


Caso Cerrado



Antecedentes Personales

- Varón de 23 años sin AP de interés
 - Residente en provincia de Barcelona
 - Hace 2 años diagnosticado de LES
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ARA Criteria for Diagnosis of Systemic Lupus Erythematosus

Criterion	Definition
Malar rash	Fixed erythema, flat or raised, over the malar eminences, tending to spare the nasolabial folds
Discoid rash	Erythematous raised patches with adherent keratotic scaling and follicular plugging; atrophic scarring may occur in older lesions
Photosensitivity	Skin rash as a result of unusual reaction to sun-light, by patient history or physician observation
Oral ulcers	Oral or nasopharyngeal ulceration, usually painless, observed by a physician
Arthritis	Nonerosive arthritis involving 2 or more peripheral joints, characterized by tenderness, swelling, or effusion
Serositis	Pleuritis – convincing history of pleuritic pain or rub heard by a physician or evidence of pleural effusion OR Pericarditis – documented by EKG, rub or evidence of pericardial effusion
Renal disorder	Persistent proteinuria greater than 0.5 grams per day or greater than 3+ if quantitation not performed OR Cellular casts – may be red cell, hemoglobin, granular, tubular, or mixed
Neurologic disorder	Seizures OR psychosis – in the absence of offending drugs or known metabolic derangements (uremia, ketoacidosis, or electrolyte imbalance)
Hematologic disorder	Hemolytic anemia – with reticulocytosis OR Leukopenia – less than 4,000/mm ³ total on two or more occasions OR Lymphopenia – less than 1,500/mm ³ on two or more occasions OR Thrombocytopenia – less than 100,000/mm ³ in the absence of offending drugs
Immunologic disorders	Positive antiphospholipid antibody OR Anti-DNA – antibody to native DNA in abnormal titer OR Anti-Sm – presence of antibody to Sm nuclear antigen OR False positive serologic test for syphilis known to be positive for at least six months and confirmed by Treponema pallidum immobilization or fluorescent treponemal antibody absorption test
Antinuclear antibody	An abnormal titer of antinuclear antibody by immuno fluorescence or an equivalent assay at any point in time and in the absence of drugs known to be associated with "drug-induced lupus" syndrome


Historia Actual

- Al mes: fiebre 39° con sudoración
- SE
 - Hb 8,6 VCM 85
 - Leu 1800 (26S 70L 2E 2M)
 - PQ 52.000
 - VSG 90
- BQ
 - Prot 75g/l gammaglobulinas 40g/l policlonal

Historia Actual

- ANA: Neg
 - HC y UC: Neg
 - Rx: Pinzamiento SCF I
 - Prednisona 90mg/d
 - Desaparece Fiebre. Persiste Pancitopenia
- 


2º Episodio

- Febrícula
 - Anti-DNA: Positivo (11 frente a 178)
 - ANA, Anti-RNP, anti-Sm: Neg
 - Azatioprina 150mg/d
- 


3^{er} Episodio

- Fiebre alta, MEG, **Dolor perianal**
- **Esplenomegalia** 4cm
- Región perianal: zona eritematosa, indurada, y muy dolorosa. No fluctua
- Más anemia, leucopenia, trombopenia
- Hipergammaglobulinemia policlonal
- OE: Normal

3^{er} Episodio

- Se suspendió Inmunosupresión
 - Se pautó: Piperacilina, Gentamicina, Metronidazol
 - HC, punción perianal: Pseudomona
 - 5d febril
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Diagnóstico diferencial

1. Brote de LES
 2. Patología relacionada con LES
 3. Patología independiente del LES
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Frequency of Symptoms of Systemic Lupus Erythematosus†

Symptoms	Percent at onset	Percent at anytime
Fatigue	50	74-100
Fever	36	40-80+
Weight loss	21	44-60+
Arthritis or arthralgia	62-67	83-95
Skin	73	80-91
Butterfly rash	28-38	48-54
Photosensitivity	29	41-60
Mucous membrane lesion	10-21	27-52
Alopecia	32	18-71
Raynaud's phenomenon	17-33	22-71
Purpura	10	15-34
Urticaria	1	4-8
Renal	16-38	34-73
Nephrosis	5	11-18
Gastrointestinal	18	38-44
Pulmonary	2-12	24-98
Pleurisy	17	30-45
Effusion		24
Pneumonia		29
Cardiac	15	20-46
Pericarditis	8	8-48
Murmurs		23
ECG changes		34-70
Lymphadenopathy	7-16	21-50
Splenomegaly	5	9-20
Hepatomegaly	2	7-25
Central nervous system	12-21	25-75
Functional		Most
Psychosis	1	5-52
Convulsions	0.5	2-20

Brote de LES

Anemia	70%
Leucopenia	65%
Trombocitopenia	15%

† Adapted from Von Feldt, JM, Postgrad Med 1995; 97:79.

Brote

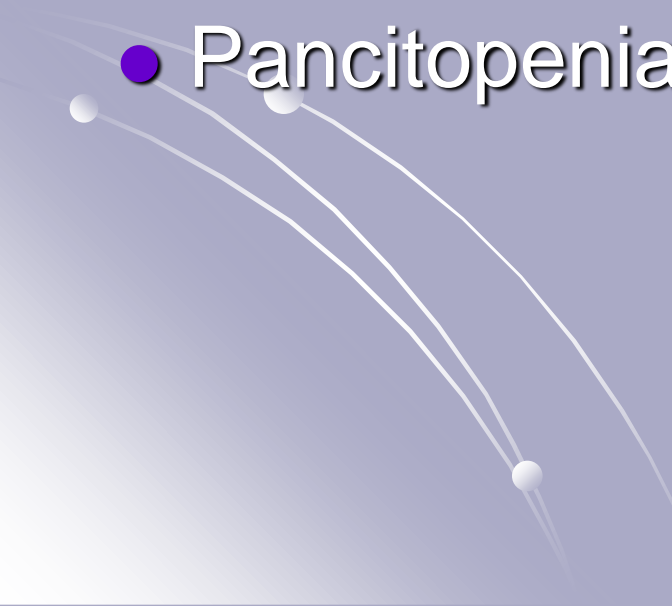
- Anticuerpos Negativos
- No derrame
- 50% de fiebre por brote
- Leucopenia más moderada
 - 4500 en 50% de los pacientes
 - 4000 en 15% de los pacientes
 - Linfopenia
- Trombopenia
 - Moderada 25-50%
 - 50000 10%

Brote

- Parcial respuesta a tratamiento
- Perspectiva del tiempo



Búsqueda

- Esplenomegalia + Fiebre
 - Pancitopenia + Fiebre
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Causas de Esplenomegalia

- Secuestro de hematíes (Esferocitocis o Anemia hemolítica)
- **Proliferación por enfermedad crónica (LES, AR, endocarditis, malaria, sarcoidosis)**
- Depósitos de lípidos (Gaucher)
- Congestivo: Hematomas, Cirrosis, ICC
- **Invasión granulomatosa o maligna (TBC, LLC, Tricoleucemia)**

Esplenomegalia

- Enfermedad Hepática 33%
- **Procesos hematológicos malignos 27%**
(Linfomas)
- **Infecciones 23%**
- Congestivo 8%
- Enfermedad esplénica 4%
- Otras 5%

Esplenomegalia masiva

- Polo inferior en pelvis o pase línea media
 - Gaucher
 - Talasemia
 - Linfoma
 - Mielofibrosis
 - VIH + MAI
 - Malaria
 - Kala-azar


Esplenomegalia, fiebre en este caso

- Proliferación por enfermedad crónica (LES, AR, Endocarditis, malaria, Sarcoidosis)
- Invasión maligna (mielofibrosis, LLC, Tricoleucemia)
- Infecciosa (TBC, Leishmania, Malaria)
- Hemofagocítico

Pancitopenia

- C3ngenita
- Invasi3n MO
 - Leucemia
 - Linfoma
 - Tricoleucemia
 - Cancer
 - Fibrosis
- Mielodispl3sicos
- Megalobl3stica
- Infeccioso
 - VIH, Parvovirus B19
 - Hemofagoc3tico por virus
- Hemoglobinuria Parox3stica nocturna

Diagnóstico Diferencial

- Actividad crónica (LES)
 - Enfermedades hematológicas malignas
 - Infecciones
 - TBC
 - Leishmania
 - Leptospira
 - Síndrome hemofagocítico
- 

S. Hemofagocítico

● Infecciones

- VEB
- VIH
- CMV
- VVZ
- VHS-8
- VIH
- Parvovirus
- Coxiella

● Autoinmunes

- LES
- AR
- Still
- Sarcoidosis
- E.Mixta del Tej.Con
- Esclerosis sistémica
- Sjögren

- Transplante renal o hepático
- Leucemias o linfomas

S. Hemofagocítico

- Clínica:
 - Fiebre 91%
 - Hepatomegalia 90%
 - Esplenomegalia 81%
 - Síntomas neurológicos 47%
 - Rash 41%
 - Linfadenopatías 42%
- No da hipergammaglobulinemia
- VSG Normal

S. Hemofagocítico

Diagnostic Criteria for Hemophagocytic Lymphohistiocytosis (HLH)[†]

Major criteria:

- (1) Fever:** Peak temperature $>38.5^{\circ}\text{C}$ for seven or more days
- (2) Splenomegaly:** Spleen palpated >3 cm below the left costal margin
- (3) Cytopenia involving two or more cell lines:**
Hemoglobin <9.0 g/dL, **or**
Platelets $<100,000/\mu\text{L}$, **or**
Absolute neutrophil count $<1,000/\mu\text{L}$
- (4) Hypertriglyceridemia or hypofibrinogenemia:**
Fasting triglycerides >2.0 mmol/L, or more than 3 standard deviations (SD) above the normal value for age, **or**
Fibrinogen <1.5 g/L, or more than 3 SD below the normal value for age
- (5) Hemophagocytosis:** Demonstrated in bone marrow, spleen, or lymph node
No evidence for malignancy. (See comments in text)

Alternative criteria:

- (a) Low or absent natural killer (NK) cell activity**
- (b) Serum ferritin level >500 $\mu\text{g/L}$**
- (c) Soluble CD25 (sIL-2 receptor) >2400 U/mL**

Diagnosis:

The diagnosis of HLH requires the presence of all five major criteria. Either criterion (a) or a combination of criteria (b) and (c) may substitute for one of the major criteria. If a patient meets only four criteria and the clinical suspicion for HLH is high, one must initiate appropriate treatment, as delays may be fatal.

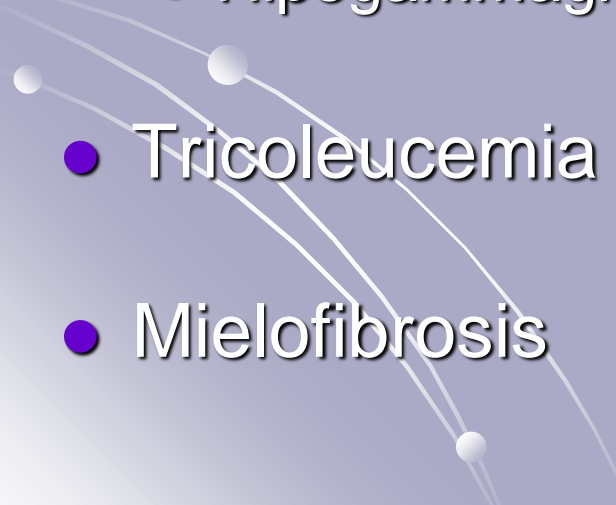
In the appropriate clinical setting, the diagnosis is justified by a positive family history of HLH; parental consanguinity is only suggestive of HLH.

[†]Adapted from Henter JI, et al. Semin Oncol 1991; 18:29.

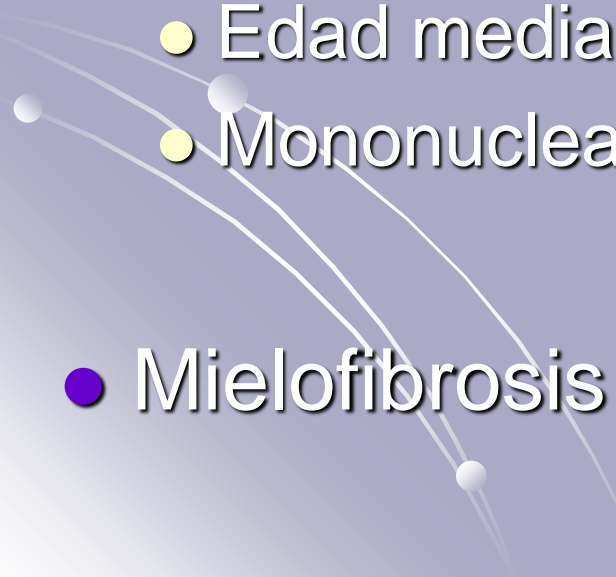
Enf. Hematológicas

- Linfoma no-Hodgkin
 - Tricoleucemia
 - Mielofibrosis
- 


Enf. Hematológicas

- Linfoma no-Hodgkin
 - 4 veces más frec
 - 2/3 tienen adenopatías (los indolentes menos)
 - Derrame pleural
 - Pancitopenia como debut
 - No linfocitosis
 - Hipogammaglobulinemia
 - Tricoleucemia
 - Mielofibrosis
- 


Enf. Hematológicas

- Linfoma no-Hodgkin
 - Tricoleucemia
 - 2% de leucemias
 - Edad media 52a
 - Mononucleares en frotis
 - Mielofibrosis
- 


Enf. Hematológicas

- Linfoma no-Hodgkin (4 veces más frec)
 - Tricoleucemia
 - Mielofibrosis
 - Esplenomegalia de 12-15cm
 - Edad media 60a
- 

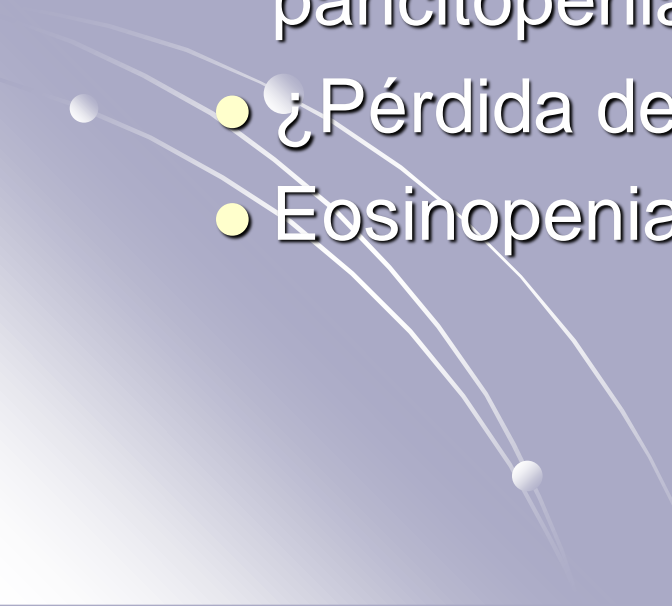
Infeciosas

- Leptospira
 - Suele tener mialgias, cefalea
 - No pancitopenia
 - Suele tener alteradas: OE, CPK, Transas, Na
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Infeciosas

- TBC
 - Múltiples Zhiel neg
 - Mantoux
 - Miliar. Más afectación hepática
- 

Infeciosas

- Leishmaniasis visceral
 - Cuenca mediterránea
 - Hipergammaglobulinemia, fiebre, pancitopenia, organomegalia
 - ¿Pérdida de peso?
 - Eosinopenia
- 

Diagnóstico

- Linfoma no-Hodgkin
- Leishmania

**BIOPSIA DE
MÉDULA
ÓSEA**