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"SCIENTIFIC RESEARCH MADE IN THE LABORATORY OF IMMUNOLOGICAL RESEARCH OF THE MINISTRY OF PUBLIC HEALTH AND SOCIAL WELFARE 1961-1962"

SCIENTIFIC RESEARCH MADE IN THE LABORATORY OF IMMUNOLOGICAL RESEARCH OF THE MINISTRY OF PUBLIC HEALTH AND SOCIAL WELFARE 1961 - 1962

The Laboratory of Immunological Research of the Secretariat of Public Health and Social Welfare has been conducting studies on onchocercosis since January 1961 from the viewpoint of investigating the pathogenesis of therapeutic shock (Mazzotti reaction) and finding more effective methods of treatment for use in public health.

As regards pathogenesis, an important point to be cleared up was the supposed participation of allergy in the Mazzotti reaction. To this end, a field study was made of symptomatology in 31 onchocercosis patients who had been treated with diethylcarbamazine.

Mazzotti reaction was positive in all patients, being very intense in 15, moderate in 12, and weak in 4, but in no case did the typical symptomatology of allergy occur; that is to say, no patient had hives or angioneurotic edema or asthma or any sings of anaphylactic shock.

Subsequently, immunochemical tests were made in 10 patients before and during the reaction to the drug. Unlike the results of an immunological reaction, no reduction of the complement or significant increase of histamine in the blood taken from the cubital and jugular veins was observed.

Serotonine in the blood taken from the jugular vein increased significantly. This finding points to the appearance of a toxic agent and to that substance's having a share in the shock symptomatology.

A fact of much interest was the appearance of Reactive Protein-C in 22 of the 26 patients treated, the amount being proportionate to the symptoms of inflammation and particularly to the presence of fever and edema. This finding confirms the destruction of tissue in the Mazzotti reaction, similar to that produced experimentally under the influence of certain endotoxins of microbial origin.

A study of the behavior of onchocerca microfilaria in the Rose chamber with coagulated plasma showed that some of them have the power to liquefy the clot, as photomicrographs and phase-contrast cinemicroscopy clearly showed the formation of channels or tunnels starting from their anterior extremities.

In fact, after attaining this knowledge, it was possible to extract from the adult parasite and from the microfilaria a proteolytic enzyme that has the characteristics of the endopeptidases and is active at pH 3.5 at a temperature of 40°C.

Another important point was the "in vitro" verification of the filaricide potency of diethylcarbamazine in dilutions of up to 1:100,000. The drug does not kill the microfilaria immediately, but rather has an initial effect of inciting motion and the secretion of endopeptidase, which ceases at 48 hours and gives place to the irreversible paralysis of 97.88 per cent of the worms (while in the control test only 69.8 per cent of paralysis in microfilaria can so far be observed).

Together, these studies make it possible to interpret the Mazzoti reaction as the result of the toxic effect of diethylcarbamazine on microfilaria, and of their secretions (endopeptidase) on the tissues of the host, with liberation of serotonine and destruction of tissues. This interpretation is consistent with the findings of Thorson in the case of hookworm in dogs, wherein the esophagus of the parasite produces an enzyme for extracorporeal digestion which at the same time acts as a virulence factor.

Once the pathogenesis of the Mazzoti reaction became known, tests were made with drugs that might prevent it. The first of the drugs tested was ciproheptadine, which is anti-serotininic and anti-histaminic, but its administration prophylactically and during the reaction barely influenced the pruritus and erythema of the initial reaction and did not diminish the later manifestations of inflammation.

To oppose the inflammatory reaction, a second experiment was made associating dexametasone with ciproheptadine: twelve hours before beginning chemotherapy with diethylcarbamazine, 31 onchocercosis patients took 1.5 mg of dexametasone and 4 mg of ciproheptadine, and this dose was repeated for two days, being administered at the same time as the diethylcarbamazine.

Under this procedure, intense itching occurred in only 2 of the patients, while 12 out of another 31 patients not given such prophylactic treatment had strong itching. Also, intense edema, high temperature, and marked adenopathy were avoided in the patients thus treated, while those symptoms did occur in 4 patients in the control group.

The outstanding fact about this therapeutic test can be summarized by saying that incapacity through prostration occurred in only one of the 31 persons who received ciproheptadine and dexametasone, while 13 of the 31 not treated prophylactically did have prostration, and that Mazzotti reaction prophylaxis with ciproheptadine and dexametason had no influence in reducing the number of microfilaria obtained in biopsies after treatment.

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