Congenital neuroblastoma with paraplegia

Author*	Age at diagnosis	Treatment	Outcome	Neurological outcome	Follow up period (years)
Moschos and Anagnostakis (1975)	6 Days	Laminectomy, chemotherapy	Alive	Improved sphincter tone, paraplegic	1·9
Kenney <i>et al</i> (1982) ¹	5 Weeks	Chemotherapy	Died	No improvement	0·3
Bodian (1963)	Not known	Laminectomy, chemotherapy	Died	No improvement	0·3
	10 Months	Laminectomy, vitamin B-12	Alive	No improvement	2·3
	3 Weeks	Biopsy, vitamin B-12	Alive	No improvement	6·6
	6 Days	Laminectomy, radiotherapy, vitamin B-12	Alive	No improvement	1·8
Katcher (1952)	3 Weeks	Laminectomy, radiotherapy, chemotherapy	Alive	Improved sphincter tone, persisting limb weakness	0·3
Hrabovsky and Jones (1979)	2 Weeks	Laminectomy, chemotherapy	Alive	No improvement	1·0
Elefant <i>et al</i> (1958)	1 Month	Laminectomy, radiotherapy	Alive	Improved sphincter tone, persisting limb weakness	1·7
Punt <i>et al</i> (1980) ²	3 Days	Laminectomy, radiotherapy	Alive	No improvement	14·0
	1 Day	Laminectomy	Alive	No improvement	11·0
	4 Months	Laminectomy, radiotherapy	Alive	No improvement	7·0
	2 Weeks	Radiotherapy, chemotherapy	Alive	No improvement	4·0
Haden and Keats (1983) ³	1 Month	Laminectomy, radiotherapy	Alive	Residual weakness of left leg	32·0
Rothner (1971)	2 Days	Laminectomy, radiotherapy	Alive	No improvement	0·8
Munro <i>et al</i> (1991)	3 Days	Chemotherapy	Alive	No improvement	0·8

*The full references for those publications not included in the list of references at the end of the paper can be obtained from Kenney *et al*,¹ Punt *et al*,² and Haden and Keats.³

Twelve patients showed no improvement in their neurological signs after treatment and four showed some improvement but were still left with significant neurological deficits. The method of treatment or the time from birth to treatment did not seem to be different between those showing some recovery and those with none. By comparison series of older children with cord compression from neuroblastoma show poorer survival, particularly in those over 1 year of age at presentation, but a much better neurological outcome. Series of patients treated both surgically^{2 4 5} and by chemotherapy alone⁶ have shown neurological recovery in 40–80% of cases. Surgery is not without its complications: significant spinal deformity is reported as affecting up to 60% of survivors after laminectomy.^{4 5} Given this high morbidity and the seemingly poor prognosis for neurological recovery we

would question the usefulness of laminectomy in congenital neuroblastoma with paraplegia.

We would postulate that in this group cord compression must occur antenatally and that by the time of birth, irreversible damage has already occurred.

1 Kenney PJ, Siegel MJ, McAlister WH. Congenital intraspinal neuroblastoma: a treatable simulant of myelodysplasia. *Am J Roentgenol* 1982;138:166–7.
2 Punt J, Pritchard J, Pincott JR, Till K. Neuroblastoma: a review of 21 cases presenting with spinal cord compression. *Cancer* 1980;45:3095–101.
3 Haden MA, Keats TE. Congenital intraspinal neuroblastoma with intraspinal calcification in the neonatal period: report of a case with a 32 year follow up. *Pediatr Radiol* 1983;13:335–8.
4 Traggis DG, Filler RM, Druckman H, Jaffe N, Cassady JR. Prognosis for children with neuroblastoma presenting with paralysis. *J Pediatr Surg* 1977;12:419–25.
5 Holgerson LO, Santulli TV, Schullinger JN, Berdon WE. Neuroblastoma with intraspinal (dumbbell) extension. *J Pediatr Surg* 1983;18:406–10.
6 Sanderson IR, Pritchard J, Marsh HT. Chemotherapy as the initial treatment of spinal cord compression due to disseminated neuroblastoma. *J Neurosurg* 1989;70:688–90.

Omenn’s disease

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Abstract
The importance of accurate pathological diagnosis is emphasised in the case of a newborn infant who presented with alopecia, a generalised erythrodermatous skin eruption, and hepatosplenomegaly. She subsequently developed generalised lymphadenopathy and recurrent septicaemia and died aged 2 months. The histological findings of widespread lymphocytic, histiocytic, and eosinophilic tissue infiltration, associated with thymic hypoplasia, were consistent with autosomal recessive Omenn’s disease.

Omenn’s disease is a rare autosomal recessive reticuloendotheliosis of infancy with similarities

to many other reticuloses but with several distinguishing features of genetic and therapeutic importance. We are unaware of any previously reported cases in the United Kingdom.

Case report
The index case was a girl who was the first child of non-consanguineous parents. The pregnancy and delivery were uncomplicated and her birth-weight was 2830 g. Hair was seen in the liquor and remaining scanty scalp hair was wiped off when she was dried. There was no other bodily hair but a generalised dry scaly rash was present with flexural cracking and extensive serous exudation. Liver and spleen were both palpable 2 cm below the costal margins and the abdomen

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was mildly distended. There were no other problems initially and she was successfully breast fed. After the first week, however, there was progressive deterioration with widespread lymphadenopathy, diarrhoea, ascites, and intolerance of feeds. Five separate episodes of septicaemia were recorded with *Escherichia coli* or *Staphylococcus epidermidis*.

Relevant investigations included: peripheral white cell count of $8.2 \times 10^9/l$ (neutrophils $1.9 \times 10^9/l$, lymphocytes $4.9 \times 10^9/l$, monocytes $0.3 \times 10^9/l$, eosinophils $1.1 \times 10^9/l$). Serum albumin concentration was 26 g/l and globulin 9 g/l. Her concentrations of immunoglobulins were (normal range): IgA 0.3 g/l (0.02–0.15 g/l), IgG 2.5 g/l (3.9–13.0 g/l), and IgM 0.2 g/l (0.09–0.4 g/l). Lymphocyte T and B cell ratios were normal but the thymic shadow was absent on chest radiography. Extensive investigations for metabolic and infective causes were unhelpful.

Examination of bone marrow revealed a normocellular marrow with an increased myeloid:erythroid ratio of 4:1 and abnormally high representation of eosinophilic precursors at 12%. A skin biopsy specimen revealed a band-like lymphocytic infiltrate in the upper dermis with occasional histiocytes and eosinophils. Basal layers of epidermis were involved with exocytosis spongiosis and eosinophilic bodies. Lymph nodes showed considerable depletion of normal lymphocytic populations, the parenchyma displaying prominent nodules of histiocytes. A few poorly cellular follicles remained and intervening fibroblastic stroma contained lymphoid cells, plasma cells, and eosinophils. A liver biopsy specimen revealed non-specific changes with mild fibrosis, cholestasis, and proliferation of biliary ductules. A rectal biopsy specimen displayed normal crypt architecture with normal lymphoid aggregates, and placental histology was unremarkable.

Initially the erythroderma responded to simple emollients with improvement in the cracking and scaling, although the skin remained taut shiny and erythematous. The child failed to gain weight despite the parenteral nutrition, had repeated episodes of septicaemia, and developed progressive ascites. Cardiac failure developed in association with an episode of septicaemia and she died at 2 months of age. In addition to the previous histological findings, postmortem examination demonstrated hypoplasia of the thymus with absent Hassall's corpuscles.

Discussion

The familial histiocytic reticuloses comprise a heterogeneous group of disorders in which the major feature is a proliferation of reticuloendothelial cells with infiltration of tissues. Classification remains difficult and the overlap of

some features such as histiocytic infiltration has led to the confusion of different diseases within the group, particularly familial haemophagocytic reticulosis and Letterer-Siwe disease.

Omenn described 12 infants in whom the major features were onset in the first month of a severe skin eruption followed by hepatosplenomegaly, lymphadenopathy, hypogammaglobulinaemia, and eosinophilia.¹ Failure to thrive and recurrent febrile illnesses progressed to a fatal outcome within six months in all cases. Skin, lymph node, and bone marrow examinations were virtually identical to those described in our case. Similar findings have subsequently been reported,^{2,3} though not previously in the United Kingdom. Further immunological defects, since outlined, include thymic hypoplasia and defective cell mediated immunity.^{3,4}

Familial haemophagocytic reticulosis was first described by Farquhar and Claireaux in 1952,⁵ since when several further cases have been reported. Although histiocytic infiltration of many tissues does occur in this condition the disease is characterised by the phagocytosis of blood cells by histiocytes, a pancytopenia, and in many cases an encephalitic process. Letterer-Siwe disease shares some common features with Omenn's disease, including seborrhoeic skin eruption and tissue infiltration by histiocytes, but is distinguished by its pancytopenia and lack of eosinophilia.

The features of eosinophilia in peripheral blood and bone marrow combined with early presentation of disease characterised by seborrhoeic skin eruption, hepatosplenomegaly and widespread lymphadenopathy, hypogammaglobulinaemia, susceptibility to infection, and rapidly fatal course appear to be unique to Omenn's disease.

The importance of the accurate diagnosis of this condition goes beyond the greater understanding of the disease processes involved. The inheritance has been shown to follow an autosomal recessive pattern in some families,¹ so that the recurrence risk of one in four is considerably greater than for other reticuloses. In addition successful treatment with bone marrow transplantation has now been described.⁶

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- 3 Och HD, Davis SD, Mickelson E, Lerner KG, Wedgwood RJ. Combined immunodeficiency and reticuloendotheliosis with eosinophilia. *J Pediatr* 1974;85:463–5.
- 4 Velders AJ, Kvis W, Va Dijk HA, et al. Omenn syndrome: familial reticuloendotheliosis with eosinophilia and combined immunodeficiency. *Br J Dermatol* 1983;108:118–20.
- 5 Farquhar JW, Claireaux A. Familial haemophagocytic reticulosis. *Arch Dis Child* 1952;27:519–25.
- 6 Junker AK, Ka Wah Chan, Massing BG. Clinical and immune recovery from Omenn syndrome after bone marrow transplantation. *J Pediatr* 1989;114:596–9.