# Pure Nucleolar Pattern of Antinuclear Factor in Systemic Lupus Erythematosus (SLE)*

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Antinuclear factor (ANF) or antinuclear antibody (ANA) is a valuable guide in both the diagnosis and prognosis of SLE patients.[1-8] Because such individuals produce antibodies against a large variety of nuclear antigens, various patterns of ANF are encountered in most of them (Fig. 1). A peripheral pattern of ANF at a titre of 1:1200 is diagnostic of SLE, whereas a speckled pattern at 1:1000 is a common picture in cases of scleroderma and mixed connective tissue disease,[4] but unlikely in SLE. A high titre of nucleolar pattern (up to 1:1024)[9] is also compatible with scleroderma but not with SLE.[1-14]

## OBSERVATION

During the past seven years (1976-1983), 4,134 serum specimens were examined for ANF at our laboratory in the Faculty of Medicine. These sera were collected from patients with SLE (57%) and scleroderma (17%); the remainder from patients with dermatomyositis, mixed connective tissue disease, and rheumatoid arthritis, among others. A pure nucleolar pattern has been observed in three cases: two scleroderma and one SLE. Details of the third case are as follow:

The SLE patient was a 17-year-old girl who first attended Chiang Mai Hospital's outpatient service on January 5, 1982 (H.N. 1081962). Her complaint of facial rash was promptly diagnosed as being due to discoid lupus. Treatment with topical corticosteroid cream gave no benefit.

Two weeks later she again visited the service, this time complaining of arthralgia of the elbows and knees, oral ulcers, alopecia and photosensitivity. Physical examination on admission (January 21, 1982), revealed a frail-looking young girl, with discoid lesions over the malar areas, buccal ulcers, moderate alopecia, arthritis of the elbows and knees, periungual erythema, vasculitic lesions on the palms and soles, and occasional premature heart beat. A haemogram disclosed: haemoglobin concentration, 11.7 g/dl; haematocrit, 33 per cent; white-cell count, 5.2 x $10^9$/litre; and platelet number, 269,000/$mm^3$. Urinalysis yielded 1+ albumin, a few white blood cells per high-dry field, and no red blood corpuscles or casts. A 24-hour urine collection contained

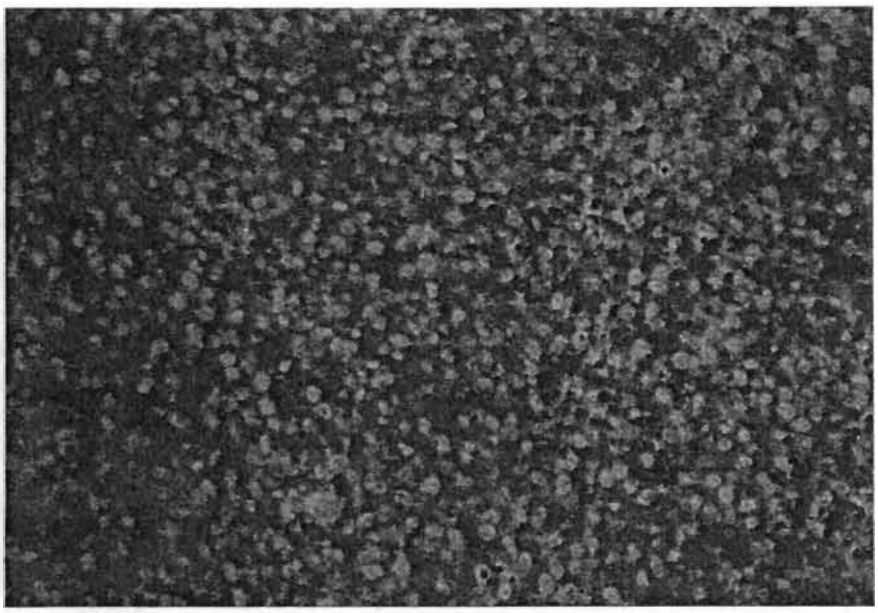

*Fig. 1* Showing mixed staining patterns of antinuclear antibodies commonly seen in patients with SLE.

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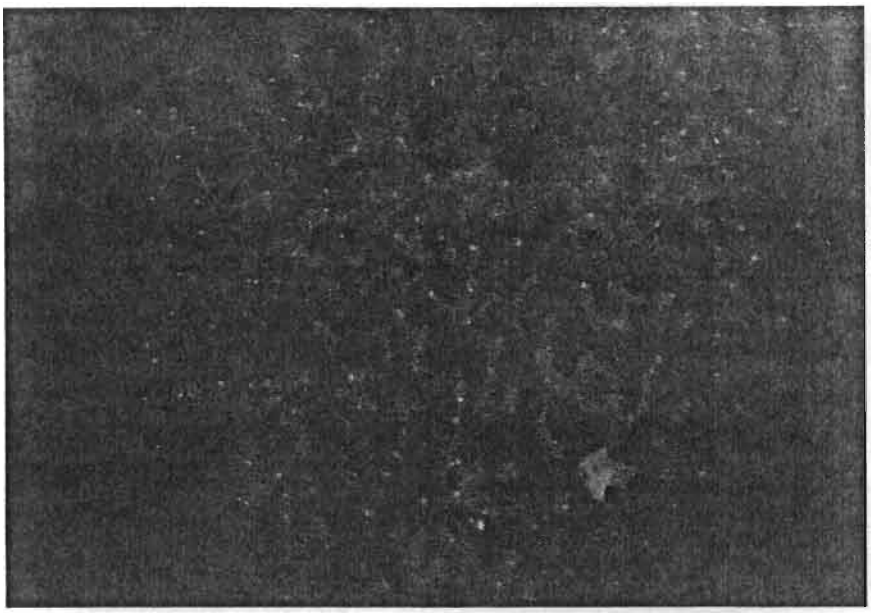

*Fig. 2* Showing antinuclear factor of pure nucleolar pattern with IgG titre at 1:1280 in the present patient.

0.765 gram of protein. Antinuclear factor revealed a nucleolar pattern with pure IgG titre of 1:1280 (Fig. 2), but was negative when using fluorescein labelled with anti-IgM, anti-IgA, anti-C3, C4 and fibrinogen. Serum haemolytic complement was 20 per cent of normal controls. LE cell preparation, rheumatoid factor, Coombs' test, anti-DNA (using immunofluorescent technique), direct antibody immunofluorescence of normal skin and VDRL were all negative. Chest radiograph was non-revealing.

At any rate, a diagnosis of systemic lupus erythematosus was established by the salient findings (discoid and butterfly facial rashes, arthritis, oral ulcers, vasculitis, photosensivity, positive ANF and low serum haemolytic complement) in conformity with the criteria of the American Rheumatology Association.[13,14] Corticosteroid therapy with oral prednisolone (1mg/kg body weight/day as a single daily dose) was started. The patient responded satisfactorily and was discharged on January 25, 1982 to continue the same medication at home. Vasculitis, oral ulcers, arthritis and albuminuria disappeared completely within two weeks of treatment; only the photosensitivity persisted. Within two months the daily dosage of oral prednisolone was tapered off gradually to 20 mg; it was supplemented with oral chloroquine (100 mg/day) and topical para-aminobenzoic acid (PABA) and corticosteroid cream.

On July 20, 1982 the patient was re-admitted because of exacerbation of SLE with leukopenia (wbc 2.0 x $10^9$/1). On examination, she showed moon face, alopecia, malar rashes, oral ulcers, cervical lymphadenopathy and vasculitis of both hands and feet. Haematocrit was 21 per cent; haemoglobin concentration, 12 g/dl; white-cell count, 2.6 x $10^9$/litre, with 70 per cent neutrophils, 28 per cent lymphocytes and 2 per cent eosinophils; and platelets, 80,000/$mm^3$. Erythrocyte sedimentation rate was 5 mm at 30 minutes and 25 mm at one hour. Urinalysis showed a trace of albumin, a few red blood cells per high-dry field and no cellular casts. Serum haemolytic complement was 80 per cent of normal controls. Other relevant investigations were within normal limits.

Despite the institution of an increased dose of oral prednisolone (40 mg/day), the patient developed two *grand mal* seizures during hospitalization. Parenteral methyl prednisolone 125 mg/day (= prednisolone 3 mg/kg body weight/day) was substituted on August 4, 1982. Five days later the white-cell count rose to 5.7 x $10^9$/litre. Hence, oral prednisolone was re-instituted with oral cyclophosphamide (50 mg/day) added on August 12, 1982. From that time, the patient's condition improved steadily; antinuclear factor (nucleolar pattern) tested on September 7, 1982 was only 1:40 and subsequently was negative on May 17, 1983 at which time she was clinically quite well. At the time of writing (September 1983), the patient is being maintained on oral prednisolone (10 mg daily) and cyclophosphamide (50 mg on alternate day).

*In conclusion,* with the authors' knowledge there has hitherto been no report in the literature of an SLE patient with high titre of pure nucleolar pattern of ANF. Although Watanabe *et al.*[12] found a nucleolar pattern of ANF mixed with cytoplasmic antibodies in SLE patients using human mononuclear cells as a substrate, they did not mention the titre range. High titre of nucleolar pattern of ANF was reported in scleroderma patients only.[9] Our patient had findings fitting the diagnosis of SLE without evidence of scleroderma or other conditions that might give a positive test for ANF. Since our case is so far the only case of its kind reported, it is as yet impossible to speculate on any significant clinical implication.

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