

expressed as the proportion of viable intracellular bacteria after 2 hours of incubation.

Results. The patient showed low levels of serum IgG and IgM, undetectable serum and salivary IgA, reduced proportion and number of circulating T-lymphocytes, and impaired *in vitro* lymphocyte stimulation response (Table). Delayed hypersensitivity was not elicited to any of the 5 common recall antigens injected intradermally. Response to PPD was absent although the patient had received BCG vaccine in early childhood. The complement system, number of B-lymphocytes, opsonic activity of plasma, and PMN functions were normal.

Discussion

The patient showed impaired immunocompetence on 2 separate occasions. Hypoimmunoglobulinaemia in the presence of normal number of circulating B-cells points to the possible existence of other pathogenetic mechanisms known to underlie common varied immunodeficiency—for example, reduced number and activity of helper T-lymphocytes, increased number and activity of suppressor T-lymphocytes, and serum inhibitors (Chandra *et al.*, 1978). In our patient, the common systemic causes of immunodeficiency (energy-protein undernutrition, anaemia, sepsis, chronic infection, Hodgkin's disease, malignancy, protein-losing enteropathy, nephrotic syndrome, immunosuppressive drugs, anticonvulsant therapy, irradiation, etc.) were excluded by history, physical examination, anthropometry, and appropriate laboratory tests. This, together with the demonstration twice of impaired immunocompetence, suggested that partial immunodeficiency affecting the humoral and cell-mediated systems was a primary event and was a part of the syndrome of laevocardia, bronchiectasis, and paranasal sinus abnormalities. The association of immunodeficiency and congenital malformations is recognised in several dysmorphic syndromes: short-limbed dwarfism, cartilage-hair hypoplasia, Kartagener's syndrome, Down's syndrome, and ataxia telangiectasia (Chandra, 1976).

Summary

In a case of laevocardia, bronchiectasis, and paranasal sinus abnormalities, assessment on 2 occasions showed the presence of moderate immunodeficiency. Serum concentrations of IgG and IgM were low, and serum and salivary IgA was not detected. T-lymphocytes were reduced in number and cell-mediated immunity *in vivo* and *in vitro* was impaired. Opsonisation, complement system, and neutrophil functions were normal.

References

- Chandra, R. K. (1976). Immunity disorders. In *Textbook of Pediatrics*, p. 204. Edited by L. S. Prasad and P. Robinson. Thompson Press: New Delhi.
- Chandra, R. K., Cooper, M. D., Hitzig, W. H., Rosen, F. S., Seligmann, M., Soothill, J. F., and Terry, R. J. (1978). *Immunodeficiency*. Technical Report Series. WHO: Geneva.
- Chandra, R. K., and Khetarpal, S. K. (1963). Levocardia with bronchiectasis and paranasal sinus abnormalities. *Indian Journal of Pediatrics*, **30**, 78–80.
- Datta, P. (1968). Letter: Chandra's syndrome. *Lancet*, **2**, 1350–1351.
- Lee, P. (1965). Letter: Chandra-Khetarpal syndrome. *Lancet*, **1**, 1398.
- Magalini, S. (1971). *Dictionary of Medical Syndromes*, p. 101. Lippincott: Philadelphia.
- Sharpe, M. V. (1963). Letter: Levocardia with bronchiectasis and paranasal sinus abnormalities. *Lancet*, **2**, 42.

R. K. CHANDRA

Department of Paediatrics, All India Institute of Medical Sciences, New Delhi

Correspondence to Professor R. K. Chandra, Janeway Child Health Centre, St John's, Newfoundland A1A 1R8, Canada.

Spontaneous maturation of stage IV–S neuroblastoma

It is recognised that a special category of disseminated neuroblastoma exists in which the prognosis is surprisingly favourable (D'Angio *et al.*, 1971). Patients fitting this stage IV–S group are those who would otherwise be stage I or II but in whom the disease is confined to liver, skin, or bone-marrow and in whom there is no x-ray evidence of bone metastases on complete skeletal survey (Evans *et al.*, 1971). Evidence from several series has shown, particularly in patients presenting under age one year, that death is more likely to result from vigorous treatment than from the disease itself (Hassenbusch *et al.*, 1976). The natural history would appear to be for the tumour and metastases either to regress completely or to 'mature' into ganglioneuroma. A case is therefore presented in which treatment, both surgical and therapeutic, has been deliberately kept to a minimum and in which gradual maturation has occurred.

Case history

A baby girl first presented to another hospital at age 4 months with 1 cm subcutaneous nodule in the right scapular region. This was not excised until 8 months by which time eight similar lesions were present on the trunk and limbs. She was otherwise

well but the lesion proved to be a metastasis from a malignant neuroblastoma (Fig. 1). Urogram and examination under anaesthesia showed there was a 5×7 cm mass above the right kidney extending almost to the midline. The liver was not enlarged and bone-marrow biopsy was normal. A skeletal survey was normal and urinary HMMA output much raised ($76 \mu\text{mol}/24 \text{ h}$; $15.05 \text{ mg}/24 \text{ h}$).

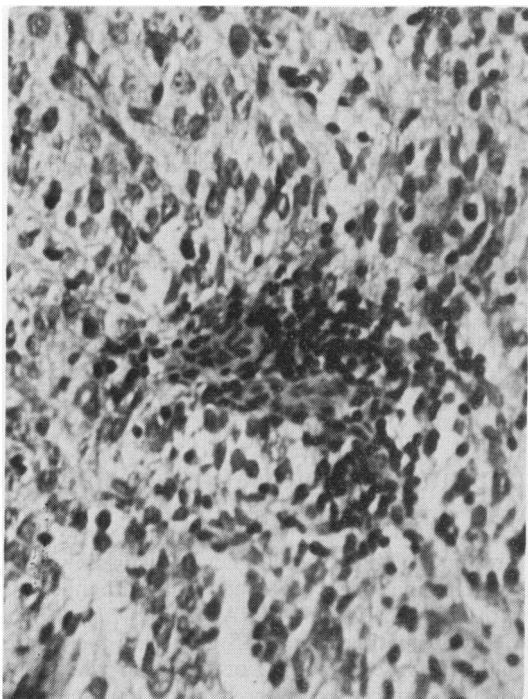


Fig. 1 *Subcutaneous metastatic nodule of neuroblastoma (child aged 8 months) showing intense perivascular lymphocytic infiltration around the vessel in the centre. $\times 180 \text{ H and E}$.*

No active treatment was planned and a period of careful observation was undertaken. Fresh skin lesions continued to appear as late as 16 months of age, but the patient remained well. Two lesions excised at 13 months again showed metastatic neuroblastoma and she continued to excrete large amounts of HMMA in urine. At 19 months, however, many of her skin nodules were decreasing in size and further excised nodules this time showed maturation to ganglioneuroblastoma and, in one nodule, to ganglioneuroma. As with previous specimens, perivascular lymphocytic infiltration was prominent and immunological studies showed an increased proportion of peripheral blood B-lymphocytes, and a blocking antibody to the tumour in the serum. Serial urograms showed the size of the primary tumour to be static,

but against these favourable signs was the fact that urinary HMMA levels remained high.

At age 2–3 years she stopped gaining weight and was noticed for the first time to be hypertensive ($160/100 \text{ mmHg}$). A urogram showed deteriorating function in the right kidney and it was felt desirable to perform a laparotomy. At operation the main mass of the tumour lay above the right kidney with no obvious normal adrenal gland present on that side. There was infiltration extending behind the major vessels and particularly around the right renal vessels causing their compression. Complete removal was clearly going to be hazardous so, to try to preserve renal function, the portion of the tumour around the renal vessels was removed as far as this was possible. Random areas of the tumour were biopsied and further skin nodules were also excised. Histologically the main tumour showed the appearances of a ganglioneuroma and the pattern of the neurofibrillary material and the presence of numerous foci of calcification was consistent with regression of a previous neuroblastoma. Once again there was a striking perivascular lymphocytic infiltration. One of the metastatic nodules however appeared to have 'lost' its ganglion cells and was more characteristic of a neurofibroma while another showed the structure of a ganglioneurofibroma (Fig. 2).

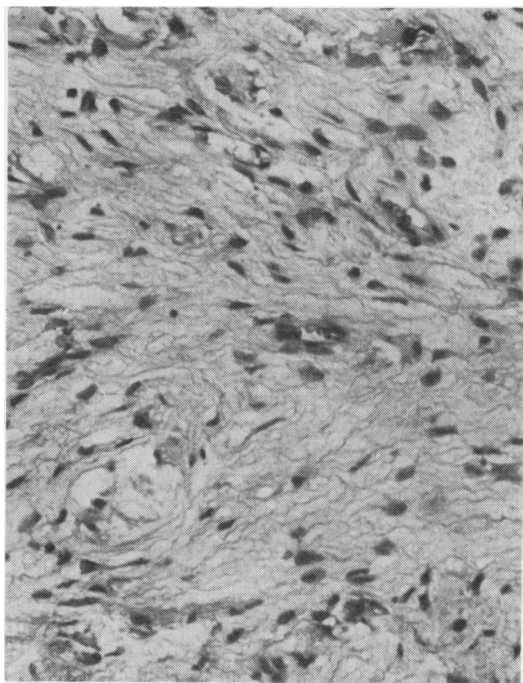


Fig. 2 *Subcutaneous nodule (child aged 2–3 years) showing neurofibromatous structure with occasional ganglion cells. $\times 250 \text{ H and E}$.*

Despite the operative intervention the child remained hypertensive and the function in the right kidney continued to deteriorate. HMMA output remains high but has shown a steady decline during the last year to near normal levels. A positive Saralasin infusion test (Streeton *et al.*, 1976) combined with increased plasma renin levels (>300 pmol/1 per min) has shown her hypertension to be renal in origin. In view of the operative findings it was decided to treat the hypertension medically and she is now well controlled on a combination of propranolol and phenoxybenzamine. Appetite and weight gain have returned to normal.

It is now 2 years 10 months since the first skin nodule was noted. Another baby girl has been born to these parents and at 7 months shows no evidence of developing neuroblastoma. HMMA levels in this sibling and in both parents are normal.

Discussion

Despite the known favourable outlook in stage IV-S neuroblastoma, most reported cases have received some treatment. The purpose of this report has been to add information on the natural history of the condition. Three previous cases have been reported in which no treatment was given and the disease regressed spontaneously (Griffin and Bolande, 1969; Schwartz *et al.*, 1974). As chemotherapy and radiotherapy have had little effect on the survival of children with stage IV neuroblastoma (Koop and Johnson, 1971) their use in stage IV-S cannot be justified as several deaths in this group can be directly attributed to their use (Griffin and Bolande, 1969; Hassenbusch *et al.*, 1976). Surgical removal of the primary tumour may be justified as late reactivation of disease can occur (Konrad *et al.*, 1973) and, as in our case, adjacent structures may be damaged. It is also desirable to establish the cause of hypertension if this should develop: the obvious explanation is the raised catecholamine levels but, as our case demonstrates, renal hypertension may occur. The Saralasin infusion test, combined with peripheral venous plasma renin estimations, appears to be a reliable and relatively noninvasive method of making the distinction (Streeton *et al.*, 1976). Major surgery involving risk to life would not seem justified.

Summary

A case of stage IV-S neuroblastoma is presented in which treatment has deliberately been kept to a minimum. Gradual maturation to ganglioneuroma has been documented and the patient's generally good progress has justified this approach.

References

- D'Angio, G. J., Evans, A. E., and Koop, C. E. (1971). Special pattern of widespread neuroblastoma with a favourable prognosis. *Lancet* **1**, 1046-1049.
- Evans, A. E., D'Angio, G. J., and Randolph, J. (1971). A proposed staging for children with neuroblastoma. *Cancer*, **27**, 374-378.
- Griffin, M. E., and Bolande, R. P. (1969). Familial neuroblastoma with regression and maturation to ganglioneurofibroma. *Pediatrics*, **43**, 377-382.
- Hassenbusch, S., Kaizer, H., and White, J. J. (1976). Prognostic factors in neuroblastic tumours. *Journal of Pediatric Surgery*, **11**, 287-297.
- Konrad, P. N., Singer, L. J., and Neerhout, R. C. (1973). Late death from neuroblastoma. *Journal of Pediatrics*, **82**, 80-82.
- Koop, C. E., and Johnson, D. G. (1971). Neuroblastoma: an assessment of therapy in reference to staging. *Journal of Pediatric Surgery*, **6**, 595-600.
- Schwartz, A. D., Dadah-Zadeh, M., Lee, H., and Swaney, J. J. (1974). Spontaneous regression of disseminated neuroblastoma. *Journal of Pediatrics*, **85**, 760-763.
- Streeton, D. H. P., Anderson, G. W., Jr, and Dalakos, T. G. (1976). Angiotensin blockade: its clinical significance. *American Journal of Medicine*, **60**, 817-824.

L. RANGE-CROFT, I. LAUDER, AND J. WAGGET
Department of Paediatrics, Hospital for Sick Children, Newcastle upon Tyne, and Department of Pathology, Royal Victoria Infirmary, Newcastle upon Tyne

Correspondence to Dr L. Range-croft, Hospital for Sick Children, Great North Road, Newcastle upon Tyne NE2 3AX.

Hypomagnesaemic hypocalcaemia with hypokalaemia caused by treatment with high dose gentamicin

We report a case of hypomagnesaemic hypocalcaemia with hypokalaemia in a 12-year-old boy after prolonged treatment with gentamicin.

Case report

After a severe road traffic accident in April 1976 the boy's injuries included a depressed skull fracture, a comminuted fracture of the left femur, a transverse fracture of the right femur, a fractured pelvis, and multiple lacerations. The frontal bone was raised and the crushed brain evacuated. The right femur was fixed internally after reduction of the fracture and a double hip spica was applied; he was then transferred from Libya to London.

At operation the left femur was found to be soundly united; the right femur was ununited and inadequately fixed, with gross surrounding sepsis.