Neonatal tumours: Glasgow 1955-86

C F DAVIS, R CARACHI, AND D G YOUNG

Department of Surgical Paediatrics, Royal Hospital for Sick Children, Glasgow

SUMMARY Fifty one neonatal tumours were diagnosed in Glasgow over a 32 year period. The most common tumours were teratomas (n=19), others being renal tumours (n=9), soft tissue sarcomas (n=8), neuroblastomas (n=7), and others (n=8). Of the total, 31% were malignant. Neonatal tumours pose difficult problems of management, and because of their comparative rarity and the great potential for cure we recommend that all centres dealing with such patients should contribute to and benefit from a Neonatal Tumour Registry.

Tumours in neonates are rare; the incidence in the United States is 3.64/100 000 live births¹ and that in the United Kingdom is 1.70/100 000.² Tumours in children display many features that distinguish them from adult tumours. Neonatal tumours also form a characteristic group. Little is known about factors responsible for the development of tumours in this age group. Genetic factors have been shown to be important in the development of certain retinoblastomas³ and a few tumours have been linked with chromosomal and congenital abnormalities.⁴ Lack of normal immune response by the fetus may be important.⁵ Exposure to ionising irradiation has long been recognised as a carcinogen,⁶ but other environmental factors acting transplacentally probably also have an important role.⁷ The aims of this study were to determine the categories of tumour seen in this age group, to determine the comparative incidence of each tumour, to assess the effectiveness of various treatments, and to see what lessons could be learned for the future.

Methods

We reviewed all solid tumours occurring during the first 4 weeks of life that presented in Glasgow from 1955 to 1986. Leukaemia and tumours of the central nervous system were not included in the study. Fifty one neonates presented with solid tumours: 30 girls and 21 boys. For analysis the tumours were divided into the following categories: teratomas, neuroblastomas, soft tissue sarcomas, tumours of the eye and orbit, hepatic tumours, and miscellaneous tumours as defined by the Childhood Cancer Research Group, Oxford.

Results

The results showed that 16 patients (31%) had malignant tumours and there were 34 survivors (67%). Table 1 shows the number of cases presenting over each time period during the study and the associated mortality. Table 2 shows the number of patients, those with malignant tumours,

Table 1 Number of survivors and deaths in patients with neonatal tumours 1955-86

	No of survivors	No of deaths	Total No
1955-60	2	0	2
1961-65	5	4	9
1966-70	2	3	5
1971-75	0	1	1
1976-80	8	4	12
1981-86	17	5	22
	34	17	51

Table 2 Types of tumour and mortality in patients with neonatal tumours 1955-86

Type of tumour	Total No	No (%) malignant	No (%) of deaths
Teratoma	19	1 (5)	4 (21)
Neuroblastoma	7	7 (100)	4 (57)
Soft tissue sarcoma	8	4 (50)	4 (50)
Renal tumours	9	0	2 (22)
Tumours of eye and orbit	4	3 (75)	0
Hepatic tumours	3	0	2 (67)
Squamous carcinoma	1	1 (100)	1 (100)
Total	51	16 (31)	17 (33)

and the associated mortality in each group. Forty of the cases (78%) presented at birth, three (6%) during the first week, two (4%) each during the second and third weeks, and four (8%) during the fourth week of life.

TERATOMAS

Eighteen of the teratomas were sacrococcygeal and one retroperitoneal. Of the sacrococcygeal teratomas, 15 occurred in girls. All except the most recent (which was diagnosed by prenatal ultrasound) were diagnosed at or soon after birth. Ten were postcoccygeal, seven both precoccygeal and postcoccygeal, and one was pelvic. The patient with a malignant sacrococcygeal teratoma was the only one who had a raised plasma α fetoprotein concentration. Of the 18, 15 (83%) survived; two died from septicaemia, and one from an intraventricular haemorrhage.

One patient had a retroperitoneal teratoma presenting with an abdominal mass. Histological examination at the initial resection showed benign tissue, but after a series of re-explorations over the next two years the patient died of metastatic carcinoma aged 3 years.

NEUROBLASTOMAS

Seven patients had neuroblastomas. Two were stage I, three were stage IVs, and two were stage IV. One localised suprarenal neuroblastoma 5 mm in diameter was noted incidentally at necropsy in a neonate with spina bifida and hydrocephalus who died of meningitis; the other survived after excision of the tumour. Operation in the stage IVs group was limited to diagnostic biopsy and, in one patient removal of the primary suprarenal tumour. All were given cytotoxic drugs, though for one this consisted of vitamin B₁₂ alone, which was fashionable at the time. The only death in this group was caused by cytotoxicity, treatment having been instigated in an attempt to decrease tumour bulk that was causing respiratory distress. Both patients with stage IV disease died without receiving definitive treatment.

RENAL TUMOURS

All nine patients with renal tumours presented with abdominal masses, and all the tumours were mesoblastic nephromas. Of the seven patients who presented before 1967, the initial histological diagnosis was known in three. All were reported as malignant, and one received actinomycin D. Two patients died of early postoperative complications (both in the 1960s) including the patient who received perioperative chemotherapy. Richmond and Dougall⁸ have previously reported the other four cases, all of whom were treated by simple

excision of the tumour and all of whom survived. Our increased knowledge of the pathogenesis of renal tumours presenting in the neonatal period has resulted in the more recent patients being treated more conservatively, that is, by operation alone.

SOFT TISSUE SARCOMAS

There were three rhabdomyosarcomas; the first rapidly deteriorated after birth and at necropsy an extensive rhabdomyosarcoma of the bladder was found.⁹ The second patient, whose mother was being treated with warfarin during her pregnancy, presented with what was thought to be a haematoma of the thigh. Confirmation of the diagnosis of rhabdomyosarcoma was obtained by xenografting a portion of the tumour, and subsequently examining it by electron microscopy. Despite aggressive treatment with cytotoxic drugs and operation the child died of metastases. The third patient, who presented with rhabdomyosarcoma of the lower limb, survived after simple excision of the tumour.

The five mesenchymal tumours were a heterogeneous group, and their management and outcome depended on the site and histological nature of the lesion. One patient presented with a left haemothorax caused by a spindle cell sarcoma in the left lower lobe of her lung. This was successfully resected and then irradiated. Although she made an excellent recovery, she presented six months later with overwhelming pneumococcal pneumonia and pneumococcal meningitis. This was presumably a result of depressed splenic function after radiotherapy in the earlier years of this review, when this risk was not appreciated. Other lesions included a mesenchymal tumour of small bowel, a benign osteocartilaginous mesenchymoma of the chest wall, and a haemangioendothelioma of thigh, all of which were successfully treated by resection alone. One patient presented with congenital neurofibromatosis and died of complications of compression by the tumour mass at the level of the thoracic inlet.

HEPATIC TUMOURS

Three patients presented with hepatic tumours, and they illustrate the problems associated with major operation in this group of patients. Two had resection of haemangioendotheliomas, but both died at early postoperative complications. More recently we have operated on a mesenchymal hamartoma (a less vascular lesion) with a successful outcome, and no residual tumour was found on follow-up examination.

TUMOURS OF THE EYE AND ORBIT

Three patients presented with retinoblastomas; two

of these were bilateral and both had strong family histories. All three were treated with a combination of operation, radiotherapy, and photocoagulation, and all survived. A benign orbital teratoma was successfully treated by enucleation alone.

SQUAMOUS CARCINOMA

A metastasising squamous carcinoma presenting as a mass over the frontal region at birth. The baby rapidly succumbed without treatment.

Discussion

When analysing the data we must consider the factors that influence both complications and survival. Complications fall into several categories. Firstly, the tumour can cause complications by local mechanical restriction of vital functions, or by metastatic disease. Each type of treatment is associated with particular complications. Operations may be complicated by haemorrhage, the necessity for organ resection incompatible with existence, and depression of the immune response. Neonatal tissues have an increased susceptibility to ionising radiation (especially brain, bone, lung, kidney, liver, and spleen) and irradiation can cause depression of the immune response. Neonates are particularly sensitive to cytotoxic drugs, and these also depress the immune response. This series illustrates complications in all the above categories. Campbell *et al*¹⁰ in a review of 102 malignant neonatal tumours also emphasised the difficulties in their management, but confirmed the great potential for cure in this group.

Tumour markers are important in the diagnosis and follow up of patients with solid tumours. The biological markers of clinical value include the tumour associated oncofetal antigen, α fetoprotein, which is useful in hepatic tumours (hepatoblastoma), teratomas, and germ cell tumours.¹¹ The products of tumour or host metabolism may also be useful as tumour markers—for example vanillylmandelic acid and hydroxymethylmandelic acid, which are produced by 90% of neuroblastomas. Inappropriate hormones may be produced, including vasoactive intestinal peptide in some neural crest tumours, and inactive renin in renal tumours of childhood.¹² Useful enzymes include neurone specific enolase, which is a tumour marker in neural crest tumours. Monoclonal membrane markers are as helpful in diagnosing T and B cell lymphomas as they are in neural crest tumours. Tumour markers will have an increasingly important role in diagnosis and monitoring of response to treatment in this difficult group of patients in the future.

Histological grade is an important indicator of

tumour behaviour.⁴ Soft tissue sarcomas, renal tumours, and neuroblastomas may be divided into groups with favourable or unfavourable prognoses.^{13 14} The description of the mesoblastic nephroma by Bolande *et al* in 1967 revolutionised attitudes towards renal tumours in neonates.¹⁵ It is now thought that half of presumed nephroblastomas in infants under 1 year of age are mesoblastic nephromas.

The importance of this review is to identify factors that could help improve survival rates for neonates who will present with tumours in the future. To achieve this, a knowledge of the natural history of histologically diagnosed tumours is vital. Examples include the excellent results achieved with conservative management of congenital mesoblastic nephromas¹⁰ and stage IVs neuroblastomas.¹⁶ Early operation is often the treatment of choice, and intensive supportive care is essential. The lower mortality seen over recent years (table 1) is probably a reflection of improved facilities for intensive care combined with a better understanding of tumour behaviour and knowing when to take a more aggressive approach. Some neonatal tumours in Glasgow, particularly in the early years of the study, have been missed as methods of record keeping have changed; recent figures are, however, more complete. A neonatal tumour registry would greatly improve documentation of these tumours. The overall survival in this study of 67% indicates that these tumours have great potential for cure and deserve to be treated actively in a coordinated way. An enthusiastically supported neonatal tumour registry would greatly assist dissemination of information on methods of treatment and outcome in these uncommon tumours. A neonatal tumour registry would also allow for surveillance of intellectual development, growth, reproduction, detection of second tumours, and identification of families at risk.

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Correspondence to Mr C Davis, Department of Surgical Paediatrics, Royal Hospital for Sick Children, Yorkhill, Glasgow G3 8SJ.

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