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FATAL GENERALIZED PROGRESSIVE VACCINIA IN AN IMMUNE DEFICIENT CHILD

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SUMMARY

A case of generalized progressive vaccinia is presented, acquired by vaccination of a child with thymic alymphoplasia. Therapeutic trials with immunostimulation were unsuccessful. There was clinical response to transfer factor and levamisole, but the child died. The rationale of mass antivariolic vaccination is discussed.

INTRODUCTION

Until the last decade dangers associated with antivariolic vaccination in Brazil were less than risk of contracting smallpox. Vaccinial complications were accepted as unavoidable disasters. Nowdays the risk of acquiring smallpox disapeared, as the disease is extinct in the whole American Continent and there is no real need of routine vaccination of all children. The United States Public Health Service recommends vaccination only for persons with a positive risk of acquiring smallpox. Even if for public health measures the routine vaccination is deemed essential, we would have grave complications in children with congenital immune deficiencies. Such children can be recognized if the correct questions are made — and precisely answered — before vaccination. It is not possible to ask those questions in field conditions here in Brazil, with mass vaccinations programs and long queues of children exposing unwillingly their left arms to the health officer; some of the children are brought to the vaccination site by their neighbours or local good samaritans, without any knowledge of their past medical stories of even the name of many of them. Some of the vaccinial complications are treatable or preventable; some are not, as is the case with vaccinia gangrenosa, myocarditis with vaccinia and arthritis, abortions when vaccinating women in the early months of pregnancy or producing foetal vaccinia when the mother is inoculated in the later months of pregnancy [2,3,4,6,7,8,10].

CASE REPORT

A ten month old female child was vaccinated, following our usual vaccination schedule. She came from São Paulo City where she was born of unrelated parents with 2.5 kg; both parents are healthy. She has an older sister, five years old, and after that child her mother had four successive abortions until being pregnant with her. She was well during her first month of life, when she was seen in our outpatient Department with oral moniliasis, that was treated with topical applications of gentian violet. Fifteen days after the first visit she was admitted to the emergency room with broncopneumonia and stayed in the hospital for eight days, being treated with ampicillin and gentamicin. Six days after her discharge she was brought again to the emergency room with bronchitis, which improved quickly with symptomatic medication; she had also oral moniliasis. Her first laboratory examinations were performed and three successive blood counts presented a pattern with low lymphocyte counts and neutrophilic leukocytosis. A

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good morphological description of these cells is not available. In the hospital the child was infected with **Salmonella typhi-murium,** and improved with symptomatic measures. She remained well at home for one month, with minor complaints of bronchitis and acute respiratory upper infections. A Mantoux test was negative. After that month she was treated with intravenous fluids for three days. For three months she was well, with good weight gain and was vaccinated with antitetanic, antidiphteric, antipertussis and Sabin vaccines without untoward reactions. In the next month she was given measles (live virus) vaccine and in 8/18/1976 she was vaccinated with antivariolic vaccine.

She was brought to the emergency room in 9/03/1976 with vesicules in the arms, buttocks and perineal region besides the local of the vaccine. The vaccination site was darker than what is generally observed, without an eschar. Her general aspect was good, and vaccinia immunoglobulin (VIG) was administered, 0.6 ml/kg.

In 9/04/1976 the original vaccination site was transformed in an eschar and the mother considered the child not well, with high fever. She was then admitted to our Department.

She was an irritable child, in the normal percentile of weight and height, with many pustular and vesicular lesions of generalized vaccinia (Fig. 1) and a big eschar, with necrotic material in the border, over the original vaccination site (Fig. 2). She was given more vaccinia immunoglobulin, 10 ml IM. White cell counts with a consistent pattern of neutrophilic leukocytosis and very few lymphocytes were obtained. Her lymphocytes were bigger than normal cells, looking like "atypical" lymphocytes, and she had a constant monocytosis. Her lymphocytes were unresponsive to phytohemagglutinin, without blastic response, and her T cells were 10%. Our normal values are 70% T cells/100 lymphocytes and results less than 45% are three standard deviations under the norm. B cells were 26%. T cells went to 16% after stimulation by thymosin and levamisole.

In 9/10/1976 she was febrile, with new lesions in her left foot, back and "alae nasi", in the corner of her mouth and over the ton-

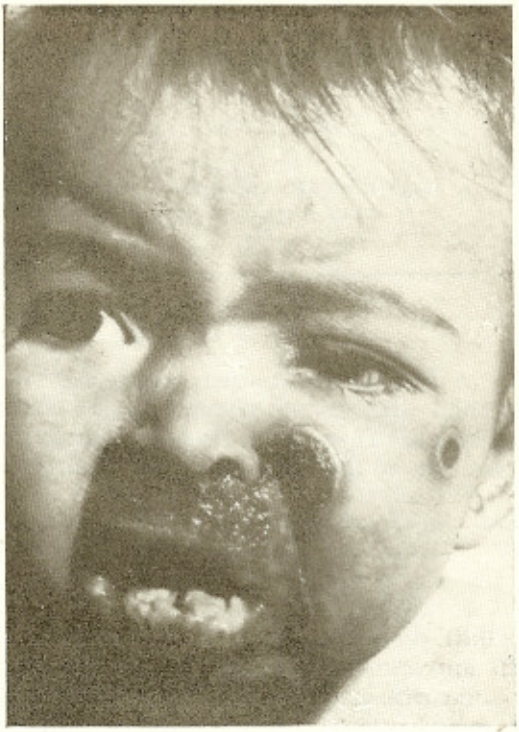

Fig. 1 — Child face, fifteen days after vaccination

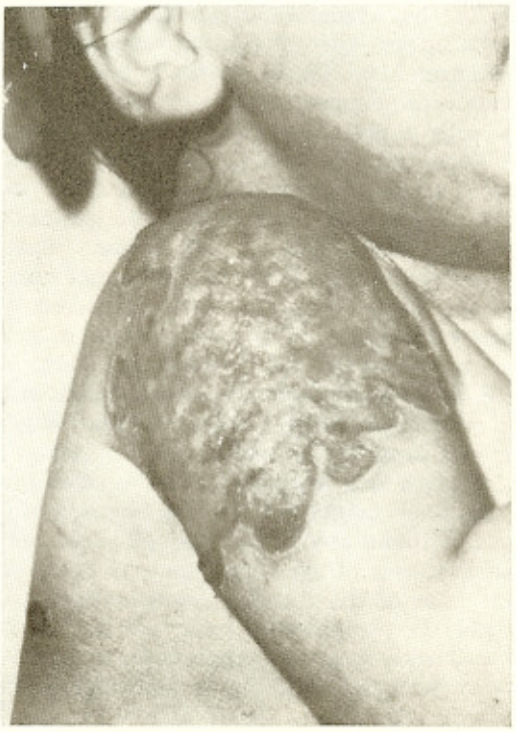

Fig. 2 — Vaccination site

gue. Results of immunoglobulin determinations, with the blood drawn before the use of VIG, showed low levels of those; she had less than 50 mg/100 ml IgA, 100 mg/100 ml IgG and normal levels of IgM, 240 mg/100 ml. Our normal values for ther age are IgA between 50 and 500 mg/100 ml, IgG between 900 and 1,900 mg/100 ml and IgM 30 to 300 mg/100 ml. Her plasma protein electrophoresis was albumin 3.6 g/100 ml, alpha$_1$-globulin 0.2 g/100 ml, alpha$_2$-globulin 0.5 g/100, beta-globulin 0.5 g/100 ml and gamma-globulin 0.5 g/100 ml. Repeat studies of T and B cells were similar to the initial ones: she had 10% of T cells and 9% of B cells. Her total lymphocyte count was 1,035/mm^3, 40% of these cells being "atypical" lymphocytes.

She received human immune plasma, from a donnor with a primary vaccination "take", levamisole and transfer factor, prepared by the Lawrence technique from a pool of normal blood bank donnors. In Brazil it is obligatory, for getting any type of work, to show proof of antivariolic vaccination, and in the São Paulo City blood donnors the prevalence of vaccination is near 100%; therefore she got "specific" transfer factor.

New studies, in 9/17/1976 showed 10% of T cells after therapy, and she was better. Immunoglobulin serum levels at this time were thought to reflect transfusion. No thymic shadow was seen in X-rays, nor shadows reflecting adenoidal tissues. She got better to 9/20/1976 with fewer lesions, better disposition and even a little weight gain. The immunological indices did not show much improvement: she had 17% of T cells in 9/21/1976.

At 9/23/1976 new crops of lesions appeared, in her buttocks, back and left arm. In 9/30/1976 she appeared less well, dispneic, with fever; she died suddenly and unexpectedly in 10/10/1976.

At autopsy she had a thymic streak, generalyzed lymph node hypoplasia (Fig. 3) and intersticial pneumonia. **Pneumocystis carinii** was not seen, even after silver impregnation techniques. The thymus gland had a blurred cortico-medulary junction (Fig. 4). The spleen was of normal size, with severe histological alterations: the folicules were without the cellular cuff, and the red pulp was made of primitive reticulum cells (Fig. 5). Material from cutaneous lesions was submitted to electron microscopy, and vaccinia virus seen. It was not found a clear cause for her demise.

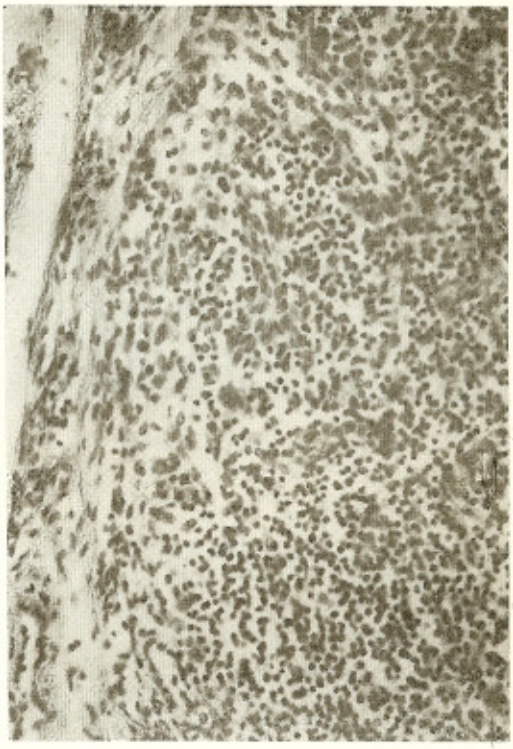

Fig. 3 — Lymph node. There is no definition in cortical and medullary portions and no germinal centers. H & E, 205 X.

Routine clinical analyses and hematological studies were performed in the clinical laboratory. B and T cell counting were made by the technique of JONDALL & col.[5]. Immunoglobulin levels were measured with reagents from Hyland Laboratories using the radial immune diffusion technique of Mancini and Heremans. Lymphocyte culture and phytohemagglutinin stimulus were made by counting blast cell response, as described by BOURONCLE & col.[1]. B lymphocytes were also counted by membrane immunoglobulin fluorescence. Stimulation of T cells by levamisole and thymosin were performed as described by SCHEINBERG & col.[9]. Vaccinia immunoglobulin was obtained from the American Red Cross.

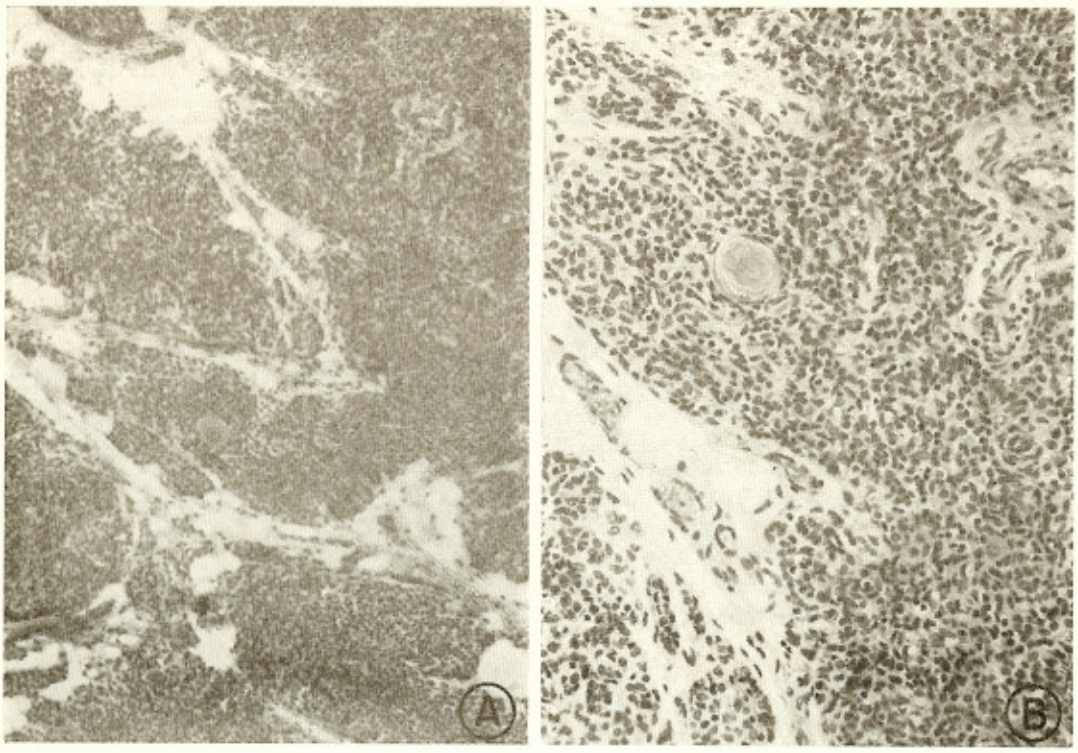

Fig. 4 — Thymus. A) There is no clear definition of cortical and medullary portions of the lobules. Hassal's corpuscules are few. H & E, 80 X. B) High power view showing depletion of lymphocytes and lymphoblasts. H & E, 205 X.

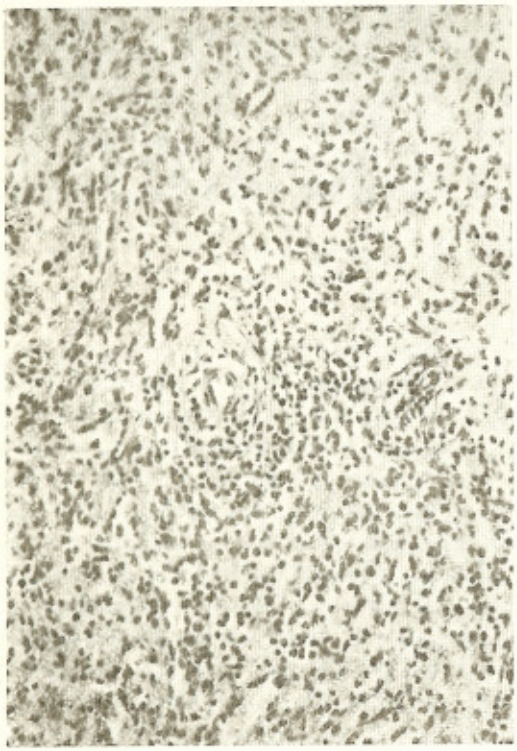

Fig. 5 — Spleen. The white pulp is made of primitive reticulum cells. The follicle is skown without the cellular cuff; the central artery stands «naked». H & E, 205 X.

DISCUSSION

Our final impression about the patient is that she had a severe T cell deficiency with humoral deficiency, which placed her under the heading of Swiss type alymphoplasia. We tried to treat her with levamisole and transfer factor, besides immune plasma and VIG. We did not find in the literature the report of any case of survival of vaccinia with these congenital immune deficiencies, with all known therapeutic resource.

RESUMO

Vaccínia generalizada progressiva fatal em criança com deficiência imunitária

São relatadas verificações referentes a acometimento definido como vaccínia generalizada progressiva, que ocorreu em criança com alinfoplasia tímica, diagnosticada na vigência do citado distúrbio decorrente da vacinação antivariólica. Diversas medidas terapêuticas foram instituídas e, entre elas, houve tentativa de imunoestimulação. Mediante emprego de fator de transferência e de levamisole sucedeu resposta favorável, mas evolução fatal não pôde ser evitada. O acontecimento é digno de

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divulgação porque representa expressiva complicação da imunização preventiva da varíola, merecedora de comentários diante do evento constatado, tendo essas considerações especial relação com os programas que dizem respeito a grandes grupos populacionais.

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