 75% of cases and is the most common cause of mortality. However, the disease can be limited to skin with a long clinical course of multiple recurrences and have a good prognosis.\cite{44-48}

Microscopically, the characteristic lesions show panarteritis involving the medium- to small-sized muscular arteries. There is necrotizing leukocytoclastic vasculitis with fibrin deposition and partial to complete destruction of the elastic lamina [Figure 9]. The infiltrate is predominantly neutrophilic with admixed eosinophils.
in and around the vessels involving the panniculus causing lobular panniculitis. In the later stages, there is intimal proliferation with thrombosis leading to ischemia and ulceration sometimes. In the healed or healing stage, there is fibrovascular proliferation and nonspecific lymphocytic infiltrate in the perivascular area.\[7,8] In a series of 16 cases with cutaneous PAN, it was observed that all cases manifested lesions in the form of nodules and/or indurated erythematous patches over their lower extremities, and on histopathologic examination, all cases exhibited necrotizing vasculitis of small, subcutaneous, muscular arteries with/without luminal occlusion. Eight of these cases were followed up for at least 5 years, with the longest follow-up period being 19 years and displayed good prognoses without any systemic involvement.\[46]

**Superficial thrombophlebitis**

Superficial thrombophlebitis usually involves lower extremities, presenting as tender, erythematous nodule, or cord-like structure. Often there is the presence of predisposing factors such as varicose veins, hypercoagulable state, oral contraceptive intake, or underlying malignancy.\[49-51]

There is involvement of small- or medium-sized veins in the deeper dermis and subcutaneous fat causing acute vasculitis and thrombosis occluding the lumina.\[52-55] In early stages, there is leukocytic infiltrate accompanied with edema, and in later stages, lymphocytes, histiocytes, and occasional giant cells are seen in the wall of the veins.\[7,29] The differential diagnosis includes PAN; however, there is no involvement of arteries. A Gram stain is always advised to rule out common bacteria causing suppurative thrombophlebitis, and a history of trauma is needed to exclude traumatic fat necrosis.\[52-54]

**LOBULAR PANNICULITIS WITHOUT VASCULITIS**

**Lupus erythematosus panniculitis (lupus profundus)**

This is defined as a specific involvement of the subcutaneous fat in patients with lupus erythematosus (LE). It is a rare manifestation of the disease, occurring approximately in 1%-3% of patients with cutaneous LE. It may be observed in patients with discoid LE or SLE or as an isolated phenomenon without systemic or other cutaneous findings [Figure 1a]. A patchy lymphoplasmacytic infiltrate in the lobules of the subcutaneous fat along with lymphocytic nuclear dust is a clue for the histopathological diagnosis of LE panniculitis (LEP) [Figure 10]. The diagnosis of LEP may be especially problematic in cases where the involvement of subcutaneous fat is the only manifestation of the disease. Clinically, LEP and subcutaneous panniculitis-like T-cell lymphoma (SPTCL) are indistinguishable; however, in SPTCL, the presence of atypical CD8-positive T-lymphocytes and the absence of septal fibrosis, B-cell follicles, and plasma cells clinch the diagnosis.\[53-58]

![Figure 9: Histopathologic features of cutaneous polyarteritis nodosa. (a and b) Inflammatory infiltrate involving medium- and large-sized arteries in the dermis and septa of subcutaneous fat (H and E, [a] ×40, [b] ×200). (c and d) fibrinoid necrosis and neutrophilic infiltrate involving full thickness of vessel wall (H and E, [c] ×100, [d] ×200)](image)

![Figure 10: Histopathologic features of lupus erythematosus panniculitis. (a) Dense collections of lymphocytes and few plasma cells in the lobules with hyalinized fat necrosis (H and E, ×100), (b) scattered lymphoid follicles with germinal centers (inset, ×200) (H and E, ×200)](image)
Sclerosing panniculitis
Sclerosing panniculitis also known as lipodermatosclerosis often affects middle-aged or elderly, overweight females with accompanying history of varicose veins, thrombophlebitis, and deep vein thrombosis. The main pathogenic mechanism is venous stasis, and hence the condition is also called stasis-associated sclerosing panniculitis.

The histopathological features are variable depending on the stage of the disease. Early lesions show centrilobular ischemia and infarction of fat cells in the subcutaneous fat along with vascular congestion and hemorrhage. No vasculitis is seen though thrombosis can be present. Lymphocytic infiltrate in the septa with hemosiderin-laden macrophages is commonly present. In later stages, there is hyalinization of the fat lobules with microcystic change and fat necrosis. Advanced lesion would reveal fibrous scarring of the septa with atrophy of the fat lobules. There are features of vessel wall thickening, chronic inflammation, and lobular capillary proliferation and fibrosis in the dermis. The differential diagnosis includes morphea profunda and scleroderma in the late stages.\(^7,59-61\)

Traumatic panniculitis
The trauma may be physical including blunt trauma, cold, excessive heat or electrical injury, or chemical injury produced by injection of noxious substances. There is quite a wide histological variation encountered in panniculitis due to physical effects (e.g., cold and pressure) or trauma to the skin.\(^62-64\)

Factitial panniculitis
Factitial panniculitides are by no means rare and should be considered in any panniculitis where there are unusual features.\(^65\) The chemical injury causes acute inflammation with focal fat necrosis and hemorrhage. Older lesions will show lymphocytic infiltrate accompanied with macrophages and fibrosis. There is no vasculitis or thrombosis. Injection of oily compounds leads to accumulation of foamy macrophages with formation of fatty cysts with surrounding fibrosis giving “Swiss Cheese appearance.” Similar appearance is seen in sclerosing lipogranuloma. The subcutaneous tissue of children’s is more sensitive to cold injury, which can cause nodules of cold injury on applying ice cubes to the skin.\(^7,62\)

Subcutaneous fat necrosis of the newborn
Subcutaneous fat necrosis of newborn occurs as a complication of forceps delivery or cesarean section in neonates. It presents as erythematous to violaceous plaques within weeks of the birth. The lesions usually subside after few weeks, however, may form nodules.

Microscopically, they show focal fat necrosis in the lobules with macrophage infiltration and foreign body type of giant cells. The macrophages and giant cells contain crystalline fat, which appear as needle-shaped clefts arranged radially. Focal small calcium deposits may also be seen.\(^7,66-70\) An important morphological differential to be remembered here is the Gouty panniculitis, wherein the needle-shaped monosodium urate monohydrate crystals are seen in the soft tissues surrounded by foreign body giant cell reaction.

Sclerema neonatorum
This is a very rare disorder commonly seen in premature infants. The characteristic appearance shows diffuse, rapidly spreading, nonpitting hardening of the subcutaneous adipose tissue of the neonates in the first few days of life accompanied with cyanosis. There is waxy appearance of the skin that is cold and tight. The condition is lethal if left untreated. The subcutaneous tissue is thickened due to increase in fat cells and wide fibrous bands. There is deposition of lipid crystals forming rosettes within the fat lobules. The inflammation is very scanty, and the lesion is rapidly progressive. Mostly the lesion is limited to subcutaneous fat but rarely can involve visceral fat, which leads to increased mortality.\(^71-76\)

Pancreatic panniculitis
Clinically, pancreatic panniculitis overlaps quite closely with that of nodular panniculitis (Weber–Christian type). Patients with nodular panniculitis have also been described with lipasemia or amylasemia but with no evidence of pancreatic disease.

The earliest histological change of pancreatic panniculitis is fat necrosis, which is probably initiated by circulating enzymes (lipases) and varying degrees of calcification. These changes may be focal, emphasizing the need for a larger surgical biopsy and serial sectioning. Inflammatory infiltrate is relatively sparse around the areas of fat necrosis, consisting mainly of neutrophils. Areas with fat necrosis show “ghost-like” adipocytes having fine basophilic intracytoplasmic granular calcification. Later on, however, the infiltrate becomes granulomatous.\(^77-81\) It should also be borne in mind that cutaneous aspergillosis and mucormycosis can closely mimic pancreatic panniculitis on histopathology, owing to the presence of “ghost-like” adipocytes.\(^82\)
OTHERS

Eosinophilic panniculitis
Eosinophilic panniculitis is characterized by a prominent infiltration of subcutaneous fat with eosinophils. It can be seen in patients with drug dependence, psychiatric illness, atopy, asthma, malignancies, immune complex vasculitis, and sarcoidosis. Eosinophilic panniculitis in EN is perhaps its most confusing presentation.\[^{82-85}\]

LOBULAR PANNICULITIS WITH VASCULITIS

Erythema nodosum leprosum
This is a Type 2 reaction occurs most commonly in lepromatous leprosy (LL) followed by borderline leprosy. Clinically, the patients present with tender erythematous plaques or nodules [Figure 4b]. It is often accompanied with fever, malaise, and arthralgia.

Histologically, the lesions show neutrophilic infiltrates superimposed on chronic multibacillary leprosy. An associated necrotizing vasculitis affecting arterioles, venules, and capillaries can be seen in some cases of erythema nodosum leprosum (ENL) [Figure 11]. Sometimes, the neutrophilic infiltration is scanty with a predominance of macrophages containing fragmented bacilli.\[^{86-89}\] In a series of 32 patients with ENL, 22 patients developed ENL before the commencement of chemotherapy, thereby highlighting the fact that development of ENL in the absence of chemotherapy is not an infrequent event and early recognition of this event is important. The authors concluded that ENL should be looked upon as a manifestation of leprosy, and not essentially as a mere complication of its therapy.\[^{87}\]

Lucio’s reaction
The Lucio’s reaction is vascular manifestation of diffuse LL, in which no treatment or inadequate treatment is given. In contrast to ENL, endothelial proliferation and thrombosis in the medium-sized vessels of the dermis and subcutis are seen leading to luminal obliteration. Strong acid-fast bacteria positivity is found in the walls and endothelium of normal looking vessels and also in vessels showing proliferative changes.\[^{90-92}\]

Neutrophilic lobular panniculitis associated with rheumatoid arthritis
Rheumatoid arthritis may be accompanied by cutaneous manifestations such as rheumatoid granuloma, leukocytoclastic vasculitis, and rheumatoid neutrophilic dermatitis.

Histopathology shows a predominantly lobular panniculitis, severe necrosis of the adipocytes in the lobule, and an inflammatory infiltrate composed of neutrophils, foamy histiocytes, and multinucleate giant cells. Small cystic spaces lined by amorphous eosinophilic material were seen in some cases as an early expression of lipomembranous or membranocystic panniculitis. Neutrophilic lobular panniculitis should be differentiated from the suppurative variant of EN, in which numerous neutrophils extend into the lobule from fibrous septa.\[^{93,94}\]

Erythema induratuum of Bazin/nodular vasculitis
NV is a multifactorial syndrome with lobular panniculitis and vasculitis, in which tuberculosis may or may not be one of its many etiologies. Thus, erythema induratuum/NV complex is classified into two variants: EIB type and NV or erythema induratuum of Whitfield type [Figure 1c]. The Bazin type has a tuberculous etiology.

Histologically, EIB/NV shows predominantly acute suppurative or granulomatous panniculitis with fibrin deposition in small vessel walls along with karyorrhexis and hemorrhage. In a series of 101 skin biopsies from 86 patients with clinicopathologic diagnosis of EIB, it was seen that vasculitis was obvious in 90.1% cases. Nearly 46.5% biopsies revealed mostly lobular panniculitis with necrotizing vasculitis of the centrilobular small vessels, 12.8% biopsies exhibited mostly lobular panniculitis with vasculitis involving both large septal veins and small centrilobular venules, 11.8% biopsies showed lobular panniculitis with vasculitis involving mainly large septal veins, without any involvement of other lobular
or septal vessels, 9.9% biopsies showed predominantly lobular panniculitis with vasculitis involving large septal vessels, both arteries and veins, and necrotizing vasculitis of the centrilobular venules, and 8.9% biopsies displayed lobular panniculitis with vasculitis involving larger septal vessels (both arteries and veins), but without any involvement of the smaller centrilobular vessels. There were 9.9% biopsies with a predominantly lobular panniculitis but without any obvious evidence of septal or lobular vasculitis, even in serial sections. The differential diagnosis of EIB/NV typically includes PAN, which can be differentiated clinically and by the presence of all stages of the lesion in the biopsy.\[^{28}\]

**Subcutaneous panniculitis-like T-cell lymphoma**

SPTCL is a very rare form of skin lymphoma and accounts for <1% of all non-Hodgkin’s lymphomas. It is localized primarily to the subcutaneous adipose tissue without the involvement of the lymph nodes. SPTCL is histologically characterized by neoplastic lymphoid cells infiltrating mainly the lobules of the subcutaneous tissue with or without the involvement of the epidermis and dermis. The neoplastic lymphoid cells have hyperchromatic, angulated nuclei, scant cytoplasm, and indistinct cell borders. In addition, interspersed histiocytes, plasma cells, neutrophils, mitoses, apoptotic bodies, karyorrhectic debris, and areas of fat necrosis are also seen. The atypical cells often show rimming of individual fat cells [Figure 12].

Based on T-cell receptor (TCR) phenotype and immunophenotypic characteristics, there are two types of SPTCL. One is TCR-αβ, associated with an indolent course and the neoplastic T-cells are usually CD4-, CD8+, and CD56-. The second type is TCR-γδ, characterized by rapid clinical deterioration and CD4-, CD8-, and CD56+ neoplastic T-cells. Nowadays, diagnosis of SPTCL is used for patients with TCR-αβ.

### Table 2: Algorithm for histopathologic diagnosis of septal panniculitis

| Assess adequacy of biopsy and location of inflammation | Predominantly septal | Vasculitis? |
|-------------------------------------------------------|----------------------|------------|
| Predominantly septal                                  |                      |            |
| Vasculitis?                                           |                      |            |
| Yes                                                   |                      |            |
| Small Vessel                                          |                      |            |
| Large Vessel                                          |                      |            |
| LCV                                                   |                      |            |
| Artery/Vein                                           |                      |            |
| Cut. PAN(Art) Sup. TB(Vn)                             |                      |            |
| Lymphos and plasma cells                              |                      |            |
| Pred. Histiocytes with granulomas                     |                      |            |
| Granulomas+                                           |                      |            |
| Necrobiosis lipoidica                                  |                      |            |
| Granulomas                                            |                      |            |
| Scleroderma                                           |                      |            |
| Granulomas+                                           |                      |            |
| Central mucin+                                        |                      |            |
| Central fibrin+                                       |                      |            |
| Cholesterol clefts+                                   |                      |            |
| Radial granulomas+                                    |                      |            |
| Erythema nodosum                                      |                      |            |

The differential diagnosis of EIB/NV typically includes PAN, which can be differentiated clinically and by the presence of all stages of the lesion in the biopsy.\[^{95-97}\]
Table 3: Algorithm for histopathologic diagnosis of lobular panniculitis

| Assess adequacy of biopsy and location of inflammation |
|-------------------------------------------------------|
| Predominantly lobular                                   |
|             | Vascultis?                                             |
|             | Yes                                                    |
|             | Large Vessel                                          |
|             | Artery                                                |
|             | CD EIB                                                |
| Few/no inflammm cells                                  |
| Pred. Lymphos                                        |
| Pred. Neutros                                        |
| Pred. Histiocytes                                    |

Figure 12: Histopathologic features of subcutaneous panniculitis-like T-cell lymphoma. (a and b) Collections of atypical lymphocytes involving both lobules and septa of subcutaneous fat with relative sparing of dermis and epidermis (H and E, x40). (c and d) Atypical lymphocytes with large, hyperchromatic nuclei with irregular nuclear margins (H and E, [c] x200, [d] x400)

A deep elliptical surgical biopsy is essential to have adequate subcutaneous fat
2. A detailed clinical history is indispensable for histopathological assessment
3. Step-wise serials to identify the pattern of panniculitis, i.e., septal, lobular, mixed, with or without vasculitis are often mandatory
4. A careful search for the diagnostic clues should be made, for example, crystals in lipocytes or histiocytes
5. Special stains in “obscure” suppurrative or granulomatous panniculitis cases, to see fungal hyphae or spores, are obligatory
6. Sometimes, polarizing the sections is important to look for sclerosing lipogranulomas or factitial panniculitis
7. Advising follow-up biopsies of representative lesions are imperative to study stages of evolution of the diseases, especially in cases with vasculitis.

In any given case of panniculitis, a diagnostic algorithm should be followed to reach to an appropriate histopathologic diagnosis with adequate clinical information [Tables 2 and 3].

**Financial support and sponsorship**
Nil.

while TCR-γδ type is designated as cutaneous gamma/delta positive T-cell lymphoma (Cyδ-TCL). [98-104]

**CONCLUSION**

Some important points to remember in cases with clinically suspected panniculitis:


**Conflicts of interest**

There are no conflicts of interest.

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