with unexplained encephalopathy and liver dysfunction of sudden onset so that prompt treatment of cerebral oedema may be instituted, if appropriate. Such an approach with this patient might have been life-saving.

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References

Atkins J N & Haponik E F
(1979) *American Journal of Medicine* **67,** 672–678
Brown R E & Forman D T
(1982) *Critical Reviews in Clinical Laboratory Sciences* **17,** 247–297
Brown T, Hug G, Lansky L *et al.*
(1976) *New England Journal of Medicine* **294,** 861–867
Crocker J F S
(1982) *Seminars in Liver Disease* **2,** 340–352
Holt J T, Arvan D A & Mayer T K
(1983) *Lancet* ii, 4–7
Lancet
(1982) i, 941–943
Lichtenstein P K, Heubi J E, Daugherty C C *et al.*
(1983) *New England Journal of Medicine* **309,** 133–139
MacSween R N M, Anthony P P & Scheuer P J *eds*
(1979) Pathology of the Liver. Churchill Livingstone, Edinburgh; pp 216–217
Morse R S, Holmes A W & Levin S
(1975) *Digestive Diseases* **20,** 1184–1190
Mowat A P
(1983) *British Medical Journal* **286,** 1999–2001
New England Journal of Medicine (1983) **309,** 179–181
Reye R D K, Morgan G & Baral J
(1963) *Lancet* ii, 749–752
Salt W B & Schenker S
(1976) *Medicine (Baltimore)* **55,** 269–289
Shaywitz S E, Cohen P M, Cohen D J, Mikkelson E, Morowitz G & Shaywitz B A
(1982) *Journal of Pediatrics* **100,** 41–46
Sherlock S
(1983) *Gut* **24,** 265–269
Sullivan-Bolyai J Z & Corey L
(1981) *Epidemiologic Reviews* **3,** 1–26
Tonsgard J H, Huttenlocher P R & Thisted R A
(1982) *Pediatrics* **69,** 64–69
Varma R R, Riedel D R, Komorowski R A, Harrington G J & Nowak T V
(1979) *Journal of the American Medical Association* **242,** 1373–1375

Severe atopic eczema, recurrent pneumococcal meningitis and recurrent eczema herpeticum[1]

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A girl is reported with exceptionally severe atopic eczema in whom recurrent infection led to the discovery of an immunological abnormality not hitherto associated with atopic eczema.

Case report

The patient, a 10-year-old Caucasian girl, is the second child of unrelated parents, both of whom have had mild atopic eczema. The pregnancy and delivery on 28.2.74 were normal; the patient was breastfed for 3 months and solids first introduced at 5 months. Atopic eczema, first noted soon after bottle-feeding was commenced at 3 months, spread to involve the entire body by 5 months. Despite therapy with topical hydrocortisone cream and Synacthen Depot 0.25 mg twice a week, her exceptionally severe eczema proved to be a major handicap. Flexion contractures of the fingers developed due to constant bandaging of her hands, and she had been unable to attend school for the 2 years prior to hospital admission at the age of 8 years. Skin infections with group A beta-haemolytic streptococci and *Staphylococcus aureus* have recurred from infancy, and on one occasion an exceptionally severe infection with the above organisms and *Pseudomonas aeruginosa* required intravenous antibiotics. Three attacks of pneumococcal meningitis and septicaemia, accompanied by major seizures and coma, occurred on 15.7.81, 18.9.81 (with subdural effusions drained through burr holes), and 25.8.82. With each attack of meningitis her skin lesions completely disappeared within two days of the onset of the meningitis, relapse occurring after 10 to 18 days. On 4.11.82 she developed primary herpetic gingivostomatitis, with oesophageal ulceration and eczema herpeticum of the face, neck and hands. Recurrences of eczema herpeticum of the face, neck and hands occurred on 8.12.82, 9.2.83 and 11.4.83. Radiological evidence of rickets of the wrists, attributed to lack of sunlight and a low dietary intake of calcium and vitamin D, was noted on 23.3.83.

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Trials of therapy with oral disodium cromoglycate, ketoconazole, evening primrose oil, and vitamin E were without benefit. Admission to hospital on 13.4.82 with urticaria and angio-oedema of the face immediately after eating whiting led to inpatient dietary manipulation. On 13.3.82 topical and systemic corticosteroids were discontinued, and all normal food and drink withdrawn. Nutrition was maintained on an elemental diet (Vivonex) for 23 days, and her skin greatly improved. Single food items were then introduced at the rate of one new item per week, and foods suspected of causing a worsening of the eczema avoided. During 8 months in hospital she was weaned off her bandages, and she was rehabilitated into a school for physically handicapped children.

The following investigations were normal: haemoglobin, total and differential white cell count (no eosinophilia), urea and electrolytes, liver function test, serum zinc, classical and alternate pathway complement activity, immunochemical C_3 and C_4, polymorph function, T- and B-lymphocyte markers, lymphocyte karyotype (with methotrexate banding), and sister chromatid exchanges. The serum immunoglobulins IgG (9.80 g/l), IgA (1.40 g/l) and IgM (0.60 g/l) were normal for her age, as was the serum IgE (35 iu/ml; normal < 80). RAST testing revealed IgE antibodies to cat (grade 3), dog (grade 1) and egg (grade 2) but not to house dust mite, grass pollen or 18 other foods. IgG subclasses showed a normal IgG1 (6.6 g/l; normal range 4.6–9.4), a low IgG2 (0.72 g/l; normal range 1.6–5.1), a normal IgG3 (0.32 g/l; normal range 0.2–1.1), and an elevated IgG4 (2.6 g/l; normal range 0.01–1.2).

Following discovery of IgG2 deficiency, polyvalent pneumococcal vaccine (Pneumovax) was given. Pre-Pneumovax, the pneumococcal antibody titre was negative, but 2 weeks post-Pneumovax it became positive at 1/256. She was also treated with intravenous Veinoglobuline (Merieux), an IgG preparation rich in IgG2 (60%, compared with 23% in plasma). Veinoglobuline was started on 24.11.82 and given in a dose of 3 grams every 2 weeks, resulting in a serum IgG2 level of 3.0–5.0 g/l. There have been no recurrences of pneumococcal septicaemia or meningitis, and her skin has slowly continued to improve. In January 1984 treatment with Veinoglobuline was reduced to 3 grams every three weeks.

Discussion

Human IgG contains four subclasses based on antigenic differences in the polypeptide heavy chains (Oxelius 1979). Deficiency of IgG2 has been reported in association with *Haemophilus influenzae* infection (Schur *et al.* 1970), meningococcal infection (Bass *et al.* 1983), the cartilage-hair syndrome (Oxelius 1979), ataxia telangiectasia (Oxelius *et al.* 1982) and children with suspected acquired immunodeficiency syndrome (Church *et al.* 1982) The finding of IgG2 deficiency in a child with atopic eczema is unique. Our patient's elevated IgG4 is a well recognized (but poorly understood) feature of atopic eczema. Although the IgE level was within the normal range, this is highly atypical in a child with severe atopic eczema where the IgE is usually very high. This inappropriately low IgE concentration may be a further feature of the patient's immune deficiency. The recurrent pneumococcal septicaemia and meningitis can be attributed to the IgG2 deficiency in view of the direct correlation between serum IgG2 concentrations and the antibody response to 11 pneumococcal antigens and to *H. influenzae* type B antigen (Siber *et al.* 1980). Recurrences of eczema herpeticum are sometimes seen in children with atopic eczema, but the severity of the recurrences in this patient is atypical.

The remission of the patient's eczema during each attack of meningitis is particularly intriguing. Maybe some part of her immune system, usually dedicated to the damaging of her skin, is temporarily 'distracted' by an overwhelming bacterial infection. Alternatively meningitis may in some way be immunosuppressive, akin to the temporary remission of atopic eczema seen after measles.

There is a clear association of atopic eczema with immunodeficiency disorders such as X-linked hypogammaglobulinaemia, the Wiskott-Aldrich syndrome, and ataxia telangiectasia. Atypical cases of eczema of unusual severity, or those with an unusual degree of infection, should prompt a search for specific underlying immunological defects.

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References

Bass J L, Nuss R, Mehta K A, Morganelli P & Bennett L
(1983) *New England Journal of Medicine* **309,** 430
Church J A, Lewis J & Spotkov J M
(1984) *Lancet* i, 279
Oxelius V-A
(1979) *Clinical and Experimental Immunology* **36,** 112–116
Oxelius V-A, Berkel A I & Hanson L A
(1982) *New England Journal of Medicine* **306,** 515–517
Schur P H, Borel H, Gelfand E W, Alper C A & Rosen F S
(1970) *New England Journal of Medicine* **283,** 631–633
Siber G R, Schur P H, Aisenberg A C, Weitzman S A & Schiffman G
(1980) *New England Journal of Medicine* **303,** 178–182