Systemic Lupus Erythematosus Flared up After Rifampicin During Active Pulmonary Tuberculosis

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The present study describes a systemic lupus erythematous (SLE) flared up after Rifampicin during active pulmonary tuberculosis (TB). A 20-year-old female was hospitalized for cough, weight loss, and apical infiltrates. Microscopy from bronchial lavage confirmed TB. After 1 week of antituberculous treatment we noted diffuse purpura, oral/nasal ulcers, leukopenia, nephritis, antinuclear antibodies, low complement (criteria for SLE). We excluded Rifampicin and introduced immunosuppressive drugs and other reserve antibiotics for TB. Clinical status improved after 2 weeks and TB cured after 9 months. Rifampicin may flare up a subjacent unknown SLE. SLE is a risk factor for TB.

Key words: tuberculosis, Rifampicin, purpura, systemic lupus erythematous

Systemic lupus erythematous (SLE) is a severe autoimmune systemic collagen disease. The lungs are commonly involved later in the evolution thru pleural effusion, interstitial lung disease, diaphragmatic dysfunction, or upper airway dysfunction [1, 2]. The 2012 SLICC (Systemic Lupus International Collaborating Clinic) established the need of a minimum 4 SLE criteria for positive diagnosis (at least one clinical and one immunologic criterion) [3]:

a). Clinical criteria – acute/subacute cutaneous lupus, chronic cutaneous lupus, oral/nasal ulcers, no scarring alopecia, inflammatory synovitis, serositis, renal and neurologic involvement, hemolytic anemia, leukopenia, and thrombocytopenia;

b). Immunologic criteria: antinuclear antibodies ANAs, anti-DNAs, antiphospholipid antibodies, low complement C3, C4, Ch50, positive direct Coombs test.

SLE is a known factor for cellular immunity impairment and thereby it could be an important risk factor for tuberculosis (TB) especially in countries with high TB endemic [4].

Some antituberculous drugs like Rifampicin and Isoniazid may induce lupus (predominantly cutaneous location) or flare up an unknown idiopathic SLE.

If the mentioned above suggestive clinical signs for SLE are associated with TB or occur during TB evolution, we have to actively search the collagen disease.

Experimental part

Materials and methods

Case report upon a patient admitted in the Pulmonology Clinic of the Clinic County Hospital Tg. Mures. Investigations including bronchoscopy and abdominal ultrasound were conducted in our clinic and we have benefited from the rheumatologic consult from the Clinic of the Rheumatology (Emergency Clinic County Hospital Mures). The chest radiography was performed using the X-ray device of the Pulmonology Clinic.

Case report

We present the case of a 20 year-old female (nonsmoker) who came in our clinic for fatigue, dry cough, sweating, low fever, polyartralgia, weight loss (4 kg/1 month) with slow onset. The chest-x-ray revealed inhomogeneous infiltrates in the left upper lobe, suggestive for pulmonary TB (fig 1.).

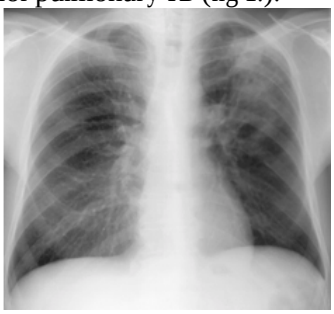

Fig. 1. Chest-x-ray: left upper lobe infiltrative TB

Three induced sputum were negative for Koch bacilli in microscopy thereby we performed bronchoscopy with bronchial lavage/brosages. Acid fast bacilli were positive and later the Lowenstein-Jensen cultures definitely confirmed TB. Bronchial aspirate was negative for nonspecific flora or tumoral cells. Abdominal ultrasound showed an enlarged liver and spleen.

We recommended the standard treatment for TB with Isoniazid, Rifampicin, Pyrazinamide, and Ethambutol. After 1 week-treatment, the patient developed diffuse purpura, oral/nasal ulcers, migraine and malar rush (fig. 2. and 3.).

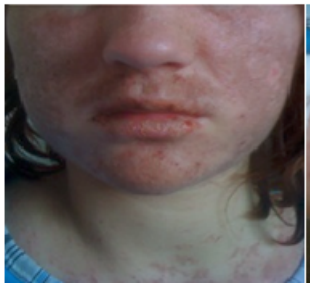

Fig. 2. Face/nose rash and edema, oral ulcers, purpura in the superior thoracic area

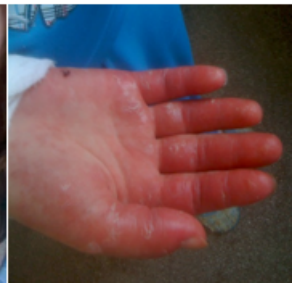

Fig. 3. Erythema and hand oedema by lupus vasculitis

A SLE was confirmed by positive serology: antinuclear antibodies 1:40 (ANAs), positive antibodies to double-stranded DNA (anti-ds DNAs), low Complement C3 - 42mg/dl. The blood tests showed severe anemia (Hb - 7.93g%, Htc - 26.1%), leukopenia (L - 2200 elements/mm^3),

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negative antistreptolysin O and anti HIV antibodies. Urine examination noticed erythrocytes 300/mm^3, proteinuria 0.6 g/24h and a positive Hamburger test (leucocytes 20.280/min, erythrocytes 33.150/min).

We excluded temporarily Isoniazid and for good Rifampicin. The patient received immunosuppressive drugs (metilprednisolon 32mg/day, hydroxychloroquin 400mg/day) and individualized treatment for TB by adding Ofloxacin and Prothionamid.

Clinical status improved after 2 weeks and the patient cured after 9 months of prolonged antituberculous treatment. Isoniazid was introduced under surveillance after 1 month with good tolerance. Treatment for SLE continued alongside with the TB treatment with favorable outcome.

Result and discussions

One of our case particularities was the very slow course of SLE and the final acute onset flared up by Rifampicin with important skin lesions, vasculitis, and nephritis. The symptoms onset after the start of the TB treatment could be interpreted by a drug-induced lupus erythematous (DILE), by side effects to Rifampicin or by really idiopathic SLE.

Identification of the offending agent in a patient taking multiple drugs could be difficult. There are not available precise tests for DILE diagnosis. We excluded both Rifampicin and Isoniazid drugs for the regime. However Isoniazid is considered a relatively low risk drug for DILE [5]. We started the immunologic investigation to reveal possible subjacent collagen disease.

There are similarities but also differences between DILE, side effects to Rifampicin and the really SLE [6]. We found clinical features suggestive for idiopathic SLE flared up by Rifampicin and less common in DILE: renal involvement, skin vasculitis lesions, migraine, leukopenia, hepatosplenomegaly. In the same time the presence of anti-ds DNAs and low C3 is suggestive for idiopathic SLE (not-found in most forms of DILE) [6, 7].

In Romania there is a high TB endemics, so people develop in high proportion primary TB in the childhood whereupon in the presence of immunodepressor factor it may occur the secondary TB episode by endogenic pathogenesis.

On the other hand mycobacteria flare up autoimmune reaction by stressing the antibodies formation in genetically susceptible host due to the failure of mechanisms for self/non-self-discrimination (*heat shock protein* from the mycobacteria) [8] such as active TB is an aggravated factor for an autoimmune disease.

Conclusions

SLE may have a long time, a less symptomatic evolution. Rifampicin may flare up a subjacent SLE thus it starts in an acute way with important symptoms. Our patient was distinguished by clinical vasculitis as main involvement (renal and skin lesions) and hematological manifestation. A major collagen disease like SLE is a risk factor for TB by immunological depression. In the same time TB mycobacteria may be a stress factor for SLE autoantibodies growth and clinical feature acceleration.

Accurate bacteriological confirmation in immunosuppressed patients often requires bronchoscopy. Long time concomitant treatment for TB and SLE healed TB and improved the collagen disease evolution.

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