Therapy Letter

Is cyclosporine a good option for the treatment of subcutaneous panniculitis-like T-cell lymphoma associated with hemophagocytic syndrome?

Sir,

Subcutaneous panniculitis-like T-cell lymphoma is a rare mature T-cell lymphoma which generally has an indolent clinical behavior. But sometimes it may be associated with hemophagocytic syndrome which leads to a rapidly progressive course.[1] We report a patient with subcutaneous panniculitis-like T-cell lymphoma and secondary hemophagocytic syndrome who responded successfully to oral cyclosporine.

A 26-year-old woman from the Philippines presented with painful, nodular lesions of size ranging from 1 to 3 cm on her limbs, abdomen, and lower back of one month duration. [Figure 1a and b].

She had associated high-grade fever and myalgia but no other symptoms like arthralgia. Laboratory tests showed abnormal liver function with elevated aspartate aminotransferase, gamma-glutamyltransferase, alkaline phosphatase, lactate dehydrogenase, and ferritin. Her CD25 was 3588 pg/mL (normal range: 0–1900 pg/mL). Investigations revealed mild anemia, leukopenia, and lymphopenia. An infectious origin was ruled out by performing urine, sputum, stool and blood culture, tuberculin test, tests for antibodies against HBV, HCV, HIV, syphilis, CMV, measles, and EBV in serum, chest and sacroiliac x-ray, and computed tomography scan of chest, abdomen and pelvis. Histopathological examination revealed a dense infiltrate of pleomorphic lymphoid cells with large nuclei and lymphocytoclasia around the adipocytes. There were no pathological changes in dermis and epidermis [Figure 1c and d]. Lymphocytes expressed CD3, CD8, perforin, and granzyme but not TIA 1 or CD4 [Figure 1e-h]. Both histopathological and immunohistochemical findings were consistent with subcutaneous panniculitis-like T-cell lymphoma. Bone marrow aspiration cytology showed an increase in the phagocytic mononuclear system with evidence of hemophagocytosis. 18 F-fluorodeoxyglucose positron emission tomography/computed tomography highlighted multiple pathological and generalized uptakes especially over the limbs, abdominal wall, and right breast. Ultrasonography showed splenomegaly. A final diagnosis of subcutaneous panniculitis-like T-cell lymphoma with hemophagocytic syndrome was made and the patient was started on oral dexamethasone 12 mg daily. Clinical and biochemical criteria of hemophagocytic syndrome resolved within 1 week, but the patient developed steroid induced hallucinations and amnesia. Hence dexamethasone was withdrawn. Magnetic resonance imaging of brain was normal. Cyclosporine A was initiated at a dose of 125 mg/day (3 mg/kg of weight) which the patient tolerated and after 6 months of treatment, the dose was tapered gradually. The disease is now well controlled with 25mg/day of cyclosporine A.

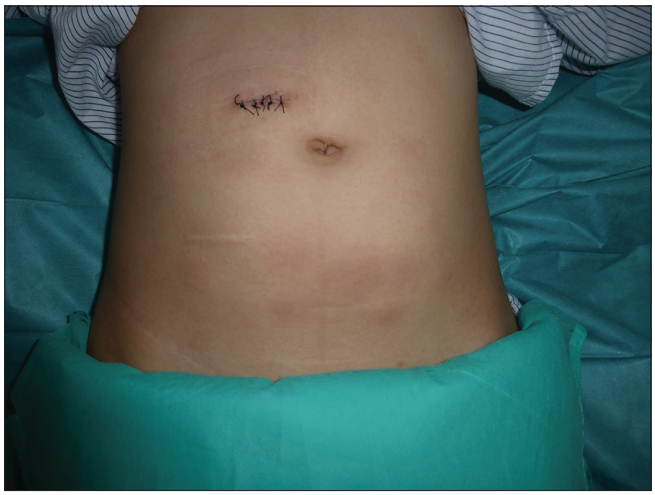

Figure 1a: Nodular lesions on trunk

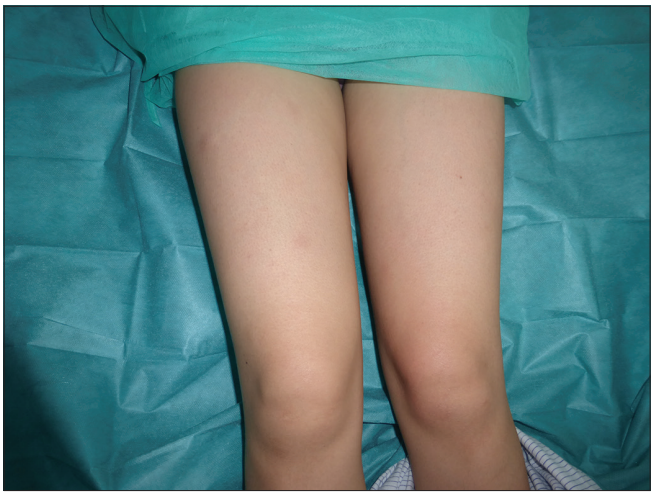

Figure 1b: Nodular lesions on limbs

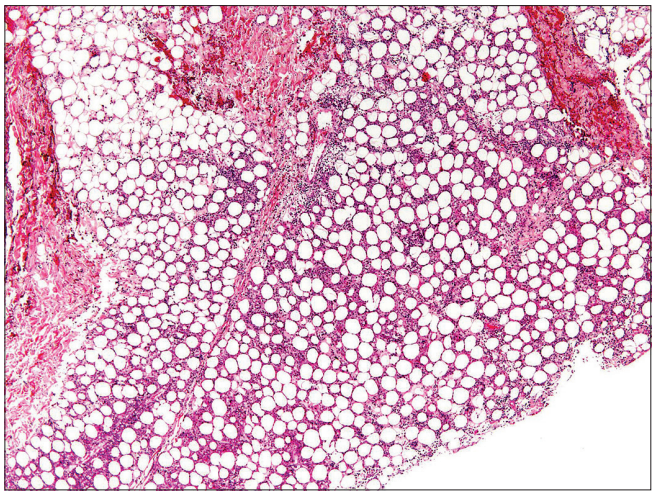

Figure 1c: Lymphocytic infiltrate confined to the subcutis producing a lobular panniculitis-like pattern (H and E, 400x)

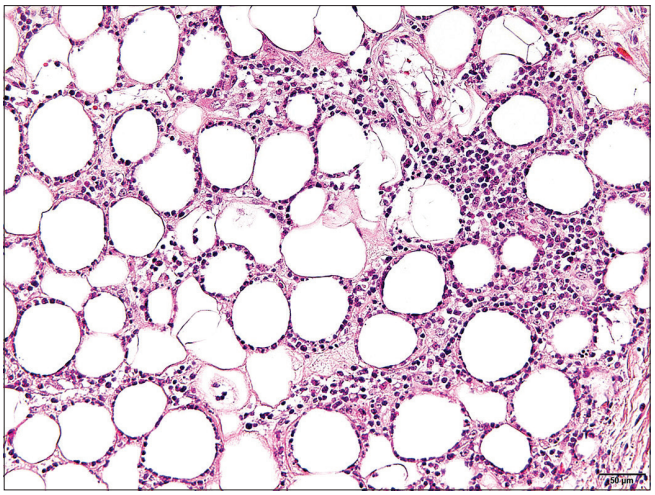

Figure 1d: Pleomorphic atypical lymphoid cells with irregular large hyperchromatic nuclei and lymphocytoclasia around the adipocytes to form a "lace-like" pattern (H and E, 400x)

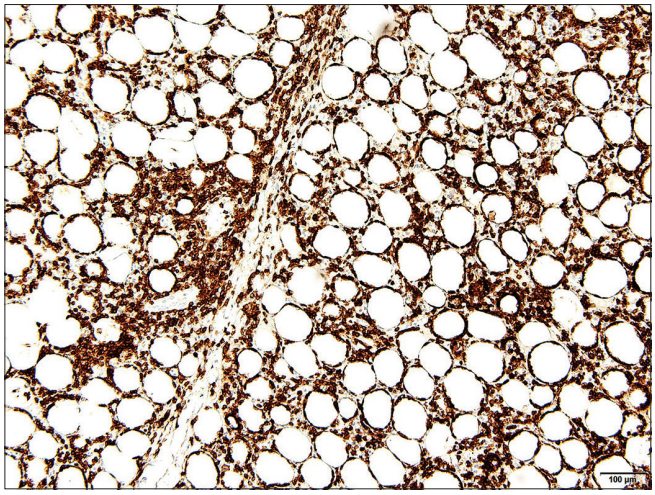

Figure 1e: The neoplastic T cells show positive CD3(CD3 stain, 400x)

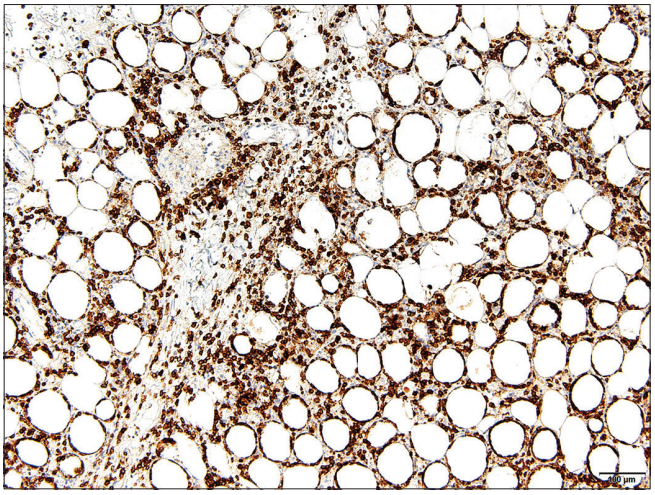

Figure 1f: The neoplastic T cells show positive CD8 (CD8 stain, 400x)

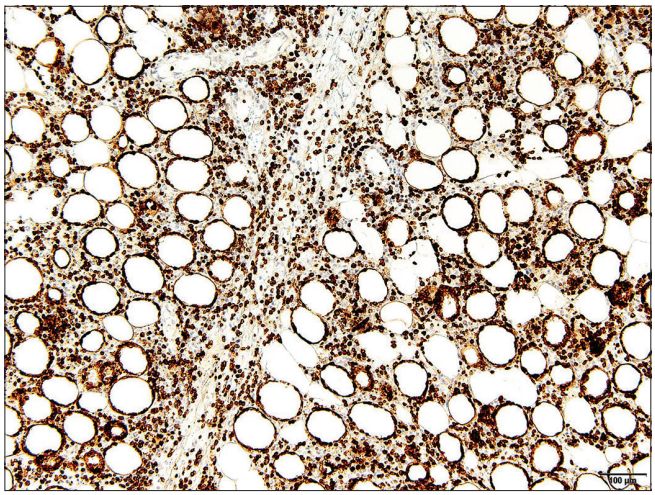

Figure 1g: The neoplastic T cells show positive perforin (perforin stain, 400x)

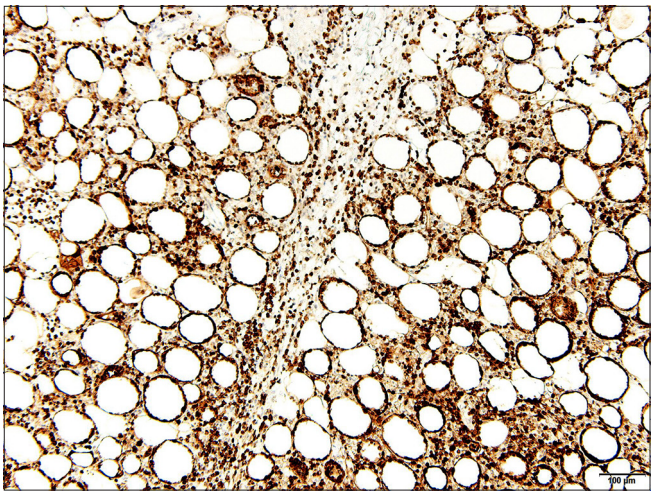

Figure 1h: The neoplastic T cells show positive granzyme (Granzyme stain, 400x)

Even at the end of 12 months the patient is in clinical remission. Hemophagocytic syndrome is an uncommon hematologic disorder characterized by at least five of the following eight findings: fever >38.5°C, splenomegaly, cytopenias, hypertriglyceridemia, hemophagocytosis in bone marrow, spleen, lymph node, or liver, low or absent NK cell activity and elevated soluble CD25 and ferritin.[2]

According to published literature, the presence of hemophagocytic syndrome might change the management approach and outcome in subcutaneous panniculitis-like T-cell lymphoma. Systemic steroids and other immunosuppressive agents are considered the first line treatment for noncomplicated subcutaneous panniculitis - like T-cell lymphoma although radiotherapy, surgery, and stem-cell transplantation can also be used in selective patients. Subcutaneous panniculitis-like T-cell lymphoma which is resistant, progressive or complicated by hemophagocytic syndrome is traditionally treated with multiagent chemotherapeutic regimens such as cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP).[1]

Since 2006, 11 patients with subcutaneous panniculitis-like T-cell lymphoma associated with hemophagocytic syndrome

Table 1: Subcutaneous panniculitis-like T-cell lymphoma with hemophagocytic syndrome treated with cyclosporin A in the literature

Author	Age (years)	Sex	Previous therapy	Response to previous treatment	Dose of CsA	Combination treatment given	Duration of treatment with CsA	Response	Follow-up
Tsukamoto *et al*. 2006	27	Male	Methylprednisolone pulse therapy	None	150 mg/day	Prednisolone 60 mg/day 7 weeks	Not mentioned	CR	6 months
Al Zolibani *et al*. 2006	17	Female	None	None	5 mg/kg/day	Prednisolone 60 mg/day	Not mentioned	CR	1 year
Rojnuckarin *et al*. 2007	52	Female	CP CHOP FC	Temporary response	200 mg/day	Prednisolone 30 mg/day	16 weeks	CR	4 months, but died due to aspergillus sinusitis
Rojnuckarin *et al*. 2007	28	Male	Prednisolone 20 mg/day CHOP	Temporary response	200 mg/day	CHOP	6 weeks	CR	9 months
Rojnuckarin *et al*. 2007	15	Female	CHOP ESHAP	Temporary response	150 mg/day	CHOP	12 weeks	CR	9 months
Chen *et al*. 2010	25	Male	Prednisone 90 mg 3 weeks CHOEP FND	Initial CR for 8 months, then relapse None None	200 mg/day	Prednisone 90 mg/day, 1 month	6 months	CR	12 months
Mizutani *et al*. 2011	38	Female	CHOP+FND	None	4 mg/kg/day	Methylprednisolone pulse therapy 1 g/day	12 months	CR	1 year
Jung *et al*. 2011	35	Female	CHOP Ifosfamide + carboplatin + etoposide Autologous HSCT	Initial CR	4 mg/kg/day	Prednisone	Not mentioned	CR	20 months
Go *et al*. 2012	18	Male	COPBLAM-V CHOP Cisplatin/cytarabine	Yes	200 mg/day at the beginning, 12 weeks. CR for 4 years 800 mg/day 7 days, then 400 mg/day	No	10 weeks	CR	3 years
Chen *et al*. 2016	35	Female	ESHAP GDP	None	300 mg/day	Dexamethasone 8 mg/day, 6 months	9 months	CR	9 months
Shen *et al*. 2016	24	Female	Dexamethasone 20 mg/day	None	250 mg/day	Dexamethasone 40 mg	Not mentioned	CR	5 months
Our case	26	Female	Dexamethasone 12 mg/day	Yes, 1 month. Developed hallucinations and amnesia	125 mg/day	No	12 months	CR	12 months

CR: complete remission; CP: cyclophosphamide/prednisolone; CHOP: cyclophosphamide/doxorubicin/vincristine/prednisolone; FC: fludarabine/cyclophosphamide; ESHAP: etoposide/steroid high dose/cytarabine/cisplatin; CHOEP: cyclophosphamide/doxorubicin/etoposide/vincristine/prednisone; FND: fludarabine/cyclophosphamide; COPBLAM-V: cyclophosphamide/vincristine/prednisolone/bleomycin/doxorubicin; GDP: gemcitabine/dexamethasone/cisplatin; CsA: cyclosporine A; HSCT: hematopoietic stem-cell transplantation

have been treated with oral cyclosporine [Table 1] with good outcome.[3,4] One of them was directly started on a combination treatment of cyclosporine A with high doses of prednisolone and had complete resolution,[3] while two patients who had no response with systemic corticosteroids alone achieved complete remission on combining with cyclosporine A.[4,5] In the remaining patients, cyclosporine A was used after relapse or resistance to chemotherapy or following autologous hematopoietic stem-cell transplantation.[4]

Our experience and recently published data suggest that the occurrence of hemophagocytic syndrome does not necessarily mean a more rapidly progressive disease and worse prognosis in all patients with subcutaneous panniculitis-like T-cell lymphoma. Response and long term remission with oral cyclosporine highlights the need to avoid too aggressive therapies. Future prospective studies with large number of patients are necessary to confirm this hypothesis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her 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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Nil.

Conflicts of interest

There are no conflicts of interest.

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