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MALIGNANT RHODESIAN TRYPANOSOMIASIS

by

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Summary — Rhodesian trypanosomiasis has become a new and serious problem in the field of imported diseases. Massive trypanosome infections are observed in « non-salted » tourists and sportsmen after a visit or a hunting party in the Parks and hunting-grounds of East, Central and Southern Africa.

The course of the disease is so critical that this trypanosomiasis has become an urgency of the same kind as the West-African falciparum primo-infection. If it is almost impossible to miss the trypanosomes in the blood-smear, the specific treatment needs to be planned very carefully and individually in order to avoid disastrous and even fatal reactions.

KEYWORDS : Trypanosomiasis, African; Trypanosoma rhodesiense; Imported Diseases.

Rhodesian trypanosomiasis has been carefully described in textbooks on tropical medicine and enabled the practitioners, beyond doubt those with training or experience in medicine in the tropics, to gain a reliable idea of the clinical aspects of a *T. rhodesiense* infection.

An increase of these infections observed mostly in safari-tourists returned from East African national parks and/or wild animal reserves has been accompanied by the emerging of unusual clinical features.

The epidemiology of these infections presents interesting peculiarities. The patients have often only been exposed a few hours to tse-tse contact and it becomes thus extremely easy to make sure of the day and even the hour of the infective bite and consequently of the precise incubation time. Moreover the man-trypanosome contact is unique in character : the human beings are without any immunologic competence against these protozoa and are as a result an uncommon model of « sentinel animals » whereas the vectors may carry a zoonotic poorly human adapted strain collected on game or the other way round transmit heavy infections collected on park wardens, acting as inapparent trypanosome carriers, as has been demonstrated.

The result of this new specific risk is the existence of a malignant variety of Rhodesian trypanosomiasis and the opening of a new chapter in the imported diseases, on which attention must be focussed.

The primary lesion, so brilliantly described in Cameroun by Graf (1929) and for East Africa by Krampitz & de Raadt (1967) occurs in the usual proportion of 1 : 2. An early rash is not unusual.

The hyperacute onset of the fever is accompanied by an impressive speedy deterioration of the general condition, by an immediate neuropsychic involvement, impaired renal and liver functions, cardiac disturbances and outspoken disturbances in the blood proteins. The lack of the classical symptoms of sleeping sickness may induce even an able physician into erroneous conclusions with disastrous results.

This malignant clinical picture is not surprising when the unusual early and heavy parasitaemia is taken into account. From the 6th-8th day the trypanosomes are present in the peripheral blood and may attain figures of 30.000/mm^3, 50.000/mm^3 and even over 90.000/mm^3.

The mental depression or confusion, the stuporous habitus, the amnesia are pointers for an *early involvement of the central nervous system*, although the clinical picture may be reminiscent of an uraemic intoxication, which is indeed increasingly present. But at this early stage the E. E. G. contains already slow δ and θ waves and furthermore one of our patients had on day 14 after the infective bite trypanosomes in the C. S. F., accompanied by 27 cells/mm^3 (lymphocytes and polymorphonuclears), which respectively disappeared and became normal again after a successful treatment.

The *renal function* is impaired at a very early stage (day 12). The kidney dysfunction is characterized by a progressive oliguria (500 ml/day) with a tendency to anuria, by uraemia, by creatinaemia, by proteinuria with granular and hyaline casts. The renal component dominates the clinical picture and becomes temporarily the major concern of the doctor in charge. It has not been possible as yet to decide on the etiology of the organ damage. Suspicion is aiming at a direct or indirect action of the trypanosomes and/or their metabolites, at a sudden release or presence of large amounts of foreign proteins inducing an immunopathological reaction, but other mechanisms may be involved.

The blood urea reaches 70-80 mg %, before any treatment, e.g. on day 12, will reach much higher values during the first two weeks of treatment (110-135 mg %) and then decreases as the treatment goes on. The creatinemia provides even more interesting data, on D 10 - D 12 the figure reaches 3-4 times the normal values and returns to normal after a few days (3) of specific treatment. The proteinuria (0,15-0,30 %) and the casts in the small amounts of voided urine disappear after one week of treatment, but may also show for a certain period of time ups and downs.

The *liver function* is also disturbed. The alcaline phosphatases (17-40 K. A. units), L. D. H. (2-4 × N. values), O. C. T. (4-8 × N. values), L. A. P. (1,5-2 × N. values), SGOT (7-10 × N. values), SGPT (7-12 × N. values) are so many examples of disturbed liver function tests. They normalize gradually after 1-1 1/2 month.

Anaemia is obvious from the early days of the infection. The mechanism is not yet elucidated. The specific treatment will take care of this condition.

The bilirubinaemia is up to 4-6 mg % (mostly direct) and down to normal again after 3-4 weeks of treatment.

Myocarditis is a common occurrence, pro parte following localisation of the trypanosomes in the interstitial spaces of the heart. The symptoms are : tachycardia, repolarisation disturbances, depressed ST-segments, inversed T-tops. The specific therapy at an early stage will restore a normal cardiac function.

The sero-proteins are also grossly disturbed : blood sedimentation remains accelerated for roundabout 2 months, γ-globulins however are up (1.3-1.9 mg %) and stay at a high level for long periods, the IgM is at 4-16 times the baseline value. C-reactive proteins are only positive during a short period of time, the thymoltest (MacLagan) reads 16-21 Units and the Hanger test (cephalin-cholesterol) 4+. After 2-3 months all of these values are normal again.

Blood

Parasitological diagnosis

The isolation of the *T. rhodesiense* is easy, both in bloodcultures and animals. Rats become positive within 24 hours to 2 days, mice after 4-6 days and guinea-pigs after 7-8 days.

Serological observations

Immuno-diagnosis in the hyperacute *T. rhodesiense* trypanosomiasis is interesting. Complement-fixation and fluorescent antibody techniques are both negative on D 12. They become however positive on D 14 : the C. F. only for 1 1/2 month with an evolution of 1 : 8, 1 : 16, 1 : 8, 1 : 2; the FAT gives 2+ or 3+ during 3-6 months. Once negativated, the serological follow-up remains unchanged (control-2 years).

Another interesting fact is the presence in the urine, a few hours after the first trypanocidal treatment, of several antigenic components of the trypanosomes.

Cerebro-spinal fluid

The C. S. F. of one of our patients (already mentioned) did contain trypanosomes and an increased number of cells, however with a normal protein content, no detectable IgM and a negative Pandy and other globulin tests. Early C. S. F. specimens show nevertheless a moderately disturbed gold colloidal test of Lange, returning to normal after 4-6 months, a further confirmation of an early involvement of the C. N. S.

The serological tests applied on the C. S. F. (CF and FAT) remain negative with the exception of the one containing trypanosomes on D 12 : the FAT became positive on D 26, but was negative after 4 months.

The electrophoresis of the CSF does not provide interesting results : the albumine is decreased ($\pm$ 60 to $\pm$ 50 %), the pre-albumin (Rho), and θ-fractions are temporarily decreased, a δ-fraction may be present, the $\alpha - 1$ and γ gammaglobulins are doubled.

Treatment

The specific treatment cannot follow any strict protocol, due to the disturbing fact of the oliguria, renal and liver dysfunction. To restore a good diuresis is fundamental and may need the administration of Mannitol 15 %, corticoids and a drastic regimen (Kempner).

Melarsoprol is an extremely active drug on *T. rhodesiense*, but also very dangerous. Having been informed of the death of one such patient immediately after the first injection and the painful experience of another patient who as been referred to us suffering of paraplegia, incontinentia, speech disturbances, decubitus (after two series of melarsoprol), hesitation to use this drug unless in the presence of imperative reasons, such as a relapse is understandable.

Our actual treatment protocol starts with one single dosis of diminazene aceturate (Berenil) 5 mg/kg, followed by a classical association of suramine, 5-7 weekly I. V. doses of 1 g (after a test dosis) and 12 I. M. doses of pentamidine 4 mg/kg. Our results have been so far excellent.

Samenvatting — **Kwaadaardige** *T. rhodesiense* **trypanosomiasis.**

De *T. rhodesiense* trypanosomiasis is een nieuwe uiterst ernstige importziekte. Toeristen en jagers, die voor het eerst in contact komen met een dergelijke besmettingsbron, in de parken en jachtgebieden van Oost-, Centraal- en Zuidelijk Africa, vertonen massieve besmettingen. Trypanosomen besmetting verloopt even acuut als een Westafrikaanse *P. falciparum* primo-infectie en dient derhalve ondergebracht bij de urgentie-besmettingsziekten.

Zo het praktisch uitgesloten is de overweldigende aanwezigheid van *T. rhodesiense* verkeerd te beoordelen, zal niettemin de behandeling met grote zorg individueel dienen gepland om ongewenste en zelfs dodelijke reacties te voorkomen.

Résumé — **La trypanosomiase maligne à** *T. rhodesiense*.

La trypanosomiase à *T. rhodesiense* est venu prendre une place non négligeable dans la pathologie d'importation. Des touristes et des chasseurs, « non-saucés », qui s'infectent à l'occasion de visites ou de parties de chasse respectivement dans les parcs ou les territoires de chasse d'Afrique orientale, centrale ou australe, font des infections parasitaires massives.

L'évolution de cette trypanosomiase est à ce point dramatique qu'elle se rapproche des accès paludéens malins produits par le *F. falciparum* de l'Afrique occidentale.

S'il est pratiquement exclu de ne pas voir les *T. rhodesiense* dans le frottis sanguin, le traitement à appliquer devra être établi soigneusement à la carte si on veut prévenir des réactions iatrogènes dramatiques, voire mortelles.

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