

Neonatal tumours

Neoplasms discovered at birth or during the first month of life are rare. Less than half are malignant but these represent a range of disease different from that seen in older children with cancer. Furthermore, some tumours which look malignant histologically may show benign behaviour while apparently benign tumours may be fatal by virtue of their position (for example, in the neck, mediastinum, or brain).

Incidence and aetiology

Estimates of incidence are imprecise. There have been few attempts at a population based assessment, most reports representing the experience of single institutions where selection bias reflects referral patterns. Some lesions raise difficulties of distinction between classification as tumours or as congenital abnormalities and most series exclude lymphangiomas, cutaneous haemangiomas, and uncomplicated melanocytic naevi. In the Third National (US) Cancer Survey (TNCS), Bader and Miller estimated the prevalence of malignancy in the first month of life to be 36.5 per million live births, or about 1:27 000,¹ while a report from the British Paediatric Pathology Society estimated the prevalence of congenital neoplasia (benign and malignant) between 1:12 500 and 1:17 300 total births.² Perinatal tumours accounted for only 2.6% of all neoplasms recorded in a 25 year period at the Children's Hospital of Los Angeles; 40% were malignant.³ This figure is somewhat lower than that from the Hospital for Sick Children, Toronto, where malignancies in the neonatal period accounted for 1.9% of all cases of cancer seen over 60 years.⁴

The aetiology of congenital tumours is unclear but an association with other congenital abnormalities is well recognised.⁵ In some cases intrauterine environmental factors may be important,⁶ and even transplacental spread of maternal tumour has been reported.⁷ There is a need for a detailed, population based study to explore the patterns of neonatal neoplasia and associated malformations more fully and to learn more of their natural history and treatment prospects. Such a study is being prepared by the United Kingdom Children's Cancer Study Group (UKCCSG).

Teratomas

These are the most frequent perinatal neoplasms, accounting for between a quarter and one third of cases.^{2,3} They are very rarely malignant—indeed they did not appear at all in the TNCS report. The sacrococcygeal region is the most common site.^{3,8} It is of interest that although two thirds of all sacrococcygeal teratomas are reported in the neonatal period, the risk of malignancy is small but increases substantially in those diagnosed later in infancy.⁹ Typically sacrococcygeal teratoma (which occurs predominantly in girls) presents as a large cystic but well encapsulated mass extruding from the coccyx, although part or all of the tumour may be presacral. Solid tumours should be viewed with greater suspicion as they are more likely to contain malignant elements.³ Total excision of the tumour is mandatory as histologically benign residual tissue may recur as malignant tumour.⁹

Soft tissue tumours

Benign and malignant soft tissue tumours are relatively common and, grouped together, exceed both neuroblastoma and leukaemia, the two most common malignant diagnoses.³ Tumours of fibrous tissue predominate and account for perhaps two thirds of soft tissue neoplasms in neonates,^{3,10} consisting mainly of the fibromatoses (infantile fibromatosis and myofibromatosis) and fibrosarcoma. They occur particularly in the head, neck, and extremities and are locally aggressive to varying degrees. Although the histological appearance of congenital fibrosarcoma is no different from that observed in the older child or adult, it seldom metastasises and has a good prognosis, although radical surgery may be required to achieve local control.¹¹ Rhabdomyosarcoma, the commonest soft tissue malignancy in older children, is very rare in the neonatal period, although presentation, prognosis, and treatment are similar.¹⁰ Haemangiopericytoma, undifferentiated sarcoma, and leiomyosarcoma have also all been reported in neonates.^{3,4}

Neuroblastoma

Neuroblastoma is the most common type of malig-

nant tumour, accounting for 30–50% of cases in most series.^{3 4 12} An abdominal mass is the commonest presentation either from the primary tumour or liver metastases, while unilateral Horner's syndrome (in cervicothoracic primaries) and spinal compression (in paravertebral tumours) are alternative signs of disease. Most neonates with disseminated neuroblastoma have stage IVS disease (a localised primary with metastatic disease confined to liver, skin, and bone marrow).¹³ Their prognosis is good, many showing evidence of spontaneous disease regression. The mode of treatment can be controversial but should be restricted to the minimum necessary to prevent life threatening complications.¹⁴ The unusually good prognosis of neuroblastoma in very young children is not restricted to those with IVS disease and patients with stage II (postoperative microscopic residual) also benefit from a conservative approach. The unusual biology of neuroblastoma is shown by the description of neuroblastoma in situ, which consists of nests of neuroblastoma tissue in an otherwise normal adrenal medulla, unassociated with gross tumour or metastases. This has been reported in 1:200–1:500 fetal and infant postmortem examinations.¹⁵ The significance is uncertain but is widely believed to represent a potentially malignant neoplasm which can regress spontaneously. Interestingly, there appears to be a high incidence of associated congenital abnormalities in this condition.^{3 15}

Leukaemia

Leukaemia occurs with a frequency somewhat less than neuroblastoma but significantly in excess of other malignant solid tumours. Unlike the disease in older children, acute non-lymphoblastic leukaemia predominates. The diagnosis is not always straightforward and it is important to consider the possibility of haemolytic disease, congenital infection, or disseminated neuroblastoma among the differential diagnoses.¹⁶ There is a well known association with children with Down's syndrome, in whom transient congenital leukaemoid reactions are also seen,¹⁷ although these have also been reported in phenotypically normal newborns.¹⁸ Skin nodules from leukaemic infiltrations are not infrequent and are often associated with monocytic subtypes, for whom an improved prognosis has been suggested.¹⁹ Overall, however, the prognosis is poor and leukaemia accounts for more deaths than any other type of neonatal malignancy.^{3 4}

Brain tumours

About 1% of childhood brain tumours occur in the

neonatal period, an incidence much lower than in later childhood.^{1 3} The commonest presenting features are hydrocephalus, which may be severe enough to cause cephalopelvic disproportion during labour, and vomiting. Differences from the pattern of disease seen in older children include a high incidence of teratoma and a predominance of tumours in supratentorial sites.²⁰ Many neonatal brain tumours are very large at diagnosis and have a high incidence of spontaneous haemorrhage into the tumour mass, factors which contribute to their poor prognosis.²⁰

Renal tumours

These are uncommon in the neonate, although renal masses are not; hydronephrosis and cystic kidneys being the most important non-neoplastic causes. Wilms' tumour occurs but is exceptionally rare and in the past was often confused with mesoblastic nephroma (fetal renal hamartoma).^{21 22} This is generally considered to be a benign condition cured by surgery alone, although local recurrence can occur and one case of metastasis has been reported.²³ True Wilms' tumour occurs much less frequently,²⁴ and both favourable and unfavourable histological variants have been reported. Neonatal diagnosis does not appear to be an adverse prognostic factor. The finding of nephroblastomatosis (nodular renal blastema) in 1:300–1:400 necropsies draws analogies with neuroblastoma in situ, and its role as a precursor of Wilms' tumour has been discussed.²⁵ It is reported in particularly high frequency in children with bilateral tumours.

Liver tumours

Liver masses in the neonatal period are most likely to be non-malignant, haemangioma and mesenchymal hamartoma being the most frequent diagnoses, although their true incidence is unknown as they are sometimes incidental findings at necropsy. The incidence of metastatic neuroblastoma or leukaemia exceeds the frequency of primary malignant liver tumour³ and although 60% of hepatoblastomas occur in the first year of life, diagnosis in the neonatal period is uncommon.²⁶ Typically, liver tumours present as an abdominal mass that may cause respiratory embarrassment. Haemangioma may be associated with anaemia, progressive cardiac failure, and consumptive coagulopathy, and the presence of cutaneous haemangiomas may provide an additional clue.

Retinoblastoma

The presentation of retinoblastoma in the neonatal

period will be influenced by the policy of elective examination of the eyes of children with a family history of the disease. This accounted for almost 25% of children with retinoblastoma in the Toronto series,⁴ which showed an unusually high incidence of neonatal diagnosis (11.5% of all cases known to the hospital). Most had bilateral tumours consistent with the inherited form of the disease.

Histiocytic syndromes

Langerhans cell histiocytosis (histiocytosis X) is no longer considered to be a neoplastic process²⁷ and its presentation in the neonatal period is distinctly uncommon.³ Haemophagocytic lymphohistiocytosis, although very rare, is usually familial and may present very early in infancy.²⁸

Management

Neonatal tumours present particular difficulties, although the broad principles of managing malignant disease are the same as in older children. The special behaviour of neonatal neuroblastoma and the relatively benign nature of infantile fibrosarcoma provide examples of a need for a conservative approach. Surgery plays the major part in the management of benign, and many malignant, tumours. The role of chemotherapy and especially radiation must be carefully considered on an individual basis. Drug doses should be calculated according to body weight rather than surface area and started at reduced levels, increasing as tolerated.²⁹ The use of radiation treatment is of concern in view of the extreme immaturity of normal tissues and the potential for late effects on growth and the risk of second malignancy.³⁰ There is increasing interest in the use of chemotherapy rather than radiation for the treatment of infants with brain tumours³¹ and in the need to replace or defer radiation as prophylactic treatment of the central nervous system in infants with leukaemia.³²

Neoplasia in the neonate is uncommon and the pattern of disease so unusual that treatment must be 'tailored' for each baby. Nevertheless, a large number of children can be successfully treated although most, including many with apparently benign disease, would benefit from the diagnostic and therapeutic resources of a paediatric oncology centre.

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