CASE REPORT

Rare zoonosis (hemotrophic mycoplasma infection) in a newly diagnosed systemic lupus erythematosus patient followed by a *Nocardia asteroides* pneumonia

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ABSTRACT

Systemic lupus erythematosus (SLE) is *per se* a disease characterized by suppressed immune response and thus susceptibility to various opportunistic infections. We describe the case of a 21-year-old woman who developed a rare zoonosis - hemotrophic mycoplasma infection in the initial stage of SLE, complicated with *Nocardia asteroides* pneumonia afterwards. Nocardia infection coincided with initiation of glucocorticoids and cyclophosphamide therapy for SLE. After the treatment she recovered completely. To our knowledge the only case of human hemoplasmosis (then referred to as eperythrozoonosis) in medical literature was the one described by a group of Croatian authors 22 years ago. No cases of a hemotrophic mycoplasma infection in a SLE patient have been published up to now.

Keywords: SLE, zoonosis; hemotrophic mycoplasma (hemoplasma), eperythrozoon, *Nocardia asteroides.*

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INTRODUCTION

The immune system in SLE patients is suppressed per se because of the autoimmune nature of the disease. Predisposing factors include lowered complement levels, impaired cell-mediated response and abnormalities in mononuclear phagocyte functions.[1-3] A long-term use of steroidal and other immunosuppressive therapy makes the patients even more immunocompromised, so it is not unexpected that various opportunistic organisms take advantage of the host and infect the body.[1-3] The list of potential pathogens is wide and includes numerous widespread Gram+ and Gram- bacteria, viruses, parasites, fungi and mycoplasma. The main causes of death of SLE patients from the onset to the later stages of the disease include cardiovascular and infectious complications equally.[4] This should be taken into consideration in the treatment of SLE patients and antibiotic prophylaxis and immunization issued to high-risk patients to lower the morbidity and mortality rate.

CASE REPORT

A 21-year-old woman worked as a hairdresser in a rural island environment and had everyday contact with sheep, pigs, poultry, cats and mosquitoes. She had a history of recurrent (nearly once a year) labial herpes and tonsillitis and often received penicillin-based antibiotics. Her medical history was unremarkable otherwise. She did not use tobacco, alcohol or illicit drugs. For about a year she complained about painful, swollen fingers and ankles, and morning stiffness which lasted approximately 1 to 2 hours.

New symptoms began with an upper respiratory tract infection and a high fever. Despite the treatment with phenoxymethylpenicillin, her condition worsened so she was hospitalized in a local hospital. Physical examination revealed cervical, axillary and inguinal lymphadenopathy (approx. 1x1 cm in diameter), mild hepatosplenomegaly and a silent systolic cardiac murmur. Laboratory findings revealed mild pancytopenia. Bone marrow aspiration cytology showed a hypoplasia of all three lines of hematopoietic system. The fever persisted so she was transferred to the Infectious Diseases Unit with the diagnosis being fever of unknown origin (FUO) and pancytopenia for further

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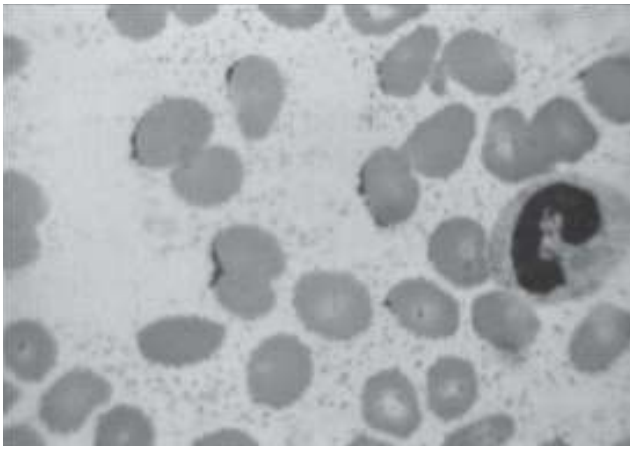
diagnostic procedures and treatment. Upon arrival blood was drawn and the diagnosis of pancytopenia was confirmed. Other routine laboratory findings and serology are also shown in Table 1.

A chest X-ray suggested a possible minor pneumonia, so she was given cephalosporin antibiotics. Another chest X-ray, performed after several days , showed bilateral vascular hili and a pronounced horizontal fissure to the right with no pneumonic infiltrates. All urine and blood cultures were negative. Serological tests for malaria, brucellosis, typhus, tularemia, toxoplasmosis and leishmaniasis were negative as well. Echosonography of the heart showed a minimal pericardial effusion with normal ejection fraction and no morphological pathology of the heart muscle and the valves. During her stay she developed vasculitis-like rash on her lower extremities around ankles. A skin biopsy was performed – perivascular lymphocytes and RBCs were found in the upper dermis and blood vessels were deformed with neutrophil deposits in the deeper dermis. A fine needle aspiration cytology of the cervical and axillary lymph nodes was performed and round, ring shaped cocci, 1-1.5 µm in diameter were found. A similar finding was revealed in a peripheral blood smear, where the same cocci were found on the surface of RBCs and free in the plasma (Figure 1). This finding perplexed the patient's physicians. Because of the positive epidemiological history, veterinarians were consulted and they recognized the cocci as the hemotrophic mycoplasma, so finally they diagnosed hemoplasmosis, zoonosis uncommon in humans.

Figure 1: Hemotrophic mycoplasma on the surface of the RBCs in the peripheral blood smear.



Pancytopenia, hepatosplenomegaly, peripheral lymphadenopathy and bone marrow hypoplasia were all signs of zoonosis. She was treated with tetracyclines for 18 days and there was a significant regression of lymphadenopathy, but her complete blood count and general condition did not get any better. Pancytopenia, intermittent fever, malaise, body weight loss, perimaleolar oedema and a vasculitis skin changes persisted. Positive immunological blood tests

Table 1. Laboratory findings

Laboratory findings	Infectious Diseases Unit	Rheumatology Unit
RBC / x 10^9 /L	3.02	3.8
Hb / g/dL	8.2	10.9
MCV / fl	80	84
WBC / x 10^9 /L	1.7	13.5
Platelets / x 10^9 /L	62	185
ESR	84-94-130	13-27
CRP / mg/L	40	5
Creatinine / µmol/L	Normal	130
Creatinine clearance / mL/min	Normal	48
Aminotransferasis	Normal	Normal
Urine	Proteins +++	Proteinuria/24h 2.4 g/L
Waaler Rose	1:256	Negative
Latex	1:320	Negative
ANA	Positive	Negative
anti-dsDNA	Positive	Negative

RBC – Red blood cells; Hb – Hemoglobin; MCV – Mean corpuscular volume; WBC – White blood cells; ESR - Erythrocyte sedimentation rate; CRP – C reactive protein; ANA – Antinuclear antibodies; anti-dsDNA – anti double stranded DNA antibodies.

aroused the suspicion that the patient may have a systemic disease of the connective tissue, so she was admitted to the Rheumatology Unit for additional diagnostic procedures and treatment. According to the ACR classification, the patient had five criteria (serositis – minimal pleural and pericardial effusions; renal disorder - proteinuria; hematological disorder - anemia, leucopenia, thrombocytopenia and immunological disorder - positive anti-double stranded DNA and antinuclear antibodies) for the diagnosis of systemic lupus erythematosus. Her complement C3 and C4 levels were low as well. Blood transfusions were administered. She received corticosteroids, first intravenously and afterwards orally (1 mg/kg/day). Within a few days, the patient's temperature fell and the complete blood count improved considerably (Table 1). This was an indirect indicator that the pancytopenia was SLE induced. Methyl-prednisolone was slowly tapered to 0.5 mg/kg/day to avoid steroid side-effects. Elevated blood pressure values, reduced diuresis

and persistent hematuria were registered. A diuretic was added. In the meantime there was a relapse of hemoplasmosis, manifested as worsening of lymphadenopathy. The relapse of the zoonosis coincided with the introduction of systemic corticosteroids in the treatment of SLE. She received additional tetracycline antibiotics. Her renal status worsened with proteinuria of 2.4 g/L, reduced creatinine clearance, severe perimaleolar oedema and hypertension. A renal biopsy was performed and mezangioproliferative lupus nephritis with segmental scleroses and membranoprolipherative changes and IgG and C3 complement fraction deposits near a basal membrane were diagnosed (according to the revised classification of the International Society of Nephrology and the Renal Pathology Society for lupus nephritis, these renal biopsy findings satisfy the criteria for class IV-S).[5] The steroid level was once again elevated to 1 mg/kg/day combined with cyclophosphamide (2x50 mg/day) and her general condition improved gradually. Within a few days she was feeling much better and laboratory findings improved as well. She was discharged with the advice of taking methyl-prednisolone 1 mg/kg/day (a 10% dose reduction every 7 days until the maintenance dose reached 20 mg/day) and cyclophosphamide 2x50 mg/day.

A month later she was hospitalized again because of cough and a high fever. Chest X-ray showed an infraclavicular cavern, 6 cm in diameter with a 1 cm thick wall (Figure 2). Bronchoscopy, bronchoalveolar lavage (BAL) and lung biopsy revealed the presence of *Nocardia asteroides* (Figure 3). She was given antibiotic trimethoprim-sulfamethoxazole parenteraly at first and orally afterwards, and within a few months there was a complete regression of the pathological findings on the chest X-ray. Complement levels (C3 and C4) remained lowered. There was no evidence of pancytopenia and polyclonal hypergammaglobulinemia. Under the maintenance therapy SLE was in remission with no signs of hemoplasmosis. Unfortunately the patient stopped coming in for regular check-ups.

DISCUSSION

Hemotrophic mycoplasma, formerly known as *Eperythrozoon* spp., is a small epicellular blood parasite without a cellular wall and is composed of circular, double-stranded DNA which encodes only the genes essential for life. The parasite is found in different species of vertebrates (sheep, goats, pigs, cattle, mice etc.). It attaches loosely to the surface of RBCs and sometimes destroys them but it can also be seen free in the plasma. Hemoplasmas are shown in the blood smear after Giemsa staining. It is most commonly found in pigs and can cause life-threatening anemia, jaundice and reproductive system problems.[6,7] The disease is extremely rare in humans and manifests with fever, swollen lymph nodes, an enlarged spleen and liver, worsening anemia, leucopenia, thrombocytopenia and sometimes mild hepatitis and subclinical myocarditis. A group of Croatian authors described this rare condition in a single human patient 22 years ago when the organism was known as Eperythrozoon.[8] To our knowledge that was the only time the human hemoplasmosis (eperythrozoonosis) was mentioned in medical literature. Cytological aspiration of an enlarged lymph node and peripheral blood smear can reveal typical rings or cocci organisms. Tetracyclines are the drugs of choice.

Figure 2: Tomogram of the infraclavicular cavern (Nocardia asteroides) on the right.

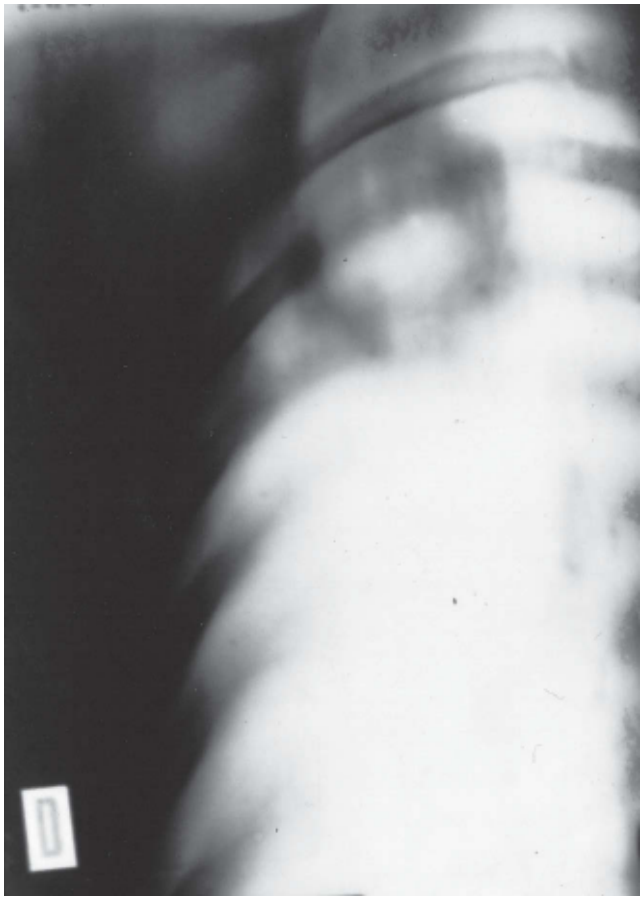
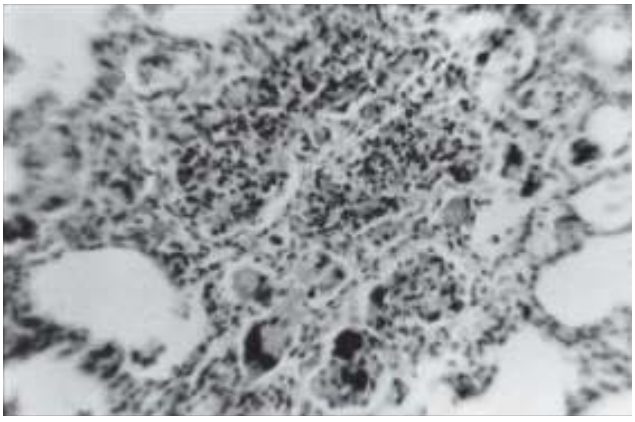


Figure 3: Nocardia asteroides in the lung biopsy.



Over time clinical improvement is seen, a rise in RBCs, WBC, platelets, reticulocyte count and the normalization of liver enzymes.

Hemoplasmas may act as a cofactor in the progression of retroviral, neoplasic and immune-mediated disease.[7] It is possible that the unrecognized initial stage of systemic lupus erythematosus suppressed the immune system of the patient and made her more susceptible to hemoplasmosis.

To our knowledge there has not been a single case of simultaneous hemotrophic mycoplasma infection and systemic lupus erythematosus in medical literature up to now. Because this parasite affects animals, mostly pigs, physicians rarely take into consideration these microorganisms in the differential diagnosis of the lymphadenopathy in humans. The relapse of the hemoplasmosis in our patient coincides with the introduction of systemic glucocorticoids in the treatment of SLE. This can be explained by the steroidal anti-inflammatory but also immunomodifying and a further immunosupressing effect on the immune molecular system.

One of them is *Nocardia asteroides*, a Gram-positive variably acid-fast aerobic bacterium, widely distributed in the environment, also in airborne dust particles, so the most common site of involvement is the lung (81%), followed by the central nervous system (13%).[9] Other sites of brain abscess, retinitis, thyroiditis and diaphragmatic infiltration.[10] A good outcome of treatment with trimethoprim-sulfamethoxazole for pulmonary nocardiosis is showed in SLE patients.[11]

An aggressive approach to immunocompromised patients, quick diagnostic procedures and early empirical therapy are essential principles of clinical management.

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