Subcutaneous panniculitis-like T-cell lymphoma

Sir,

We would hereby like to report a case of subcutaneous panniculitis-like T-cell lymphoma (SPTCL), presenting as a persistent swelling over face.

The World Health Organization–European Organisation for Research and Treatment of Cancer classification defines SPTCL as a tumor confined to the subcutaneous fat composed of αβ CD8 cytotoxic lymphocytes, having an intermediate prognosis.[1]

A 25-year-old, Hindu, married male, resident of central India, presented with the chief complaint of intermittent swelling over face for 10 months, persistent since 6 months, occurring initially over both lips, which then spread to involve both cheeks, front and sides of neck, and bilateral periocular areas. The patient also developed progressive hoarseness of voice, for the last 6 months associated with inability to close the eyes fully. Cutaneous examination revealed bilaterally symmetrical, woody hard facial swelling extending from the forehead up to the submandibular and submental regions and laterally up to the ears. After about 3 months, the swelling became persistent and was associated with appearance of linear purpura predominantly noted over the forehead and front and sides of neck [Figure 1]. There was no palpable cervical lymphadenopathy. The patient was treated as recurrent angioedema by other dermatologists, before presenting to our center, with initial partial response to treatment.

The laboratory and radiological investigations that were conducted have been briefly outlined in Table 1. Figure 2 shows the histopathological and immunohistochemical findings.

A persistent, progressive leucopenia and thrombocytopenia, raised reticulocyte count and serum ferritin levels accompanied with hepatosplenomegaly and fever were suggestive of hemophagocytosis. Taking this into consideration along with the histopathological and immunohistochemical profile, a diagnosis of SPTCL was confirmed.

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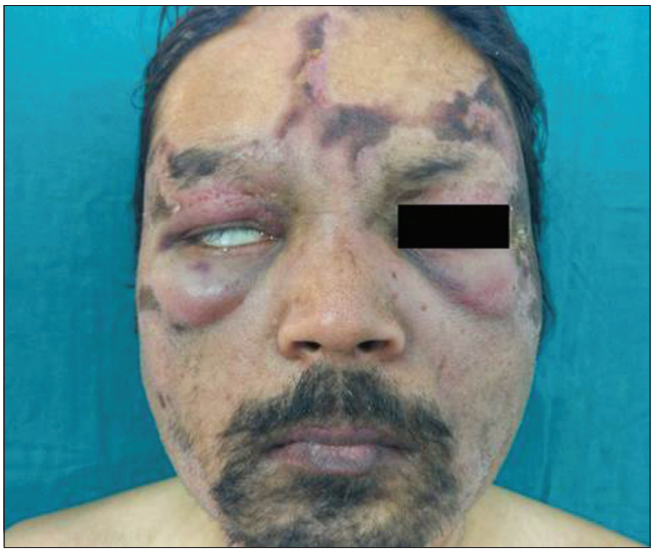

Figure 1: Bilaterally symmetrical swelling with woody hard induration and purpuric plaques overlying the skin, involving the face. Bell's phenomenon visible in the right eye

A stepwise diagnostic approach was followed to rule out cellulitis, deep fungal infection, solid facial edema, Melkersson-Rosenthal syndrome and acute sarcoidosis, as other causes of persistent facial swelling.

The patient was started on intramuscular methotrexate 15 mg/week and tapering doses of prednisolone, leading to a resolution of facial swelling and apparent lipoatrophy [Figure 3] and return of all the hematological parameters to near normal values by 12 months.

Several cases of cutaneous lymphomas presenting as facial plaques, nodules and facial nerve palsies, as well as cases presenting with facial swelling, have been published so far. A comparative analysis is summarized in Table 2.

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Table 1: Investigations summary

Investigations	Summary of findings
Complete hemogram with peripheral smear	Progressive leucopenia and mild thrombocytopenia, with a normal hemoglobin value (11 g %); an absence of any circulating atypical lymphocytes on peripheral smear, reticulocyte count - 2%
Serum lactate dehydrogenase	460 IU
Serum ferritin levels	>2000 pg/mL
Liver and renal function tests, serum antinuclear antibodies, serum complement and C1 esterase levels, serum acetylcholinesterase levels	Within normal limits
Bone marrow biopsy	Trilineage hematopoesis
Local part ultrasonography of face and neck	Nonspecific subcutaneous tissue water logging involving the face and anterior aspect of neck, upto the level of thyroid gland, without any abnormalities in salivary glands or any significant regional lymphadenopathy
CT scan	Head and neck - no abnormality detected Thorax and abdomen - mild hepatosplenomegaly
Direct laryngoscopy	Right vocal cord paralysis, suggestive of right recurrent laryngeal nerve paralysis
Nerve conduction studies	Bilateral facial nerve palsy (lower motor neuron type)
Histopathology and IHC	Diffuse, lymphocytic infiltrate throughout the subcutis without epidermotropism and lobular panniculitis, with abundant lymphocytic infiltrate rimming the fat lobules. IHC profile study was done on the tissue biopsy block from the face which revealed the following results: LCA, CD3, CD43, CD8, CD2, CD5: positive; CD56, CD20, CD4: negative

CT: computed tomography; IHC: immunohistochemistry; LCA: leukocyte common antigen

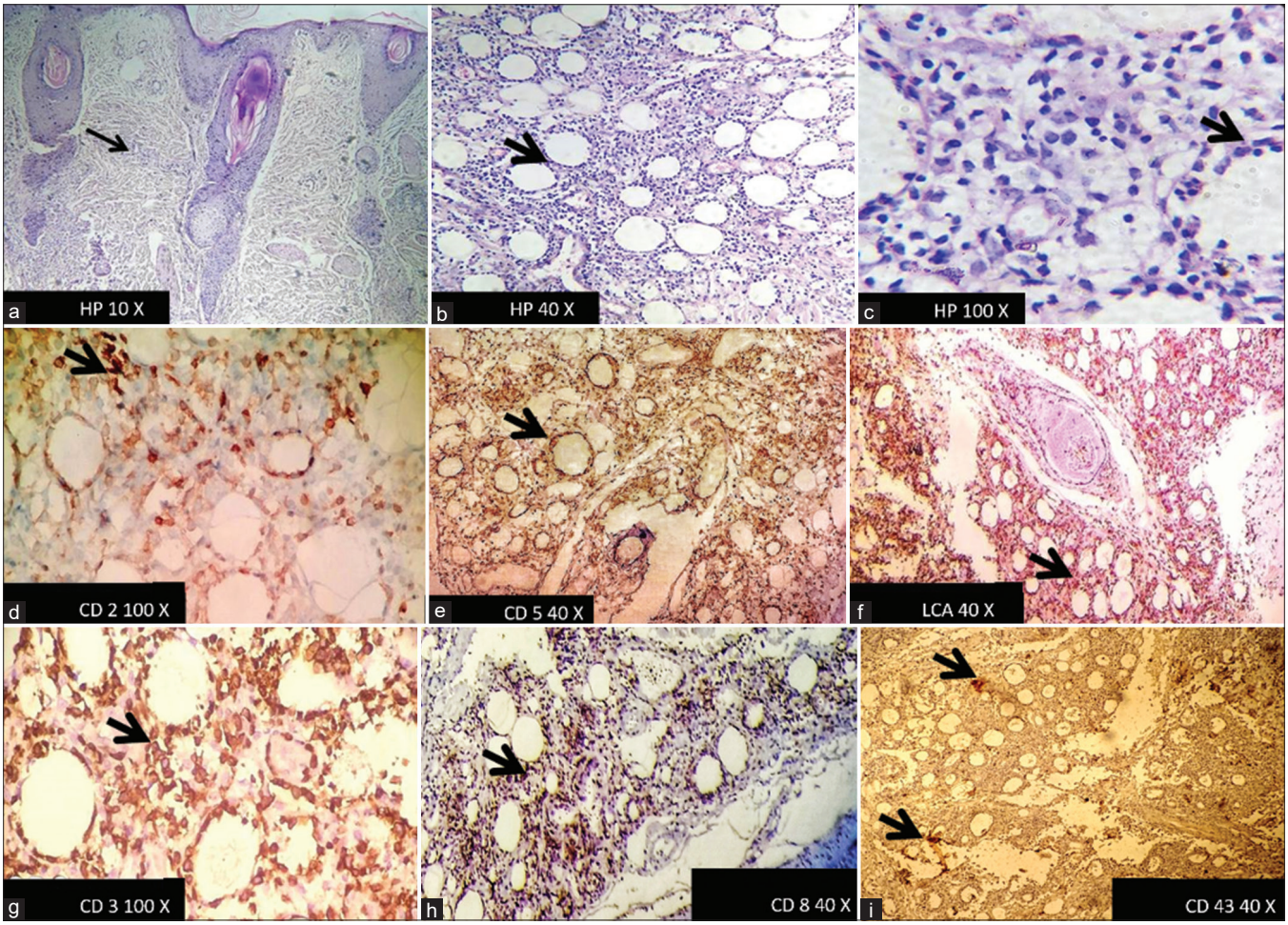

Figure 2: (a-c) Histopathology ×10, ×40, ×100 magnification respectively showing A lobular panniculitis with lymphocytes rimming the fat lobules. (d) Positive staining by CD2 IHC marker on ×100 magnification, (e and f) Positive staining by CD5 & LCA on ×40 magnification, (g) Positive staining by CD3 on ×100 magnification, (h and i) Positive stain by CD8 & CD43 markers respectively

Table 2: Review of Literature

	Case reports						
	Willemze *et al.* (Review article)[1]		Au *et al.*[2]	Park *et al.*[3]	Amo *et al.*[4]	Kawachi *et al.*[5]	Present case
	αβ T-cell phenotype (63 out of 83 cases)	γδ T-cell phenotype (20 out of 83 cases)					
Age (years)	Mean: 36	Mean: 59	55	47	75	1	25
Sex	Female:male ratio=2:1	Female:male=1.9:1	Female	Female	Male	Female	Male
Median duration of symptoms (months)	7	Not available	2	2	1	3	10
Clinical presentation	Typical nodular skin lesions or deep seated plaques, of varying sizes, involving legs > arms, trunk >> face, healing with lipoatrophy	Nodular or plaque-like lesions simulating a panniculitis, with or without ulceration involving legs > arms > trunk	Facial swelling and inflammation, facial weakness with lip swelling, sagging features and bell's phenomenon, normal auditory, gutate and tactile function	Erythematous, indurated oval patches, with surface scaling on the trunk	Facial palsy followed by development of erythematous indurated plaques over left cheek and nose within 1 month	Multiple subcutaneous nodules on cheeks, upper and lower extremities	Bilaterally symmetrical, woody hard, facial swelling extending from the forehead up to the submandibular and submental regions and laterally upto the ears Linear purpuric patches over forehead and neck Progressive hoarseness of voice, associated with inability to close eyes fully
Associated findings	Constitutional symptoms in 58.73% patients, hemophagocytic syndrome in 11.46% patients, associated autoimmune condition in 19% patients	Constitutional symptoms ion 70% cases, 1 patient had history of etanercept therapy for rheumatoid arthritis for 3 years Hemophagocytic syndrome in 45%	Bilateral facial nerve palsy, with residual lip swelling	Constitutional symptoms, including fever, malaise, general weakness, left-sided facial paralysis, and paraesthesia on the right side of the face	Facial hemiplegia, paraesthesia	None	Right recurrent laryngeal nerve palsy, bilateral facial nerve palsy
Lymphadenopathy	7.93%	70%	None	None	None	None	None
CBC serum chemistry	Anemia, leucopenia, thrombocytopenias, and combined cytopenias, elevated liver function tests	Cytopenias, elevated liver function tests in 70%	Not available	CBC normal, raised lactate dehydrogenase, and serum alaninie aminotransferase levels	Not available	Within normal limits	Progressive leucopenia and thrombocytopenia, raised serum lactate dehydrogenase levels, elevated reticulocyte count on peripheral smear; raised serum ferritin levels >2000
Bone marrow	Hemophagocytosis in 17.46% patients, myelodysplastic syndrome in one patient	Histiocytic hyperplasia, hemophagocytosis or decreased cellularity in 35% patients; no evidence of lymphoma	Normal	Normal	Not available	Normal	Normal; trilineage hematopoesis

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	αβ T-cell phenotype (63 out of 83 cases)	γδ T-cell phenotype (20 out of 83 cases)					
Histopathology	Predominantly lobular panniculitis with occasional mild septal involvement, atypical lymphoid infiltrate; rimming of adipocytes by neoplastic T cells	Predominant subcutaneous lymphoid infiltrate but with additional involvement of dermis and epidermis, keratinocyte necrosis, angioinvasion and angiodestruction; less pronounced rimming	Lip biopsy showing heavy infiltration of lymphoid cells with frequent mitoses, no lymphocytic rimming	Skin biopsy - atypical panniculitis-like lymphohistiocytic infiltrate through the dermis and subcutis	Skin biopsy: dense infiltrates of large lymphocytes with irregularly shaped nuclei and prominent nucleoli Muscle biopsy from facial muscle in the area of erythematous plaque: massive muscle tissue destruction by lymphomatous infiltrate	Skin biopsy: lobular panniculitis composed of atypical lymphoid cells with hyperchromatic nuclei and prominent nucleoli; fat rimming by atypical lymphoid cells and phagocytosis	Diffuse, lymphocytic infiltrate throughout the subcutis without epidermotropism and lobular panniculitis, with abundant lymphocytic infiltrate rimming the fat lobules
Immunophenotyping	CD3+, CD8+, CD 4 - strongly expressing Granzyme B, perforin, loss of CD2, CD5 and/or CD7, CD30 always negative, CD56 positive in a single case	CD3+, CD8+, CD4 - strongly expressing Granzyme b, perforin (17 cases), CD8−, CD4+, CD3+ 2 cases, CD56+ (60%) CD30+ in 3 cases	CD2+, CD3+, CD7+, CD5+ (weak) CD4, 4, 20, 56, 79 a negative	CD3, CD56, CD45 RO - positive CD20, CD68 - negative	L26, CD79a	CD2, CD 3, CD 8, Granzyme B, T-cell intracellular antigen-1 - positive CD4, CD20, CD30, CD56, CD123 - negative	LCA, CD3, CD43, CD8, CD2, CD5 - positive CD56, CD20, CD4 - negative
Molecular studies	Beta F1 positive in all cases	TCR δ1 positive in all 6 tested cases, beta F1 negative in rest of the 14 cases	TCR δ1 positive	Germline configuration of γ chain of T-cell receptor by PCR amplification studies		α/β T-cell phenotype, oligoclonal pattern for TCR β Gene, polyclonal pattern for TCR γ gene	Not done
Subtype of cutaneous lymphoma	SPTCL-αβ	SPTCL γδ	Primary mucocutaneous γδ T cell lymphoma	Cutaneous γδ	Diffuse large B-cell lymphoma	SPTCL-α/β subtype	SPTCL subtype unknown
Magnetic resonance imaging	-	-	Infiltrative changes and contrast enhancement in facial subcutaneous tissue	Focal areas of high T2 and FLAIR signal intensity and a low T1 signal with a nonenhancing lesion in the right occipital lobe, consistent with a metastatic lesion	Not available	Not done	Not done; however, computed tomography scans of head and neck were normal Computed tomography of thorax and abdomen revealed hepatosplenomegaly
PET			FDG uptake	Multiple hypermetabolic lesions in pancreas, adrenal glands, breast, inguinal, paraaortic, external iliac lymph nodes suggesting metastatic lesions	-	Not done	Not done

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	αβ T-cell phenotype (63 out of 83 cases)	γδ T-cell phenotype (20 out of 83 cases)					
Treatment	50% - CHOP regimen (31/63), 38% (24/63) - less aggressive therapy (prednisolone, cyclosporine, chlorambucil, methortrexate, cyclophosphamide, 5 patients - radiotherapy or surgery)	70% CHOP regimen	Fludarabine, mitoxantrone, dexamethasone 6 courses	CHOP regimen	Not available	No treatment as there was no systemic involvement	Tapering doses of prednisolone and weekly methotrexate 15 mg subcutaneous injections
Response to treatment	CHOP therapy: 19 of the 31 patients had complete remission, 8 had ongoing disease, 4 died Other therapies: 16 of 24 had complete remission, 5 partial remission, and 3 no response Surgery or radiotherapy: all 5 complete remission, 1 case showed a cutaneous relapse	At the time of last follow up, 15 of 20 patients had died of HPS or progressive lymphoma, 4 were in complete remission, and 1 was alive with progressive disease	Complete metabolic remission, no facial recovery by medical management	Initial radiological and cutaneous remission along with improvement of facial paralysis followed by aggravation and death within 1 month	Not available	Spontaneous resolution after 1 year of diagnosis, no systemic involvement	Resolution of facial swelling and apparent lipoatrophy and returning of all the hematological parameters to near normal values, at the end of 1 year of follow-up

CBC: complete blood count; CHOP: cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (oncovin) and prednisone; FDG: fluorodeoxyglucose; FLAIR: fluid-attenuated inversion recovery; PCR: polymerase chain reaction; SPTCL: subcutaneous panniculitis-like T-cell lymphoma; HPS: Hemophagocytic syndrome

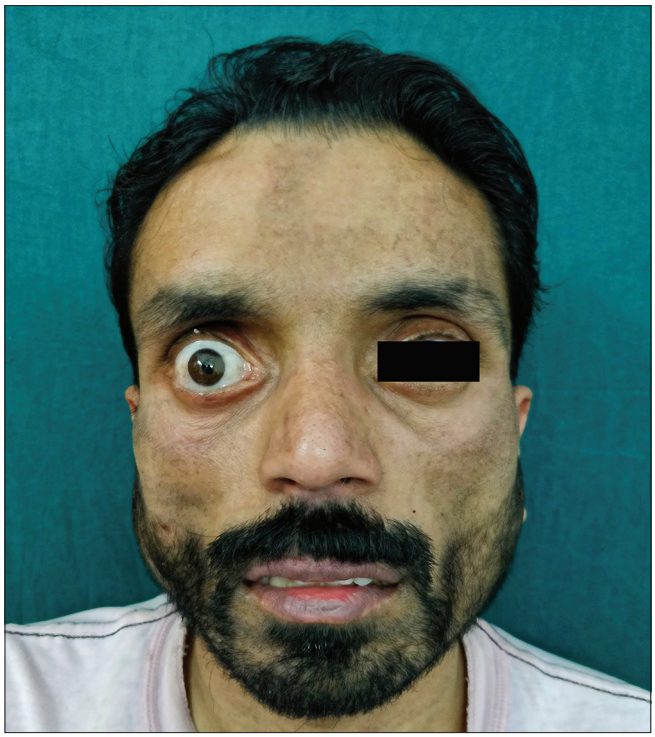

Figure 3: Posttreatment (1 year): complete resolution of the swelling along with clinically apparent lipoatrophy; persistent facial nerve palsy

Our limitation in this case is the lack of T-cell receptor gene rearrangement studies for molecular subtyping of this case into α/β or γ/δ types, as well as absence of positron emission tomography studies, due to a resource-poor setup.

The gradual clinical course of the disease in our case coupled with an excellent response to less aggressive systemic therapy favor the relatively indolent nature of SPTCL. However, involvement of cranial nerves has usually been noted in the more aggressive forms of this disease. The rare, but unique diagnosis of SPTCL should definitely be kept in mind while assessing any case of facial swelling.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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References

1. Willemze R, Jansen PM, Cerroni L, Berti E, Santucci M, Assaf C, *et al.* Subcutaneous panniculitis-like T-cell lymphoma: Definition, classification, and prognostic factors: An EORTC cutaneous lymphoma group study of 83 cases. Blood 2008;111:838-45.
2. Au WY, Yeung CK, Loong F, Li GK. A γ-δ T cell lymphoma with a mask face. Leuk Lymphoma 2012;53:728-9.
3. Park J, Park KY, Li K, Seo SJ, Hong CK. Cutaneous γδ T-cell lymphoma presenting as facial palsy. Br J Dermatol 2011;164:205-7.
4. Amo Y, Tanei R, Yonemoto K, Katsuoka K, Mori M. Diffuse large B-cell lymphoma associated with skin, muscle and cranial nerve involvement. Eur J Dermatol 2000;10:306-8.
5. Kawachi Y, Furuta J, Fujisawa Y, Nakamura Y, Ishii Y, Otsuka F. Indolent subcutaneous panniculitis-like T cell lymphoma in a 1-year-old child. Pediatr Dermatol 2012;29:374-7.