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KAZUISTIKA *CASE REPORT*

LUPUS PROFUNDUS ALEBO LUPUS ERYTHEMATOSUS S PANIKULITÍDOU

I. JAJIC, Z. JAJIC, S. GRAZIO, T. NEMCIC, M. BELICZA

LUPUS PROFUNDUS OR LUPUS ERYTHEMATOSUS PANNICULITIS

Department for Rheumatology, Physical Medicine and Rehabilitation and Clinical Institute of Pathology "Ljudevit Jurak", Medical Faculty of Zagreb, University Hospital "Sestre milosrdnice"

Súhrn

Lupus profundus je zriedkavá choroba. Vyskytuje sa samostatne alebo zriedkavo aj spolu s diskoidným alebo systémovým lupus erythemtosus. Vo väčšine prípadov postihuje táto choroba ženy vo veku 30—60 rokov. V podkožnom tukovom tkanive sa objavia bolestivé, modrasté uzlíky veľkosti 1—2 cm. Po mesiaci sa vyvinie atrofia kože a podkožného tukového tkaniva a pozoruje sa priľnavosť kože k svalom a kostiam. V typických prípadoch sú patohistologické nálezy bohaté na lymfocyty a histiocyty. Terapia pozostáva z podávania antimalarík buď samostatne, alebo v kombinácii s kortikosteroidmi a príležitostne cytostatikami.

Uvádzame kazuistiku ženy s 20-ročným trvaním tejto choroby, kontinuálnou progresiou, nevratnými zmenami a rezistenciou proti leičbe.

Kľúčové slová: lupus profundus, lupus erythematosus panniculitis, panikulitída, kožné choroby.

Summary

Lupus profundus is a rare disease. It occurs independently as a separate entity or rarely along with discoid or systemic lupus erythematosus. In most cases, it is a disease of women between there thirties and sixties. Painful and bluish nodules develop in subcutaneous fat tissue ranging in diameter 1—2 cm. After one-month atrophy of skin and subcutaneous fat tissue occur with adherence of the skin to muscles and bones. In typical cases pathohistological finding is rich of lymphocytes and histiocytes. Therapy consists of anti-malarial drugs alone or in combination with corticosteroids and occasionally cytotoxic drugs.

We present female patient with 20-year duration of the disease manifesting continued progression with irreversible changes and resistance on therapy.

Key words: lupus profundus, lupus erythematosus panniculitis, panniculitis, skin diseases.

INTRODUCTION

Panniculitis is a term regarding to progressive chronic inflammation of subcutaneous fat tissue, characterized by infiltration of lymphocytes and histiocytes ending with fibrosis (1). Panniculitis granulomatosis appears when histiocytes make the base of inflamed infiltrate.

Accurate nature of the infiltrates may be confirmed by biopsy (2). Panniculitis is divided according to histological criteria into four categories: 1. septal panniculitis; 2. lobular panniculitis; 3. mixed septal and lobular; and 4. panniculitis along with vasculitis (3). Lupus profundus or lupus erythematosus panniculitis belongs to mixed panniculitis (1—5). As it is a rare form of panniculitis, we present female patient with 20-year duration of the disease that manifest continued progression with irreversible changes.

A CASE REPORT

D.B., disease history number 328915, born 1943, retired, has three children. *Family history:* There was no similar disease. *History:* Often sore throat in the childhood. Menarche when 13-year old. Two births, one gemini pregnancy. No abortion. *Present disease:* Since 1967 has suffer from morning headache and paresthesia in all fingers.

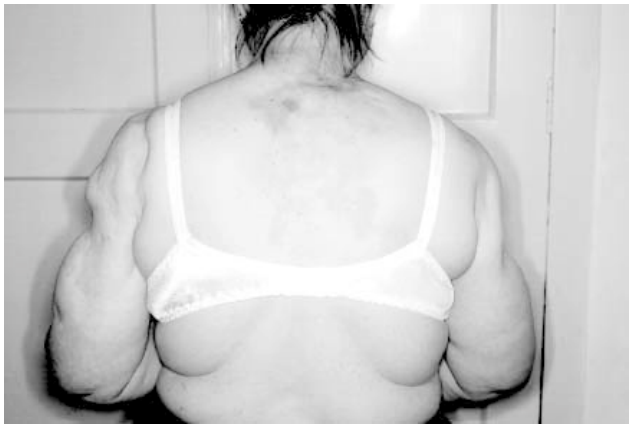

Fig. 1. Atrophy of the skin and subcutaneous tissue on the thorax between scapulas, on shoulders, upper arms and scalp.

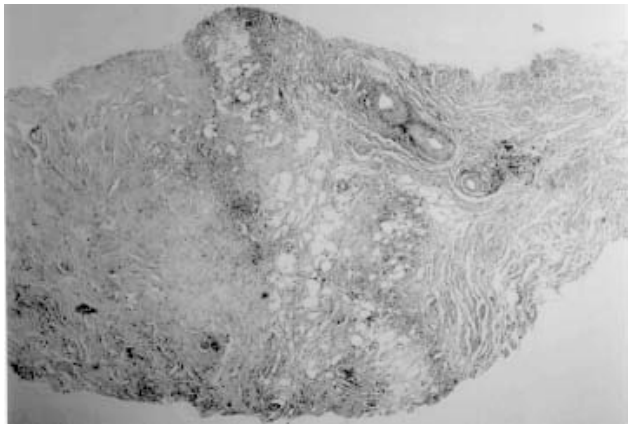

Fig. 2. Atrophic flat epidermis, mixoid degeneration of papillary corium, inflammed focal infiltrates (lymphocytes, histiocytes) and subcutaneous fat necrosis (reticular layer and connective tissue).

Since 1980 the headache has been worse. At the same time, some blue spots appeared on the skin of the left forearm and scalp. They were transformed into nodules during 2—3 days. The nodules were located in subcutaneous tissue. They were also blue coloured, painful, rigid and immobile from the base (Fig. 1). For some length of time, 3 weeks to one month, atrophy of the subcutaneous fat tissue developed at the sites of nodules and consequently scars grew together with base (muscle, bone). Such a nodules appeared three to four time a year in variable time intervals. Development of the nodules did not depend on seasons. During 1999 nodule on right gluteal region and right thigh appeared just as alopecia.

Status: Atrophy of the skin and subcutaneous tissue on the thorax between scapulas, on shoulders, more right one, upper arms and scalp (Fig. 1). At these regions the skin was thinner and livid coloured. The size of atrophic skin was from coin to palm size. The patient felt the pain while palpation on atrophic skin. Alopecia was present sporadically.

Laboratory findings: ESR 23 mm/h (never up to 30 mm/h); erythrocytes $3.74x10^{12}$/L; hemoglobin 114 g/L; leukocytes $5.0x10^{9}$/L; urine pH 6.0; CBC: nonsegmental 0.02, segmental 0.60, lymphocytes 0.34, monocytes 0.04; alkaline phosphatase 62 U/L; ALT 10 U/L; CK 62 U/L; LDH 256 U/L; bilirubin 6.2 Ţmol/L; urea 6.8 mmol/L; creatinine 54.0 Ţmol/L; urine acid 147.1 Ţmol/L. Electrophoresis of serum proteins: alpha-1 4.5, alpha-2 9.5, beta 12.5, gamma 19.5, albumins 66. Immunoelectrophoresis: IgG 12700 mg/L, IgA 3200 mg/L, IgM 660 mg/L, C3 complement 880 mg/L, C4 complement 340 mg/L, ceruloplasmin 350 mg/L, haptoglobin 2200 mg/L, CRP less than 5 mg/L. Waaler-Rose test negative; PLT 1.4; Latex test negative; LE cells negative; ANF negative.

Histological findings: In the histological sample of the skin and subcutaneous fat tissue pathological changes involved all layers (Fig. 2). Microscopically, there was atrophic flat epidermis with less manifested epidermal extensions and mixoid degeneration of papillary corium. In dermis there were extensive inflamed focal infiltrates, mostly consist of lymphocytes and some histiocytes, especially near hair follicle. In the reticular layer of dermis and subcutaneous fat tissue there were foci of necrosis, sporadically with erythrocyte extravasation. Vessels with thickened endothelium and perivascular lymphocyte infiltrates, focal necrosis of fat cells and scar connective tissue with infiltrates of lymphocytes, plasma cells and macrophages were found in subcutaneous fat tissue.

Radiological findings of the region of developed nodules was normal.

Treatment: Therapy with corticosteroids and azathioprine has taken place since 1980 and it lasted only year with minor therapeutic effects. After that, there was therapeutic trial with doxycycline, but without any significant improvement. Since 1982 the patient has been treated by nonsteroidal anti-inflammatory drugs that also did not influence on clinical picture of the disease. In 1999 has started therapy with antimalarials (Resochin) that have lead to rarely relapses and milder clinical picture. Now, there are no signs of disease progression and the patient feels better.

DISCUSSION

Original description o lupus panniculitis was derived from Kaposi in 19. century (4): Term "lupus profundus" dates from thirties of 20. century. In the fifties of the same century

was discovered that patients with lupus profundus often do not have characteristics of systemic lupus but changes of discoid lupus (2). Characteristic pathohistological picture of lupus profundus was described and treatment with antimalarials and corticosteroids has been introduced in the sixties of 20. century.

Lupus profundus or lupus erythematosus panniculitis most often appears in adult women (5, 6). Some cases in children were described too.

The changes consist of nodules in subcutaneous tissue that are sensitive on palpation and could ulcerate. The nodules most often develop in subcutaneous tissue of the face, upper extremities or gluteal region and thighs, as it was in our patient.

Histologically, lupus profundus is clear and it appears as a primary entity in patients without evidence of SLE or some other autoimmune disease (6, 7, 8).

Performed histological examination of epidermis and dermis confirm lobular panniculitis (lupus profundus) as it was stated in literature (2, 7). However, in the lesion in subcutis that was old two days we found inflamed infiltrate corresponding to septal panniculitis, and in the second sample of the same patient that was old five days we found lobular picture of fatty necrosis that is characteristic of pancreatic panniculitis. These findings show that mixed form of panniculitis, in which belong lupus profundus too, is changing during its definitive forming.

Categorization of lupus panniculitis into mixed panniculitis could be useful in the future due to definition of pathogenesis and treatment of this rare disease.

Lupus profundus was described along with discoid and very rarely with systemic lupus erythematosus, Sjögren's syndrome, sialoadenitis, rheumatoid arthritis, mixed connective tissue disease, Hashimoto's thyroiditis, immune hemolytic anemia and immune thrombocytopenic purpura, but in 50 % cases a s a primary entity.

Lupus panniculitis differs from other forms of panniculitis by its clinical presentation and distribution of the changes. Lesions develop mostly on proximal parts of upper extremities, trunk, face and head. They rarely appear on lower extremities.

Other states that could clinically resemble lupus panniculitis are necrotic vasculitis that involves subcutaneous fat tissue, cytophagic histiocytic panniculitis and false panniculitis (6). They have different pathohistological findings (9). Panniculitis appearing in pancreas diseases or trauma has different clinical and pathological characteristics and panniculitis caused by the lack of alpha-1-antitrypsin, has different clinical, pathological and laboratory findings. Panniculitis of connective tissue appears rarely and differs pathologically by its lobular panniculitis and caseous necrosis. Weber-Christian's panniculitis is clinically characterized by fever.

Antimalarials are useful for the treatment, but in case of their omission, relapses appear again. Better results have been achieved by combination of antimalarials and corticosteroids (10). Dapson and azathioprine are reserved for the resistant cases. Single cases react to thalidomide.

Lethal cases have not been described.

In conclusion, lupus profundus panniculitis occurs independently as a separate entity or rarely along with discoid or systemic lupus erythematosus. Serological abnormalities are extremely rare. That is why the diagnosis is based on histological finding and clinical picture. Antimalarials and corticosteroids are recommended therapy, but it is hardly to define its real worth.

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Address to author: I. Jajic, Vinogradska 29, 10 00 Zagreb, Croatia.

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RHEUMATIC FEVER — IS IT STILL A PROBLEM?

C. OLIVIER

REUMATICKÁ HORÚČKA — JE STÁLE PROBLÉMOM?

J Antimicrob Chemotherapy, 45, 2000, s. 13—21.

Incidencia reumatickej horúčky v priebehu posledných 50 rokov klesla v rozvinutých krajinách na priemernú ročnú incidenciu 0,5 prípadu na 100 000 detí v školskom veku. V rozvojových krajinách však zostáva endemickým ochorením a ročná incidencia je 100—200 prípadoc na 100 000 detí. V industrializovaných krajinách sa občas zaznamenajú izolované epidémie (napr. v USA v rokoch 1985—1987). V súčasnosti stále prevláda koncepcia, že vznik reumatickej horúčky je odrazom autoimunitnej odpovede organizmu na infekciu betahemolytickým streptokokom skupiny A. V posledných rokoch však narastá záujem o štúdium faktorov virulencie streptokokov a pozornosť sa sústreďuje predovšetkým na proteín M, podľa ktorého možno diferencovať viac ako 80 rôznych sérotypov. Otázka, prečo určitý sérotyp má výraznejší reumatogénny potenciál, nie je zodpovedaná. Diagnóza reumatickej horúčky v rozvinutých krajinách je v súčasnosti ťažká aj vzhľadom na jej nízku incidenciu. Navyše ďalším problémom je spoľahlivá diferenciácia medzi reumatickou horúčkou a poststreptokokovou reaktívnou artritídou. Preto vo väčšine európskych krajín stále platí odporučenie, že treba liečiť antibiotikami všetky prípady faryngitíd a tonzilitíd napriek tomu, že asi iba 20 % prípadov je zapráčinených betahemolytickám streptokokom skupiny A.

F. MATEIČKA

IMMUNOSUPPRESSANT USE WITHOUT BONE LOSS — IMPLICATIONS FOR BONE LOSS AFTER TRANSPLANTATION

G.R. GOODMAN, I.R. DISSANAYAKE, B.R. SODAM, E. GORODETSKY, J. LU, Y.F. MA, W.S.S. JEE, S. EPSTEIN

IMUNOSUPRESIA BEZ STRATY KOSTNEJ HMOTY —DÔSLEDKY PRE POSTTRANSPLANTAČNÝ ÚBYTOK KOSTNEJ HMOTY

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Liečba cyklosporínom A (CsA) je asosiovaná s posttransplantačnou kostnou chorobou. V poslednom čase boli vyvinuté účinné imunosupresíva ako rapamycín (sirolimus, SRL), ktoré majú menej výrazné nežiaduce účinky. Nedávne experimenty ukázali, že pri vysokej imunosupresívnej účinnosti má SRL relatívne nižší negatívny účinok na kostný metabolizmus. Kombinácia nízkych dávok CsA a SRL preukazuje in vivo synergické imunosupresívne vlastnosti.

Cieľom tejto štúdie bolo preskúmať efekt kombinovanej liečby nízkymi dávkami CsA a SRL na kostný metabolizmus ako potenciálnu kosť šetriacu alternatívu posttransplantačnej imunosupresie. 119 potkanov bolo rozdelených do 6 skupín: kontrola, vehikulum, CsA — vysoká dávka, CsA — nízka dávka, SRL — nízka dávka, kombinácia CsA a SRL — nízke dávky. Kontrolná skupina bola usmrtená v deň 0 a vyšetrená histomorfometricky. Odber krvi a váženie v ostatnýc skupinách sa robili 0., 28., 56. a 84. deň pokusu. Potkany boli usmrtené 84. deň pre potreby histomorfometrie. V odobratých vzorkách bol analyzovaný močovinový dusík, kreatinín a osteokalcín.

Osteokalcín bol signifikantne zvýšený na 28. a 56. deň v skupine s vysokou dávkou CsA. V tejto skupine zároveň histomorfometria preukázala prítomnosť osteopénie. V skupine s nízkou dávkou CsA sa pozoroval mierny úbytok kostnej hmoty, kým nízka dávka SRL a kombinovaná nízka dávka CsA a SRL boli bez negatívneho účinku.

Synergická kombinácia nízkej dávky CsA a SRL predstavuje nádejnú verziu posttransplantačnej imunosupresie s minimalizovanými nežiaducimi účinkami na kostný metabolizmus.

R. IŠTOK