

France : an ageing country with ageing infection

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France

- Mr C 71 year-old, Martiniquan
- Past Medical history : Tolosa Hunt Syndrome treated with Anti-TNF α
 - Positive IDR : Isoniazid+ Rifampicin prophylaxis
- History of Presenting complaint : Fever during 1 month (8 months after the onset of anti TNF α therapy)

Initial presentation

- Temperature : 40°C
- No urinary or pulmonary or gastrointestinal symptoms.
- Clinical examination revealed an isolated hepatosplenomegaly

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Blood results :

- Na 146 mmol/l, K 4,3 mmol/l
- Urea 26 mmol/l creatinine 268 µmol/l
- AST 74 UI/L, ALT 32 UI/L, ALP 278 UI/L, GGT 264 UI/L
- Hb 9,6 g/dl, MCV 76, Platelet 51 G/L
Leucocyte 0,3 G/L
- TP 98%, ratio TCA 1,1

Initial presentation



Main hypotheses



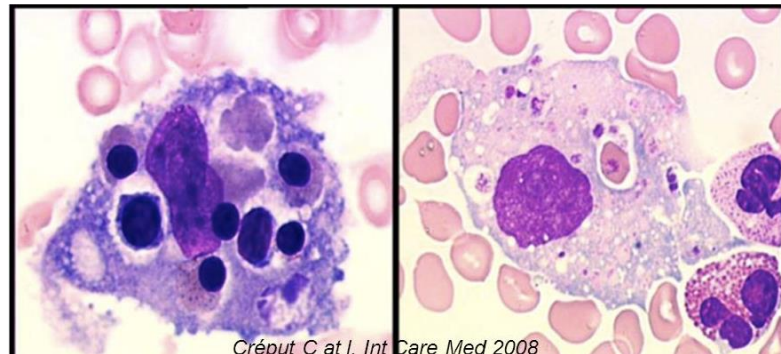
Main hypotheses

- Hemophagocytic Lymphohistiocytosis (HLH)
- Subacute Endocarditis



Further investigation

- Infection : CBU, hemoculture, Echocardiogram, CT scan
 - No infection
- HLH : TG 2,7 g/L, ferritin 4000 $\mu\text{g/l}$, fibrinogen 2,4 g/l
 - myelogram : hemophagocytosis
 - H Score 317



Diagnosis method for HLH

Table 4. The HScore

Parameter	No. of points (criteria for scoring)
Known underlying immunosuppression*	0 (no) or 18 (yes)
Temperature (°C)	0 (<38.4), 33 (38.4–39.4), or 49 (>39.4)
Organomegaly	0 (no), 23 (hepatomegaly or splenomegaly), or 38 (hepatomegaly and splenomegaly)
No. of cytopenias†	0 (1 lineage), 24 (2 lineages), or 34 (3 lineages)
Ferritin (ng/ml)	0 (<2,000), 35 (2,000–6,000), or 50 (>6,000)
Triglyceride (mmoles/liter)	0 (<1.5), 44 (1.5–4), or 64 (>4)
Fibrinogen (gm/liter)	0 (>2.5) or 30 (≤2.5)
Serum glutamic oxaloacetic transaminase (IU/liter)	0 (<30) or 19 (≥30)
Hemophagocytosis features on bone marrow aspirate	0 (no) or 35 (yes)

If HScore > 169, HLH Diagnosis : Se = 93% and Spe = 86%

Etiology of HLH

- Infectious :
 - Negative Influenzae PCR , HBV-, HCV-, HIV -, EBV-, HSV-, Parvo B19 serologies, HHV6-, HHV8-, EBV- PCR
 - Negative Rickettsi- and Coxiella-, Chlamydia trachomatis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Bartonella serologies, legionella antigenuria, Koch bacillus sputum/urinary
 - Negative Anguillulose (Strongyloidiasis) antigens
- Immunology :
 - Negative ANA, ANCA, increased complement, ACE
- Haematology :
 - Negative Leukocyte immunophenotyping
 - PET scan : rate and liver hyperfixation
 - Bone Marrow : no evidence of lymphoma or Castelman

Clinical Course

- Clinically worsening with
 - Confusion
 - Dyspnea
 - Pancytopenia
 - Hemostasis



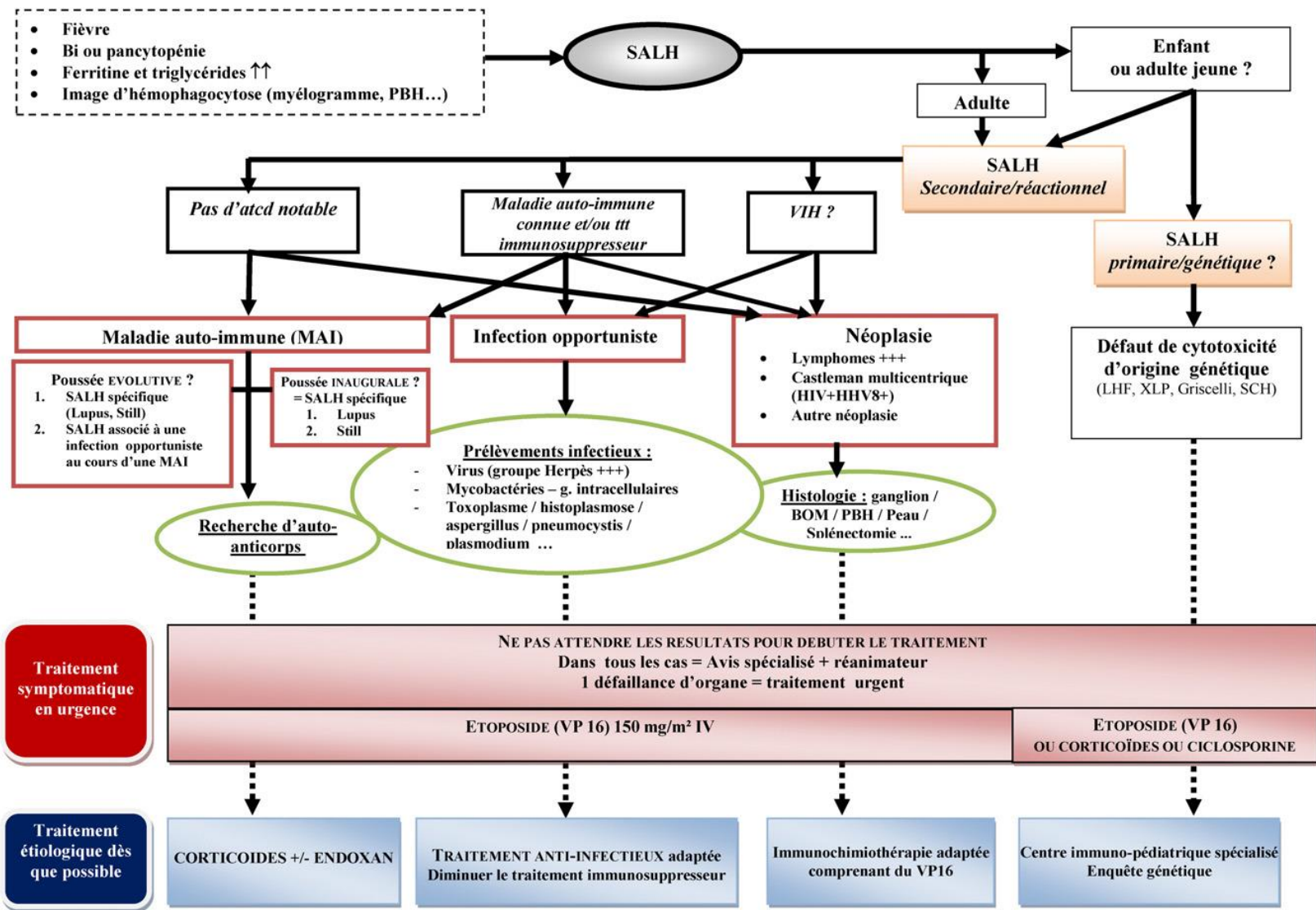
Treatment?

Clinical Course

- Clinically worsening with
 - Confusion
 - Dyspnea
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 - Hemostasis

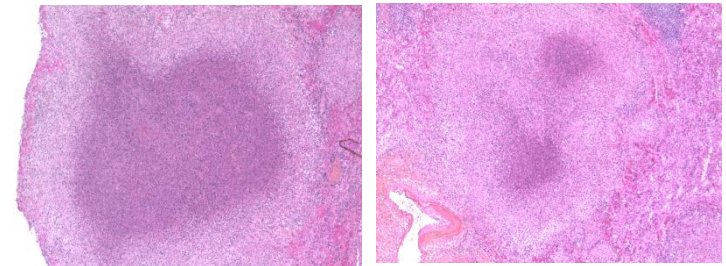


Etoposide (VP 16)



New Investigation

- Liver biopsy :
 - Histology : HLH and granuloma formation without caseum area
 - No evidence of an infection (negative mycological and bacteriological Culture (with leishmanie), Koch bacillus PCR, EBV PCR, HHV8 PCR)
 - No B or T cell clone
- Splenectomy
 - Histology : caseating granuloma
 - Koch bacillus +



Treatment

- Isoniazid (5 mg/kg) + Rifampicin 10 mg/kg+ Ethambutol (15 mg/kg) + Pyrazinamide (20 mg/kg)
 - + B6 vitamin supplementation
- Vaccination after splenectomy:
 - Haemophilus, meningococcus ACYW135, pneumococcus
- Amoxicillin post splenectomy

Key learning points

- Biotherapy
 - Infection risk
 - Indeed prophylaxis
- Non invasive test :
 - expansive tools
 - Could be negative
- Splenectomy :
 - Invasive test
 - Should be realized without delay if the first result were negative

In France, we're not Chauvinist

