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MEDICAL MEMORANDA

Dysgammaglobulinaemia Complicated by Disseminated Measles

HELEN MAWHINNEY, INGRID V. ALLEN, J. M. BEARE, J. M. BRIDGES, J. H. CONNOLLY, MARGARET HAIRE, N. C. NEVIN, D. W. NEILL, J. R. HOBBS

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We report the case of a boy with dysgammaglobulinaemia who died with giant cell pneumonia and disseminated measles seven weeks after receiving live attenuated measles vaccine.

Case Report

From the age of 6 weeks the patient had frequent infections associated with a rash on the face, scalp, and limbs. He was given three doses of triple antigen (diphtheria, pertussis, and tetanus) and oral live attenuated poliomyelitis vaccine; the third dose at the age of 8 months. Fifty-six days later live attenuated measles vaccine was given. One week later he developed a pyrexial illness with a skin rash. There was no known contact with measles. An elder brother had a similar illness when 2 days old and died at 7 months with staphylococcal bronchopneumonia, a cervical abscess, and boils on neck.

Queen's University of Belfast, Belfast BT7 1 NN
HELEN MAWHINNEY, M.B., M.R.C.P., Tutor and Registrar, Royal Victoria Hospital
INGRID V. ALLEN, M.D., M.R.C.PATH., Senior Lecturer and Consultant in Pathology
MARGARET HAIRE, M.D., Senior Experimental Officer, Department of Microbiology
N. C. NEVIN, M.D., M.R.C.P.ED., Senior Lecturer and Consultant in Human Genetics

Royal Belfast Hospital for Sick Children, Belfast BT12 6BE
J. M. BEARE, M.D., F.R.C.P., Consultant Dermatologist
J. M. BRIDGES, M.D., M.R.C.PATH., Consultant Clinical Pathologist

Royal Victoria Hospital, Belfast BT12 6BJ
J. H. CONNOLLY, M.D., M.R.C.PATH., Consultant Virologist
D. W. NEILL, M.SC., F.R.C.PATH., Consultant Biochemist

Westminster Hospital Medical School, London S.W.1.
J. R. HOBBS, M.D., M.R.C.PATH., Professor of Immunology

At 11 months the patient had an unusual skin rash, confluent on the face, extensive on the limbs, and less pronounced on the trunk (Figs. 1 and 2). This was hyperkeratotic, purpuric, and reticulate in pattern and was not that of eczema or measles. He had pyrexia, generalized lymphadenopathy, splenomegaly, nasal and urethral bleeding, oral thrush, and photophobia.

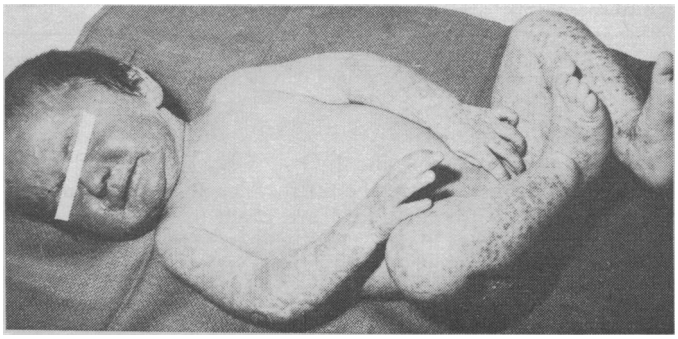

FIG. 1—Generalized symmetrical rash most pronounced on face and limbs.

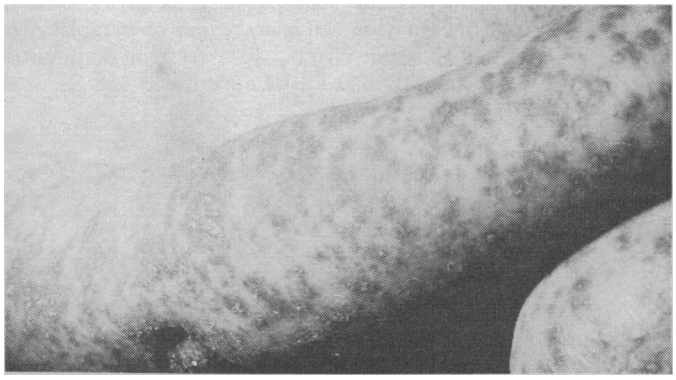

FIG. 2—Close-up showing reticulate and hyperkeratotic rash on the arm.

Investigations.—Chest *x*-ray films showed progressive patchy consolidation of both mid-zones. Haemoglobin was 10.7 g/100 ml but fell terminally to 7.7 g/100 ml. The platelet count ranged from 64,000 to 40,000/mm^3. The initial total white cell count was 5,300/mm^3, with 3,000 lymphocytes/mm^3, but fell to 1,900/mm^3, with 600 lymphocytes/mm^3. A skin biopsy showed patchy dyskeratosis,

with parakeratotic crusting in the epidermis extending into the follicles with associated inflammation. Dyskeratotic cells were most prominent towards the granular layer but some basal cells were also affected. Abnormal shrunken pyknotic, nucleated, and prematurely keratinized cells were seen.

Protein Chemistry.—An IgGλ paraprotein (Fig. 3) was detected at a concentration of 2,300 mg/100 ml but was not associated with any detectable Bence Jones protein. The serum IgM-globulin was 35 mg/100 (normal range, 48-200 mg/100 ml). He had group B red cells but no isohaemagglutinins (A, B, or H). The serum IgA and IgE levels were normal at 75 mg/100 ml and 120 ng/ml respectively. The residual normal IgG-globulin was low. Full protein studies carried out on the parents and four sibs were normal.

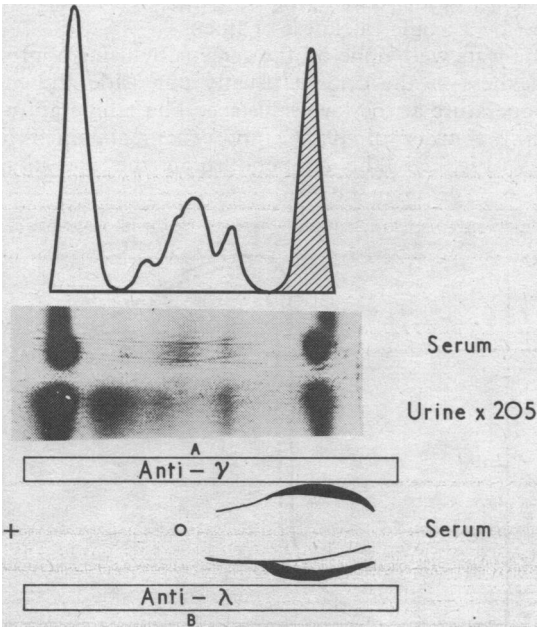

FIG. 3—Protein chemistry. (A) Electrophoretic separation of the proteins of serum and urine (concentrated × 300). (B) Characterization of the protein with respect to its light chains (Bence Jones fraction).

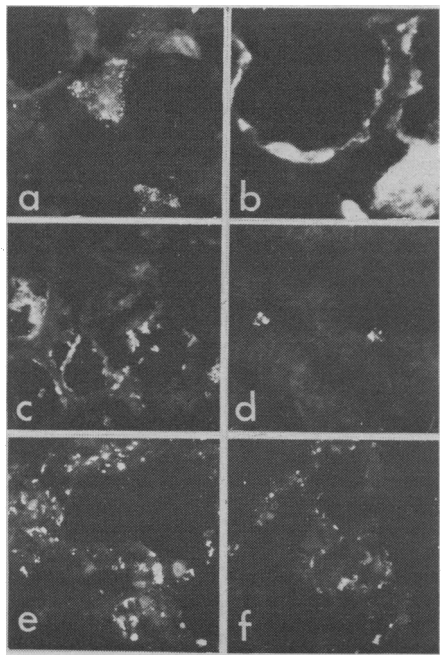

FIG. 4—Measles virus antigen demonstrated by direct immunofluorescent staining: (a) giant cell in lung; (b) alveolar cells in lung; (c) necrotic areas in liver; (d) lymp node; (e) bone marrow; and (f) thymus. (× 360.)

Despite systematic antibiotics, prednisone, topical steroids, and antifungal agents he died on 10 December 1968.

Histological Investigations.—The lungs showed severe intra-alveolar haemorrhage with peribronchial lymphocytes, polymorphonuclear leucocytes, and numerous large multinucleated cells containing intranuclear inclusions. The liver and pancreas showed patchy necrosis with giant cells. The extremely small thymus was not differentiated into cortex and medulla and was noticeably hypocellular with only a few Hassall's corpuscles. Germinal centres were absent. The spleen, especially the Malpighian corpuscles, was hypocellular and contained small necrotic areas with giant cells. Lymph nodes were enlarged and hypocellular, with poorly developed germinal centres. Plasma cells and giant cells were present in the pulp. Peyer's patches were poorly developed. The bone marrow was hypocellular.

Virology.—Cryostat sections were stained by the direct immunofluorescence technique with controls (Haire, 1969). In the lung measles virus antigen was found in the giant cells and in the cells lining the alveoli (Fig. 4 a and b). Large quantities of antigen were seen in the necrotic areas of the liver (Fig. 4 c), but less in the spleen, lymph nodes, bone marrow, and thymus (Fig. 4 d, e, and f).

Measles virus which was isolated from lung, spleen, and a lymph node behaved as an attenuated strain. Measles complement fixing and haemagglutination inhibiting antibodies and poliovirus types 1, 2, and 3 neutralizing antibodies were measured (Connolly *et al.*, 1967; Connolly, 1968) in a serum sample obtained 93 days after the final dose of oral poliomyelitis vaccine and 37 days after the live attenuated measles vaccine. Measles antibody was absent from the serum at a dilution of 1:8. Measles specific IgM and IgG were absent in undiluted serum when measured by the indirect immunofluorescence technique (Haire and Hadden, 1970). The poliovirus neutralizing antibody titres were: type 1, 1:42; type 2, 1:682; type 3, 1:256. Tetanus antibody was <0·01 international antitoxin units/ml.

Comment

The diagnosis of dysgammaglobulinaemia is suggested by the deficiency in IgM and functional IgG antibody. The deficiency in IgM was shown by the low serum level, the absence of isohaemagglutinins, and the absence of a measles-specific IgM response to infection, while the deficiency of IgG was shown by the low residual normal IgG level in serum, the absence of detectable tetanus antibody, and the absence of a measles-specific IgG antibody response.

Our patient was able to recognize and respond normally to the three poliovirus antigens in the oral vaccine. Since, however, neutralizing antibody to the three poliovirus types may be IgA as well as IgG immunoglobulin and the patient had a normal IgA level the antibody response can be explained. Mitus *et al.* (1962) described the case of a child who died three months after receiving live attenuated measles vaccine with giant cell pneumonia and disseminated measles. Our patient had measles virus antigen in the lungs, liver, spleen, lymph nodes, and bone marrow, and also in the thymus, which may have inhibited recruitment of thymus-differentiated immunocytes (Burnet, 1968). Live vaccine viruses which are attenuated in virulence for normal children may be pathogenic for immunologically incompetent children.

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Requests for reprints should be addressed to Dr. J. M. Beare, Skin Department, Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BJ, Northern Ireland.

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