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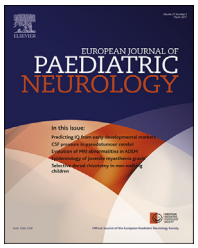

Original article

Where are the opportunities for an earlier diagnosis of primary intracranial tumours in children and young adults?

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ABSTRACT

Background: Childhood brain tumours have some of the longest time to diagnosis. A timely diagnosis may have a role in reducing anxiety in waiting for a diagnosis and subsequent morbidity and mortality. We investigated where the opportunities for an earlier diagnosis were, and for which anatomical locations this strategy will most likely to be effective.
Methods: A record-linkage cohort study of patients diagnosed aged 0–24 years with a primary intracranial tumour between 1989 and 2006 in England, using records from the National Cancer Registry linked to hospital admission records from Hospital Episode Statistics (HES, 1997–2006) and primary care consultation records from Clinical Practice Research Datalink (CPRD, 1989–2006). Relevant neurological presentations were extracted from HES and CPRD. Temporal changes in presentation rates were estimated in generalised additive models.
Results: Frequency of presentation began to increase six months before diagnosis in primary care and three months before diagnosis in hospital. Supratentorial and midline tumours had the longest presentation history before diagnosis. Peri-ventricular tumours presented frequently in hospital (rate ratio = 1.29 vs supratentorial tumours; 95% CI = 1.12–1.48) or as an emergency (1.24; 1.01–1.51), and in primary care (1.12; 0.62–1.85).
Conclusions: Opportunities for an earlier diagnosis are greater in supratentorial, midline or cranial nerve tumours, which have a longer presentation history than peri-ventricular, cerebellar or brainstem tumours. Common features before diagnosis include headache, convulsions, and growth or endocrine disorders. Focal neurological deficits are uncommon and emerge late in the pre-diagnosis period.

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1. Introduction

Primary intracranial tumours account for 25% of all childhood cancers, and are associated with the greatest number of cancer deaths.[1] This has generated substantial interests in improving the prognosis of intracranial tumours through earlier detection,[2–8] and culminated in the identification of early diagnosis as one of the top 10 priorities for clinical research in neuro-oncology by The James Lind Alliance and by the National Cancer Research Institute Brain Supportive and Palliative Care sub-group in the United Kingdom.[9] The James Lind Alliance is a non-profit making initiative bringing together patients, carers and clinicians to identify unanswered questions that they agree are most important.[10]

Evidence on early diagnosis of intracranial tumours in children and young adults, and particularly its relationship with survival, is scarce because of the logistical cost in recruiting sufficient patients to create a traditional cohort for identifying earlier diagnostic opportunities. Advances in statistical methodology and computing power in linking routinely collected patient care records have enabled creation of a population-based cohort with histologically verified intracranial tumours for examining temporal changes in the symptoms and signs at each primary care or hospital visit, thus allowing us to investigate if an earlier diagnosis of an intracranial tumour would have been possible.[11–14] Our aims are to investigate if such opportunities were limited to tumours in certain locations or existed uniformly for tumours in any location to tailor recommendations on early diagnosis for specific intracranial neoplasms. This will provide evidence for a more focused approach in developing guidelines and evaluating interventions on early diagnosis to achieve the maximum possible effect in the population.

2. Patients and methods

We identified patients aged 0–24 years when diagnosed in England with a benign, borderline or malignant primary intracranial tumour from the National Cancer Registry. We have included patients up to the age of 24 years as those patients are often managed in specialist teenage cancer units in the United Kingdom.

Intracranial tumours were defined as those with a relevant morphology (diagnostic groups III, IX.b.2, IX.d.8 and X.a in the third edition of the International Classification of Childhood Cancer[15]) and arising from one of the following sites (the 9th or 10th revision of the International Classification of Diseases, ICD[16,17]): the supratentorial compartment, midline, cerebellum, brainstem, ventricular system, meninges, cranial nerves and other intracranial sites. Records were excluded if they contained invalid dates or unknown sex or vital status. Records which failed Office for National Statistics validity checks, those of secondary or metastatic tumours, synchronous or multiple primary tumours were also excluded.[18]

We obtained records of primary care consultations between 1989 and 2006 from Clinical Practice Research Datalink (CPRD), a database of longitudinal records of primary care consultations from over 600 practices from anywhere in the UK.[19,20] Patient data in CPRD are representative of the UK population in age, sex and ethnicity (compared with UK Census 2011), with high level of validity in data on diagnoses (over 95% of cases confirmed in internal and external validations for neoplasms).[20,21] We also obtained records of admissions between 1997 and 2006 from Hospital Episode Statistics (HES), which collates data on in-patient stays in National Health Service (NHS) hospitals in England.[22] CPRD and HES records were linked to the National Cancer Registry by matching on NHS number, sex, date of birth and postcode.[23,24]

2.1. *Presentation rates*

Over 800 clinical features relevant to an intracranial tumour presentation were identified from manually searching the list of Read and ICD-10 codes.[25] Read coding is a hierarchical system for coding symptoms, signs, diagnoses, interventions and administrative events in primary care. We retained for analysis records of primary care or hospital visits containing one or more coded features that may be explained by the presence of an underlying intracranial tumour. Each episode of hospital stay was also classified as "non-emergency" or "emergency" based on how the patient was admitted. An emergency admission came from any of the following sources: the Accident and Emergency department, general practice (direct admission or after consulting the duty hospital doctor), outpatient clinics, or by urgent transfer from another hospital.

We calculated presentation rate, which was the unit of analysis, by dividing the number of visits by observation time. Changes in the pattern of hospital presentations were estimated using a cohort of patients with linked HES records, and changes in the pattern of primary care presentations were estimated from a separate cohort of patients with linked CPRD records. The observation time for each patient in HES began on the later of the date of birth or the start date of the HES data and ended with the earlier of the date of death or the end date of HES data. The observation time in CPRD began on the date of registration with the general practice (most took place within a few weeks after birth) and ended with the earliest of the date of death, transferring out (if a patient had moved to a practice not contributing data to CPRD) or last collection date (when a practice last submitted data to CPRD). Presentation rates may thus be interpreted as the number of visits per month in a cohort of 100 patients. We described temporal changes in the presentation rates from the date of diagnosis in the National Cancer Registry for 0–1, 1–3, 3–6, 6–12 and over 12 months in the main text.[26,27] But Since time from diagnosis when patients presented is continuous in nature, we have also illustrated changes in presentation rate graphically (in Supplemental materials) to overcome the arbitrariness of dividing time into intervals, especially for presentations that took place exactly at the boundary of those intervals. Although we are primarily interested in presentations before the diagnosis of an intracranial tumour, presentations after diagnosis have been included for two reasons: (a) to demonstrate, rather than to assume, that the intensity of healthcare use falls after a diagnosis and thus emphasise the importance of reaching a correct diagnosis; and (b) to reduce statistical uncertainty in estimating rates around the time of diagnosis