Current therapeutics for visceral leischmaniasis

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Intoduction

- The visceral leischmaniasis is an anthropozoonose caused by a protozoar, the *Leishmania infantum*
- The VL rages in Tunisia under its Mediterranean shape
- The declared children come from farming regions and modest environment
- Yearly impact : 100 – 150 cases/year
- Mortality regressed thanks to the present treatment

- 30 to 40 cases / year
- Elevated impact after the season of rain
- Delay of diagnosis: 30 days
- Splenomegaly (99%), constant fever, paleness
- Hypotrophy (57,4%)

- Anemia:
  - < 9 g/100 ml (90,9%)
  - < 6 g/100 ml (40%)
- Diagnosis gotten thanks to the puncture of the bone marrow, and blood serology
- Treatement: *Glucantime* in IM
- Evolution:
  - Favorable
  - Mortality: 5%
  - No mortality registred during the last five years
  - 3 cases of resistance in 20 years

The antimony and the antimony derivates

- The two antimonies used: N-methyl-glucantime (glucantime*), and the stibiogluconate of sodium (pentostam*)
- The glucantime is presented in bulbs of 5 ml, or 1500 mg and its concentration in antimony is of 85 mg/ml
- The glucantime acts on the synthesis of the ATP at the time of the bioenergetic metabolisms.

- **Glucantime:**
  - 90 mg/Kg/ml in intramuscular way, during 21 days, 3 times per day
- **1st protocol:**
  - 60 mg/Kg/day, during 15 days (2 cures occasional of 15 days)
- **Resistance:** 3 cases
- **Relapse:** 3 cases

Resistance to the glucantime: 3 cases

	Product	Clinical state at the end of ttt	Biology at the end of ttt	Treatement after	Evolution
1st case	Glucantime 60 mg/kg/day	SMG w/aw= 84% No fever after 5 days	wc= 4000 Hb=10g/dl Pl=23500	Glucantime 90 mg/kg/day, 21 days	recovery
2nd case	Glucantime 80 mg/kg/day	SMG w/aw= 84% No fever after 8 days	wc=4400 Hb= 7g/dl Pl= 154000	Amphotericin B	recovery
3rd case	Glucantime 60 mg/kg/day	SMG w/aw= 72% No fever after 8 days	wc= 5000 Hb= 7g/dl	Amphotericin B	recovery

Relapse: 3 cases

	Treatement receved	Clinical evolution after ttt	Biological evolution after ttt	Relapse
1st case	Glucantime 70 mg/kg/day 15 days	SMG No more fever after 3 days	wc= 7400 Hb= 9,6g/dl Pl=279000	SMG Fever pancytopenia
2nd case	Glucantime 60 mg/kg/day 15 days	SMG= 0 No more fever after 4 days	wc= 14100 Hb= 9,5g/dl	SMG Fever pancytopenia
3rd case	Glucantime 60 mg/kg/day 15 days	SMG= 0 No more fever after 7 days	wc= 6300 Hb= 10g/dl Pl=250000	SMG Fever pancytopenia

The diamidines

- Isethionate of pentamidine (l*omidine**) can be indicated in the different shapes of leischmaniasis
- Some resistance is frequently described
- The dose is from 3 to 4 mg/kg every 2 days
- Secondary effects: alteration of the renal function, hematological desorders, cardiovascular unrests (unrests of the rythm)

In case of relapse or resistance to the treatement by glucantime, the WHO recommends a treatement by the antimony in the same posology, but of double length (6 weeks). In case of new failure,the pentamidine becomes useful during a period adapted to its tolerance

Amphotericin B

- The efficiency of the amphotericin B in the treatement of the LV is recognised throughout the endemic regions, at the dose of

  1 mg/kg/day during 21 to 28 days
- Its renal toxicity limits its use
- Ambisome (liposomal form)
- The protocol of 6 injections limits the cost related to hospitalisation

Other therapeutics

- **Allopurinol** (Zyloric*):
  - Hypourecemic activity
  - Its action against the protozoar has been recognised at the end of the 1970's
- In our set, 20 children received the glucantime associated to zyloric (no superority compared to glucantime in monotherapy)

Immunotherapy

Other therapeutics

- **The miltefosin** is the first therapeutic against leishmaniasis which can be used orally

- It healed 95% of the patients treated during the clinical tests.

Conclusion

- The treatement of visceral leischmaniasis in the mediterranean countries is not uniform
- The pentavalent antimonies are used at the dose of 20mg/kg/day in IM during 21 days
- Exellent results
- Association: antimony + zyloric➔ no superiority compared to antimonies used only
- Amphotericin B liposomale (ambisome*): 3mg/kg/day
- In case of relapse or resistance, a 2nd cure of 28 days with glucantime is prescribed