Clinico-microbial correlation in 95 patients with SPPT / PTLDS.

Dr Muriel Manant-Blanc

- Emergency ward, University Hospital of Besançon, France

Prof. Christian Perronne, MD, PhD

- Infectious and Tropical Diseases

- University Hospital Raymond Poincaré, Garches

- Greater Paris University Hospitals

- University of Versailles – Paris Saclay

Patients and Methods

- Open-label prospective study

- 95 patients with SPPT: persistent polymorphic syndrome after a possible tick-bite), close to PTLDS

- All the patients were followed by only one physician (**Dr Muriel Manant-Blanc**)

- Two year follow-up: December 2017 to December 2019

- Microbial diagnosis was made with serologies and PCRs (ADNucleis technique, Prof. Michel Franck, Lyon, France)

- A clinical questionnaire was filled by the physician during consultation

Questionnaire. Items with a severity score, graded from 0 (no sign or symptom) to 5 (maximum intensity):

- Asthenia, weight variations

- Fever, chills, hot flushes, alternating hot/cold feeling

- Abdominal pain, digestive transit disorders

- Dyspnea, cough, oedema

- Palpitations

- Joint pain, myalgias, fasciculations,

- Intervertebral dysfunction (first or second degree)

- Cephalalgias, concentration problems

- Neuropathic pain, vertigo, visual disorders, hearing impairment

- Episodes of anger, sadness/depression

- Sleeping disorders, craving for food

- Capillary microcirculation disorders

Intervertebral dysfunction

• Osteopathic medicine:

A musculoskeletal disturbance that can be detected with manual palpation and corrected with manipulation

Questionnaire. Other items only noted present or absent:

- Nail mycosis

- Chronic rhinitis/sinusitis

- Thrombocytopenia

- Cardiovascular events

- Cancer

- Erythema migrans

- Red striae, dermographism, cutaneous erythema

- Night sweats

Biological tests

- **Serologies for:**

  – *Babesia, Candida , Ehrlichia, Rickettsia, Bartonella, Coxiella, Francisella, Mycoplasma pneumoniae, Chlamydia pneumoniae.*

- **PCRs:**

  – Realized by ADNucleis lab in Lyon, France or Espacelab in Geneva, Switzerland.

  – Wide spectrum PCRs on samples from **venous blood**, **capillary blood, urine** and **saliva**.

Results

- **Mean age: 46 years (7 to 75)**

- **Mean duration of the disease: 8 years (1 to 35)**

- **Mean number of signs or symptoms per patient: 22/35**

- **Mean number of micro-organisms per patient: 2.8 (1 to 7)**

Most frequent crypto-infections identified in 95 patients

- *Babesia*:   39 (41.1%)
- *Theileria*:   16 (16.8%)

- *Candida*:   47 (49.5%)

- *Mycoplasma*:   62 (65.3%)
- *Borrelia*:   29 (30.5%)
- *Rickettsia*:   24 (25.3%)
- *Bartonella*:   22 (23.2%)
- *Ehrlichia*:   21 (22.1%)

Less frequent crypto-infections identified in 95 patients

- *Chlamydia*:   6 (6.3%)

- *Coxiella*:   2 (2.1%)

- *Anaplasma*:   2 (2.1%)

- *Francisella*:   1 (1.1%)

- *Neoehrlichia mikurensis*:   1 (1.1%)

- CMV: 2 (2.1%)

- West Nile virus: 1 (1.1%)

Mean scores (1)

5 = maximum intensity

- **Asthenia:** 4.5

- **Abdominal pain:** 2.9

- **Weight variation:** 2.3

- **Hot flushes:** 1.9

- **Alternating hot/cold feeling:** 1.9

- **Oedema:** 1.8

- **Fever:** 0.8

Mean scores (2)

- **Intervertebral dysfunction (first degree):**   **4.95**
- **Muscular pain:**   **4.2**
- **Joint pain:**   **4.1**
- **Troubles du transit :**   **3.4**
- **Dyspnea/cough:**   **2.9**
- **Intervertebral dysfunction (second degree):**   **2.7**
- **Palpitations:**   **1.4**

Mean scores (3)

- **Cephalalgias:**   3.9
- **Concentration problems:**   3.7
- **Sadness/depression:**   3.2
- **Vertigo:**   3
- **Fasciculations:**   2.6
- **Craving for food:**   2.5
- **Capillary microcirculation disorders:** 2.5
- **Anger:**   2.4
- **Hearing impairment:**   2.2
- **Visual disorders:**   1.8
- **Neuropathic pain:**   1.06

Frequency of other signs and symptoms

- **Night sweats:**   **48 %**
- **Nail mycosis:**   **48 %**
- **Thrombocytopenia:**   **44 %**
- **Chronic rhinitis/sinusitis:**   **25 %**
- **Red striae, dermographism, erythema:**   **18 %**
- **Cardiovascular events:**   **10 %**
- **Erythema migrans:**   **7 %**
- **Cancer:**   **7 %**

Correlation of clinical pattern, involved micro-organism, age of the patient and duration of the syndrome

Statistical analysis by linear least-square regression method

Threshold of significance : p<0.01

Intensity and number of signs and symptoms, correlation with co-infections and the duration

❖ **Number of identified micro-organisms (co-infections)**

  ❖ **Intensity of signs and symptoms: $p<0.0006$**

  ❖ **Number of signs and symptoms: $p<5 \times 10^{-5}$**

❖ **Duration of the syndrome**

  ❖ **Intensity of signs and symptoms: $p<5 \times 10^{-5}$**

  ❖ **Number of signs and symptoms: $p<0.001$**

Signs and symptoms

❖ **Correlation with the duration of the syndrome and with a specific micro-organism**

- ❖ **Chills, p<0.01** (*Babesia*, p<0.0005)
- ❖ **Hearing impairment, p<0.01** (*Ehrlichia*, p<0.001)
- ❖ **Neuropathic pain, p<0.003** (*Borrelia*, p<0.001)
- ❖ **Intervertebral dysfunction (second degree), p<0.0007** (*Theileria*, p<0.002)

❖ **Correlation with the duration of the syndrome alone**

- ❖ **Palpitations, p<0.0005**
- ❖ **Sleeping disorders, p<0.002**
- ❖ **Weight variations, p<0.01**

Correlation of the age of the patient with some specific signs or symptoms

- **Abdominal pain, p<0.009**
  - Younger the patient, higher the pain

- **Intervertebral dysfunction (first degree), p<0.003**
  - Older the patient, more frequent the dysfunction

Correlation of thermic disorders with some specific micro-organisms

- **Fever:**
  - *Babesia*, p<0.01
- **Chills:**
  - *Babesia*, p<0.0005   (Duration, p<0.01)
- **Alternating hot/cold feeling:**
  - *Babesia,* $p < 1 \times 10^{-8}$
  - *Theileria,* p<0.03, NS
  - *Borrelia*, p<0.02, NS
- **Night sweats:**
  - *Babesia*, $p < 3 \times 10^{-9}$
  - *Theileria*, p<0.008

. *Babesia*

- Fever, p<0.01

- Chills, p<0.0005   (Duration, p<0.01)

- Alternating hot/cold feeling, p<1×10^{-8} (*Theileria*, p<0.03,
  NS   *Borrelia*, p<0.02, NS)

- Night sweats, p< 3×10^{-9} (*Theileria*, p<0.008)

- Dyspnea/cough, p<0.0008

- Vertigo, p<0.0009   (*Mycoplasma*,
  p<0.002)

- Episodes of anger, p<0.0005   (*Borrelia*, p< 0.01)

- Fasciculations, p<0.01

- Cephalalgia, p<0.01   (*Borrelia*, p<0.01)

- Thrombocytopenia, p<0.01

Mycoplasma

- Vertigo, p<0.002   (*Babesia*, p<0.0009)

Borrelia

- **Erythema migrans,** $\quad$ **p<1.10^{-5}**

- **Alternating hot/cold feeling: p<0.02** $\quad$ (*Babesia*, p<1x10^{-8}; *Theileria*, p<0.03, NS)

- **Cephalalgia:** $\quad$ **p<0.01** $\quad$ (*Babesia*, p<0.01)

- **Episodes of anger:** $\quad$ **p<0.01** $\quad$ (*Babesia*, p<0.0005)

- **Visual disorders:** $\quad$ **p<0.02, NS**

- **Neuropathic pain:** $\quad$ **p<0.001 (Duration, p<0.003)**

Ehrlichia

- **Hearing impairment, p<0.001   (Duration, p<0.01)**

Theileria

- **Night sweats, $p < 0.008$ (*Babesia*, $p < 3 \times 10^{-9}$)**

- **Alternating hot/cold feeling, $p < 0.03$, NS (*Babesia*, $p < 1 \times 10^{-8}$; *Borrelia*, $p < 0.02$, NS)**

- **Intervertebral dysfunction (second degree), $p < 0.002$ (Duration , $p < 0.0007$)**

- **Episodes of sadness/depression, $p < 0.01$ (Duration $p < 0.004$)**

- **Capillary microcirculation disorders, $p < 0.0006$ (Duration, $p < 0.007$)**

Bartonella

- Red striae, dermographism, cutaneous erythema, $p<2.5\text{x}10^{-5}$

- Chronic sinusitis, $p<0.008$

Candida

- **Craving for food, p<0.007**

Conclusion
SPPT / PTLDS

- *Serologies: interest for some micro-organisms*

- *PCRs: interest to:*
  - *Search a wide range of micro-organisms*
  - *Take samples from several matrices (venous blood, capillary blood, urine and saliva)*

- *An accurate microbial diagnosis may allow correlations with some signs and symptoms*