Case 24

Persistent periorbital edema and erythema

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Patient: A 46-year-old Thai woman from Yasothon

Chief complaint: Periorbital edema and erythema for 3 months

Present illness:

Six months earlier, the patient developed an asymptomatic rash on her face and scalp causing localized hair-loss.

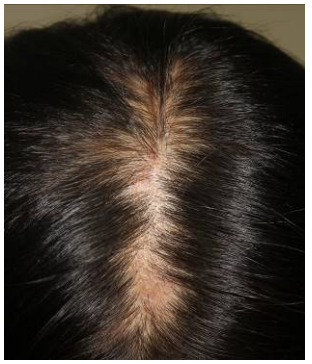
Three months earlier, she noticed the swelling and redness of both eyelids and periorbital areas associated with mild discomfort, but no pain or pruritus. The lesions were persistent and aggravated by sun exposure. There were no systemic symptoms, such as fever, joint pain, discolored fingers or weight loss.

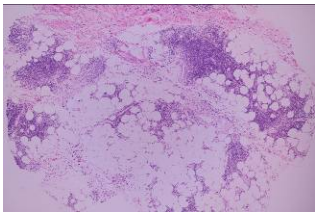
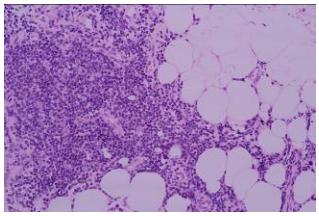
Past history: Healthy

Family history: No autoimmune diseases or malignancies

Skin examination:

- Ill-defined, erythematous edematous plaques of both eyelids and periorbital areas, admixed with thin scales on the upper eyelids
- Multiple round and oval erythematous to brownish patches and plaques with some follicular plugging, adherent scales and central atrophy, distributed on the forehead, chin, cheeks and V-shaped area
- Few patches of scarring alopecia with follicular plugging, admixed with two round-shaped patches of non-scarring alopecia with mild erythema on the overlying skin, located mainly on the vertex of the scalp



Histopathology: (S14-14225, periorbital area)
- Dense perivascular and periadnexal infiltrate of lymphocytes in the dermis and subcutaneous fat lobule

Direct immunofluorescense:
- IgM deposition in the superficial blood vessels
- Few C3 deposition in the subepidemal colloid bodies

Investigation:
Laboratory tests

CBC: **Hct 28.2%**, WBC 6390 (N62%, L31%, M7%), Plt 264,000/mm^3
MCV 54.9 fL, MCH 16 pg, RDW 27.3%
Cr 0.58 mg/dL
LFT: ALP/GGT 79/84, AST/ALT 56/69, TB/DB 0.4/0.2, TP/alb 81.7/34.7
UA: sp.gr. 1.005, protein & glucose negative, RBC & WBC 0-1/HPF
ESR 63 mm/hr, CPK 48 U/L
CH50 100%, C3c 1210 µg/mL (900-1800), C4 251 µg/mL (100-400)
ANA: positive coarse speckled titer 1:320
ANA profile 12 specific nuclear antigens: **SS-A (Ro) 3+, Jo-1 3+**
Serum iron 18 µg/dL, TIBC 401 µg/mL, ferritin 18.9 ng/mL
Coomb's test: Negative
Hemoglobin typing: EA (HbA 75.2%, HbE 19.8%, HbF 5%)

Imaging studies

Chest X-ray: Unremarkable

Diagnosis:
- **Lupus erythematosus profundus over the periorbital areas**
- **Discoid lupus erythematosus of the head and neck**
- **Hemoglobin E trait with iron-deficiency anemia**

Treatment:
- Sun protection and sun avoidance
- Hydroxychloroquine 200 mg/day
- Prednisolone 20 mg/day with calcium, vitamin D and PPI
- Betamethasone dipropionate ointment apply DLE lesions twice daily
- Iron supplement

Discussion:

Lupus erythematosus (LE) panniculitis, principally characterized by involvement of the subcutaneous tissue, is an uncommon clinical variant of chronic cutaneous lupus erythematous (CCLE), demonstrating in 1-3% of patients with cutaneous LE.[1] Although "LE profundus" is interchangeably used

with LE panniculitis by many authors, some authors reserve it only to the cases of LE panniculitis with overlying discoid LE (DLE) changes. LE panniculitis (LEP) mostly affect young adults (30-40 years) with a marked predilection for female; however, it may occur in any ages, including children.[2-5]

Clinically, LE panniculitis presents as tender subcutaneous nodules or plaques. The overlying skin is often normal though it occasionally shows erythema, DLE changes or ulceration. Lesions can be single or multiple areas, but generalized form seems to be extremely rare.[3] The usually involved sites are the face (particularly cheeks), upper arms, scalp, hips and trunk.[2-5] Sometimes, a history of previous trauma in the lesion site can be obtained.[3] Besides, the LEP lesion may eventually resolve leaving depressed atrophic areas which might be disfiguring cosmetically.

There are also other more uncommon clinical presentations of LEP described as follows. LEP involves the fatty breast tissue, so-called lupus mastitis.[3] LEP presents as periorbital edema. This LEP variant occurs much more frequently in South Africans, compared to Asians and Caucasians. It also tends to have a more benign clinical course.[4,6] LEP is arranged in linear or annular configuration. This clinical presentation shows a predilection for the scalp of Asian child and adolescent patients. The lesion is usually non-scarring and sometimes following the Blaschko's lines. It also tends to resolve without leaving atrophic areas.[1,7] LEP simulating alopecia areata presents as circumscribed non-scarring alopecia with probably containing exclamation mark hairs. Scalp tenderness, erythema of the overlying skin and histological findings of LEP are the key to diagnosis of this variant of LEP.[8] In addition, not only LEP located on the parotid area[6] or the earlobe[3], but also LEP clinically mimicking morphea[3] is another rare variant of LEP.

Coexisting with DLE lesions elsewhere is observed in one-third to one-half of patients with LEP, whereas in general it is only about 10% of patients who meet the criteria for systemic LE (SLE).[2-5] However, a higher proportion of coexistent SLE was demonstrated in the case series of LEP from Singapore[5] and Japan[2], accounting for about 40%. Interestingly, when LEP occurs in combination with SLE, the severity of SLE appears to be less serious.[3] Apart from SLE, LEP can also be observed in other autoimmune diseases, such as dermatomyositis, rheumatoid arthritis and Sjögren's syndrome.

Although serologic analyses may be normal, it is common for LEP patients to have low-titer antinuclear antibodies (ANA). It appears that LEP patients who have positive ANA test with a titer of 1:80 or more than indicate a higher probability of coexistent SLE or later developing SLE.[2-5] Less frequently, other circulating autoantibodies, such as anti-dsDNA, can be detected. Other possible laboratory abnormalities include lymphopenia, anemia and decreased C4 level. It is also notable that C4-deficiency is associated with LEP in children, especially those who have a widespread distribution.[3]

Regarding histology, LEP lesions show a pattern of lymphocytic lobular panniculitis with variable degree of inflammation. The characteristic features are hyaline fat necrosis and mucin deposition. Other features are lymphoid follicle formation, lymphocytic vasculitis, calcium deposition and infiltration of plasma cells and eosinophils. It is noted that eosinophils are frequently seen in LEP, but not in other variants of cutaneous LE.[3] The presence of DLE features at dermo-epidermal junction in the lesions of LEP varies ranging from 50% to 75% of patients, and this presence is very useful for LEP diagnosis.[2-5]

Considering immunofluorescence, a positive lupus band can be

established in the overlying skin in a high percentage of LEP patients, even in the lesion of LEP without DLE changes.[2-5] The immune deposition also can be seen in the vessel wall located in the deep dermis and subcutis. C3 complement appears to yield the highest rate of positive DIF tests in both patterns.[2]

In terms of treatment, antimalarials are widely considered to be the first choice of treatment for LEP. They are effective, but slow acting, taking up to 3 months to demonstrate the results.[3] Systemic steroids are also highly effective in LEP treatment, with commonly prescribed dose at 0.5 mg/kg/day of prednisolone. Although thalidomide is suggested to be the most effective drug for LEP therapy as it showed complete remission in 80% of patients within 1-2 months[3], it is not frequently used because of its adverse effects. Other systemic therapies include dapsone, IVIg and cyclophosphamide.

Our patient presented with an uncommon manifestation of LEP, periorbital edema, in her 40s. Although the presence of overlying DLE changes was not appreciated clinically, it was histologically confirmed. Therefore, the diagnosis of LE profundus was established. Besides, DLE lesions were found elsewhere not only on the face, but also on the scalp leaving scarring alopecia. Interestingly, patches of circumscribed non-scarring alopecia are also observed on the scalp. This might be another uncommon presentation of LEP which is mimicking alopecia areata or might be true alopecia areata occurring concominantly with DLE lesions. Unfortunately, the confirmed histology was not done on the scalp. Patient did not meet the criteria for SLE, even though she had a rather high titer of ANA. She was treated with prednisolone at a dose of 0.5 mg/kg/day combined with hydroxychloroquine 200 mg/day and high-potency topical steroids for DLE lesions. She also was advised to practice adequate strategies for sun protection. As a result, the lesions appeared to be partly improved.

References:

1. Mitxelena J, Martinez-Penuela A, Cordoba A, Yanguas I. Linear and annular lupus panniculitis of the scalp. Actas Dermosifiliogr. 2013; 104(10): 936-9.
2. Arai S, Katsuoka K. Clinical entity of Lupus erythematosus panniculitis/lupus erythematosus profundus. Autoimmun Rev. 2009; 8(6): 449-52.
3. Fraga J, Garcia-Diez A. Lupus erythematosus panniculitis. Dermatol Clin. 2008; 26(4): 453-63.
4. Jacyk WK, Bhana KN. Lupus erythematosus profundus in black South Africans. Int J Dermatol. 2006; 45(6): 717-21.
5. Ng PP, Tan SH, Tan T. Lupus erythematosus panniculitis: a clinicopathologic study. Int J Dermatol. 2002; 41(8): 488-90.
6. Perez-Pastor G, Valcuende F, Tomas G, Moreno M. [Lupus erythematosus panniculitis presenting as palpebral edema and parotiditis]. Actas Dermosifiliogr. 2007; 98(8): 549-52.
7. Chiesa-Fuxench ZC, Kim EJ, Schaffer A, Fett N. Linear lupus panniculitis of the scalp presenting as alopecia along Blaschko's lines: a variant of lupus panniculitis not unique to East Asians. J Dermatol. 2013; 40(3): 231-2.
8. Kossard S. Lupus panniculitis clinically simulating alopecia areata. Australas J Dermatol. 2002; 43(3): 221-3.