DI-051:Rifampicin-induced systemic lupus erythematosus

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Background:

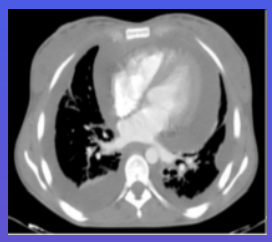
Rifampicin is an antimicrobial agent active against cocci gram positive usually prescribed in prosthetic-joint infections , in combination with other antibiotic. Rifampicin is usually well tolerated, but it can, rarely, induced **systemic lupus erythematosus** (SLE). We report a case of SLE in a man treated since four months by rifampicin for *Enterococcus faecalis* hip prosthetic infection.

Drug-induced SLE (DISLE) represents **10% of all SLE**. DISLE has been reported with over 40 drugs. It is important to diagnose DISLE because stopping the drug allows the disease to be controlled.

Case report:

A 75 years old man was hospitalized in March 2005 for bilateral oligo-arthritis of the inter-phalangeal joints, with pleuro-pericarditis. He has diabetes mellitus with renal insufficiency. **Since four months he was treated for *E. faecalis* infection associated with left hip prosthesis.**
Joint prothesis has been removed.

He was treated with an antibiotic course including **amoxicillin (initially IV followed by 2 g every 6 hours PO) + rifampicin (1200 mg /12 hours).**
At admission his temperature was 38°C.
He had peripheral oedema of the hand and joint swelling. Clinical examination suggested pleural and pericard effusion. Chest tomodensitometry confirmed them. Laboratory tests showed the following :



Hemoglobin (g/dL)	white cell count (G/L)	Platelet count (G/L)	creatinine (mmol/L)	Creatinine clearance (mL/min)	Sedimentation rate /C-reactive proteine (mg/L)
10.2	4.41	233	300	20	92/89
Antinuclear antibody (ANA) (indirect immunofluorescence on HEp2 cells)	double-stranded DNA antibodies (normal < 75 UI, Elisa)	Antihistone antibodies (normal < 20 kU/L)	Anti-ENA (extractable nuclear antigens) antibodies	rheumatoid factor	antineutrophil cytoplasmic antibody
1/1280 with homogeneous pattern	177 UI	52 kU/L	negative	negative	negative

Pleural and pericardial fluid analysis revealed lymphocytic and exudative effusion without neither microbial agent nor neoplastic cells. Mycobacterium tuberculosis was absent by PCR and culture.

Rifampicin induced SLE was diagnosed. Rifampicin was stopped. The patient underwent pericardial window for the treatment of effusion. Corticosteroid were used for the systemic signs (arthralgia and pleuro-pericardis, 0.5 mg/kg body weight oral prednisone) and were stopped 6 months later. In October 2006 patient was free of symptom.

Discussion:

Rifampicin is a **well tolered** antibiotic.

-The main problem in clinical practice => **Drug-drug interactions**
- The most adverse events: **nausea, vomiting and hypertransaminasemia**
- Only few cases of rifampicin-induced SLE have been reported in the literature

Clinical and laboratory features are similar in DISLE than in idiopathic SLE, **but patients fully recover after the offending medication is discontinued**.

Mechanisms of DISLE are complex and different from one drug to another. Several mechanisms for induction of autoimmunity will be possible.

⇒ **Oxidative metabolites of the drug compound trigger autoimmunity**

⇒ **Drug can act as hapten to form stable complexe to stimulate T lymphocytes**.

⇒ Cytotoxicity of drug, or drug metabolite, can release autoantigens and drug metabolite can disrupt central immune tolerance.

	Characteristics of DISLE
	- **no sex difference** whereas in the SLE a female prevalence exists -**HLA-DR4 allele, and slow acetylator phenotype** are two group of genetic factor associated with the DISLE
Characte-ristic symptoms	-**Arthalgia and myalgia**: 50 to 90%, are often the only clinical symptom - **fever, pleurisis and pericarditis** -Analyze of pleural or synovial fluid: the findings are **similar to those in SLE** -**ANA**: positive in up to 90% of DISLE, with homogenous pattern -**Antihistone antibodies**: positive in 75 to 95% of the DISLE, while they are found only in 20% of idiopathic SLE - Complement levels in DISLE: normal
Rare symptoms	-skin involvement, mucosal ulcers, lymphadenopathy and Raynaud's phenomenon: less frequent in DISLE, compared to idiopathic SLE -renal and hematologic involvements: usually absent

Our patient satisfied the criteria for DISLE

-presence of **at least one clinical symptom** of idiopathic SLE with **positive lupus serology**
-rifampicin was administrated over **an appropriate period of time**: roughly from 3 weeks to 2 years before development of symptom
-clinical signs promptly improved **after discontinuation** of rifampicin

Conclusion:

In the litterature there is no predictors for the occurrence of DISLE. It is important to know that rifampicin can induced SLE. When DISLE is suspect, it is necessary to measure **ANA and antihistone antibody** to confirm the diagnostic and to promptly stop the treatment.