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Overview

Management of Central Nervous System Tumours in Children

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Abstract

This article reviews current approaches to management of central nervous system tumours of childhood, highlighting aspects particularly pertinent to the paediatric population.

Key words: Brain; paediatric; radiotherapy; tumours

Introduction

Primary central nervous system tumours are the most frequent solid tumours and the most common cause of cancer-related morbidity and death in childhood (Figure 1). They constitute a heterogeneous group of diseases in terms of histology, biology, clinical course and prognosis. Compared with adult practice, a different spectrum of histological subtypes is seen, reflecting the different stage of development of the nervous system during which tumours arise. Histologically low grade pilocytic astrocytomas are the most frequently occurring, while medulloblastomas are the most common malignant brain tumour. Conversely, high grade astrocytic tumours seen frequently in adults are relatively uncommon in children. In paediatric neuro-oncology practice significant numbers require the technically challenging technique of craniospinal RT. In common with adult practice an understanding of tumour molecular biology is now in the process of being incorporated into decision making in addition to conventional pathological parameters. However, these molecular biological features frequently differ between adult and paediatric series despite similar appearances on conventional histology. There are important overlaps with adult practice with respect to neurosurgery and imaging.

Management of brain tumours in children is highly specialised and should only be carried out by specialist MDT's in accredited centres. Radiotherapy, normally integrated with surgery and chemotherapy in treatment protocols, continues to play a pivotal role in spite of concerns regarding late effects. Particular challenges for the paediatric clinical oncologist include immobilisation of the young, uncooperative child, psychosocial aspects and the organisation of long term follow up. Modern radiotherapy approaches are evolving to improve the therapeutic ratio including hyperfractionation, IMRT and proton therapy. An improved understanding of molecular biology may enable individualisation of management in the future.

Epidemiology

In the UK, the incidence of childhood CNS tumours is reported as 31.4 per million [1]. The cause of most (95%) is not known but there are well recognised risk factors. These include a family history of brain tumour, exposure to ionising radiation (in particular prior therapeutic CNS irradiation) and familial genetic syndromes (for example, neurofibromatosis 1 and 2, tuberous sclerosis, Von Hippel Lindau disease, Li Fraumeni and Gorlin's syndrome) [2]. CNS tumours are more common in males.

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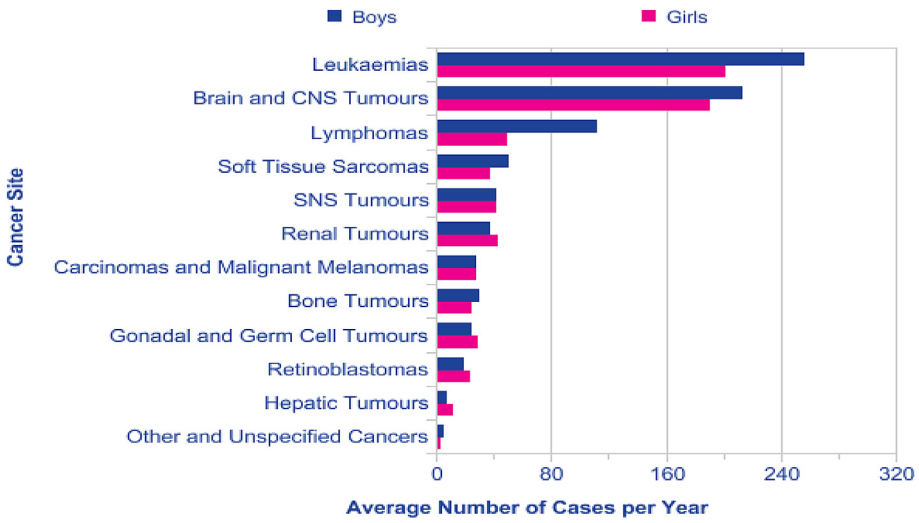

Fig 1. All childhood cancers, average number of new cases, children (0–14), great Britain 2006-2007 (source CRUK http://www.cancerresearchuk.org/cancer-info/cancerstats/childhoodcancer/incidence/).

Pathological Classification

Pathological classification is according to the 2007 WHO classification of tumours of the nervous system and is based on histology (Table 1) [3].

Over 90% of CNS tumours originate in the brain. Of these, astrocytomas constitute approximately 43% and these are most frequently low grade lesions. Approximately 19% are embryonal tumours, three quarters of which are medulloblastomas and which are more frequent in younger children. Ten percent of CNS tumours in childhood are ependymomas and choroid plexus tumours with the greatest incidence in very young children [4]. In contrast with the adult setting, high grade gliomas occur relatively infrequently and appear to be biologically distinct from those occurring in adulthood [5].

Molecular profiling of paediatric brain tumours provide opportunities to further enhance understanding of tumour biology. It is anticipated that integration with clinical and histological data in prospective clinical trials may enable further risk stratification and create new opportunities for individualised therapy as well as new therapeutic targets [6].

Clinical Features

Presenting symptoms include those of raised intracranial pressure such as morning headache and vomiting, visual disturbance, cranial nerve palsies, ataxia, impairment of motor skills, seizures, endocrine, growth abnormalities and lethargy. Very young children may present with failure to thrive or irritability. As the symptoms of a brain tumour are often non-specific other, more common diagnoses are often explored initially and delayed diagnosis is a well recognised problem internationally [7]. Once a brain tumour is suspected, imaging to confirm the presence of a space occupying lesion should be initiated with minimum delay. Contrast enhanced MRI is the imaging modality of choice but where this is not readily available a CT scan is acceptable as initial imaging. There is increasing recognition that advanced imaging techniques such as MR spectroscopy, perfusion MRI, functional MRI, diffusion tensor imaging and tractography may assist in diagnosis and in treatment planning [8,9].

Management

Management of children with brain tumours requires a well-organised multidisciplinary approach in specialist centres experienced in the management of these diagnoses [10]. In the UK children should only be treated at a Children's Cancer and Leukaemia Group (CCLG) accredited centre subject to peer review according to the standards outlined in National Institute for Health and Care Excellence (NICE) Improving Outcomes Guidance (IOG) [11]. This defines a series of multidisciplinary and multiprofessional standards for management of the patient and family. Recommended standards for radiotherapy centres are also outlined in the CCLG/Royal College of Radiologists (RCR) Paediatric Good Practice Guide [12].

The NICE IOG and CCLG/RCR guidelines recommend that the team caring for a child with a brain tumour should comprise paediatric and clinical oncologists, neurosurgeons, radiologists, endocrinologists, ophthalmologists, neuropathologists and specialist nurses. There should also be ready access to neuropsychologists and clinical psychology, paediatric radiographers, play therapists (or child life specialists), an anaesthetic team and a rehabilitation team including physiotherapy, OT and speech therapy.

The aims of treatment should be to maximise tumour control and minimize toxicity (in particular long term effects) through judicious incorporation of the three main modalities of surgery, radiotherapy and chemotherapy into treatment protocols preferably within the context of a clinical trial [13].