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Why are brain tumours still being missed?

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Abstract

The prediagnosis period of 74 children with primary brain tumours was assessed to examine their presentation and reasons for any delay in diagnosis. Medical case notes were reviewed and parents were interviewed and asked to complete psychological questionnaires. Mean (SD) duration of clinical history was 20·0 (29·1) weeks. Most common symptoms were vomiting (65%) and headache (64%). Only 34% of headaches were always associated with vomiting and only 28% occurred 'early morning'. Changes in the child's personality (47%) were also common. The average number of consultations before diagnosis was 4·6. Migraine was diagnosed in 24% of children and a psychological aetiology in 15%. One quarter of the children had altered levels of consciousness on arrival at the unit. Results indicate that delay in diagnosis still occurs, despite strong parental concern. The non-specificity of symptoms and a high incidence of psychological symptoms may confound the clinical picture and are considered along with other possible contributory factors.

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Previous studies have indicated delays in the diagnosis of childhood brain tumours. Half of the children studied by Gjerris had a clinical history of more than six months, and delay was significantly longer in supratentorial compared with infratentorial tumours.[1] Flores *et al* found a mean interval of 26 weeks between symptom onset and clinical diagnosis compared with a mean of 4·5 weeks in acute leukaemia and 2·8 weeks in Wilms' tumour.[2] They reiterated the non-specificity of symptoms associated with childhood brain tumours but recommended that a high level of suspicion accompanied by thorough neurological examination and neuroimaging should lead to earlier diagnosis.

In their review of the nature of headaches accompanying brain tumours in children Honig and Charney emphasised the importance of neurological and ocular examination.[3] They outlined a diagnostic approach to the assessment of childhood headaches, which in conjunction with more aggressive use of computed tomography, would potentially have diagnosed brain tumours in 96% of patients within four months of headache onset. Barlow drew attention to the importance of changes in behaviour or in school performance, with or without headaches,[4] and Gjerris noted the frequency of changes in mood and behaviour in the presentation of childhood brain tumours.[4] In his experience, however, these symptoms rarely led to admission.

Given these findings and the increasingly widespread availability of neuroimaging, diagnosis would perhaps nowadays be expected at an earlier stage. In our experience this was not the case. In an effort to identify where, and how, delay occurs, the duration and characteristics of symptoms and signs, and the nature of consultations before diagnosis were examined in a group of children with primary brain tumours.

Patients and methods

A retrospective study was undertaken of 74 children, aged 0–16 years, with primary brain tumours admitted consecutively to the Maudsley Neurosurgical Unit in London between 1990 and 1994.

METHODS

Medical case notes and histopathology reports were reviewed and the parents of all living children contacted by letter. The Office of Population Censuses and Surveys was consulted for death registrations, in which event the general practitioner was telephoned before contacting the parents.

A semistructured parental interview was used to gain information on symptoms and signs, their duration before diagnosis, and the nature of consultations with health professionals.

GRADING OF SEVERITY

Severity of symptoms and signs on presentation to the neurosurgical unit was graded as: grade 1 symptoms only; grade 2 symptoms plus papilloedema; grade 3 as grade 2 plus focal neurological deficits; and grade 4 decreased level of consciousness.[2]

PSYCHOLOGICAL QUESTIONNAIRE

At interview parents were asked to complete a questionnaire detailing any changes in their child's psychological functioning in the six months before diagnosis. For the 5–16 year olds parents completed the modified Rutter parent questionnaire[5]: an expanded version of the original for school age children.[6] It contains 40 items inquiring about the child's behaviour in addition to items on health and habits and can be scored for hyperactivity, emotional disorder, conduct disorder, prosocial behaviours, and total deviance.

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Table 1 Mean duration of clinical history in weeks

Population	*Symptom onset to diagnosis**	*Initial consultation to diagnosis**	*Symptom onset to diagnosis*
All children (n=74)	3	16	20
Currently alive (n=60)	3	17	23
Died (n=14)	1	8	13
Age (years)			
0–2 (n=13)	2	3	6
2–5 (n=15)	3	12	19
5–16 (n=46)	5	30	34
Children presenting with:			
Headache and vomiting (n=38)	5	19·5	23
No headache or vomiting (n=15)	1·5	15	16·5
Headache, no vomiting (n=9)	1	7·5	29
Vomiting, no headache (n=9)	1	9	10
No headache (n=24)	1	13	14
Morning headache and vomiting (n=7)	2	22	24
Nocturnal headaches (n=9)	1	27	27
Psychological symptoms (n=16)	7	25	31
No psychological symptoms (n=35)	2	15	20

*Incomplete data – not all parents were approached.

The Richman's behaviour checklist,[7] a modified version of the behaviour screening questionnaire,[8] was used for the 2–5 year olds. This uses the same 12 items of behaviour but is completed by parents.

None of the existing questionnaires adequately covered the range of symptoms indicative of brain tumour in the 0–23 month group[9] and we therefore devised our own. Many items were extrapolated from other checklists while a few new items were included bearing in mind the age of the sample and the diagnosis.

Ethical approval was granted by the ethical committee of the Bethlem Royal and Maudsley Hospitals. Information was analysed using Epi-Info (version 5).

Results

SURVEY STATISTICS

Medical case notes and histopathology records of all 74 children were available for inspection. There was an 88% response rate to the initial letter sent to the parents of surviving children; of whom two declined to participate. Fourteen children had died. In discussion with general practitioners it was considered inappropriate to contact parents of four of these children, and the family of a fifth could not be located. Of those contacted, six agreed to participate in the study and three declined. Thus the overall participation rate was 80%. Complete psychological data were available for 90% of these.

PATIENT CHARACTERISTICS

The ages ranged from 0–16 years (mean (SD) 6·9 (4·5) years, mode 10 years). The male:female ratio was 1:1·5. Sixty three of the 74 children were white, five Afro-Caribbean, four Oriental, and two were of mixed race. Of the parents on whom information was available, English was the first language in 90%.

TUMOUR LOCATION

The ratio of supratentorial to infratentorial tumours was 1:1·3. The most common location was the cerebellum 42%. Twenty one per cent were midline and 13% in the brainstem.

DURATION OF CLINICAL HISTORY (TABLE 1)

This ranged from less than one week to 130 weeks (mean (SD) 20·0 (29·1) weeks). One month after symptom onset 68% children were not yet correctly diagnosed and after six months 20% were still not diagnosed. The mean (SD) duration of signs and symptoms before parents consulted a health professional was 3·0 (13·4) weeks (range 0–104 weeks). In 92% of cases parents took their child to a doctor within one month of symptom onset. The mean (SD) duration of clinical history between initial consultation with a health professional and clinical diagnosis was 16·0 (24·4) weeks (range 0–130 weeks). One month after initial consultation 58% of children had not yet been diagnosed and 18% were yet to be diagnosed six months after initial consultation. Although supratentorial tumours had a longer clinical history than infratentorial, and benign longer than malignant, the differences were not significant.

CONSULTATIONS BEFORE DIAGNOSIS

Before diagnosis there was a total of 257 (mean 4·6; range 1–12) consultations with professionals in the 56 children for whom this information was available. Of these, 45·5% were with a general practitioner and 9% with an accident and emergency department. Seven children were referred for scanning after first consultation, but 62% were seen on four or more occasions before the correct diagnosis was made. In 35% a second opinion was requested, and 10% of parents arranged private consultations. Other health professionals consulted were: paediatricians (13%), opticians (9%), neurologists (2%), and psychologists (1%). Two children had inappropriate lumbar punctures.

Doctors were unable to make a diagnosis in 19% of children and in a further 15% could find nothing wrong. Symptoms and signs were confused with those of migraine in 14 children. A psychological aetiology was proposed in 13 and a virus or allergy in nine.

In 11 of the 52 schoolchildren teachers had noticed deteriorating school performance. Others had problems with balance, or complained of being unwell at school, but not all parents had been informed of these concerns.

FREQUENCY OF SIGNS AND SYMPTOMS (TABLES 2 AND 3)

On presentation to the neurosurgical unit 7% of children were classified as grade 1, 20% as grade 2, 47% as grade 3, and 26% as grade 4.

Vomiting occurred in 65% and headache in 64% of the children. Detailed analysis of those with headaches showed: a mean (SD) duration of 21 (34) weeks (range 0–130 weeks); 34% were always associated with vomiting; 47% were sometimes associated with vomiting; 16% were never associated with vomiting; and 3% had pernicious vomiting. In 33% of cases headaches increased in severity; 15% were early morning and associated with vomiting; 27% increased in both severity and frequency;

Table 2 Frequency of signs on presentation to neurosurgical unit

Presenting signs	*No (%) of children*
Gait ataxia	36 (49)
Decreased level of consciousness/drowsiness	35 (47)
Papilloedema	28 (38)
Visual field defects	19 (26)
Hemiplegia	12 (16)
VI nerve palsy	10 (14)
Torticollis	8 (11)
Increasing head size	7 (9)
Diplopia	6 (8)
Sunsetting	4 (5)
Proptosis	1 (1)
Unequal pupils	1 (1)

Table 3 Frequency of symptoms before diagnosis

Presenting symptoms	*No (%) of children*
Vomiting	48 (65)
Headache	47 (64)
Changes in personality and mood	35 (47)
Squint	18 (24)
Out of character behaviour	16 (22)
Deterioration of school performance	11 (21)*
Growth failure	15 (20)
Weight loss	12 (16)
Seizures	12 (16)
Developmental delay	12 (16)
Disturbance of speech	8 (11)
Polyuria/polydipsia	5 (7)
Collapse	4 (5)
Abdominal pain	2 (3)

*Out of 52 school aged children.

60% occurred every day; 27% occurred most days; 45% had no diurnal pattern; 27% occurred in the morning; 27% occurred at night; and 59% interfered with activity and were not relieved by simple analgesia. There was no relationship between site of tumour and location of headache and the nature of pain was very variable.

PSYCHOLOGICAL RESULTS (TABLE 4)

Initial symptoms were psychological or behavioural in 52% (33% of 0–2 year olds, 80% of 2–5 year olds, and 47% of 5–16 year olds) of children in whom information was available. The prevalence of psychological difficulties in the 5–16 years age group using the Rutter questionnaire was 48%. The total deviance score (cut off point 13) ranged from 3–40/62 with a mean (SD) of 14·5 (8·7). The scores for Richman's behaviour checklist for children aged 2–5 years indicated that 31% of children had psychological difficulties. The range of scores was 3–16/16 (cut off point 10) with a mean (SD) score of 8·0 (4·1). The range of scores derived from the checklist for children aged 0–2 was between 1–9/15 with a mean (SD) of 5·3 (3·4). Table 4 shows the most common concerns of parents for each age group. There was no relationship between site of tumour or duration of clinical history and incidence of psychological difficulty for any age group.

MORTALITY AND MORBIDITY

The mortality rate was 17%. There were no perioperative deaths. The high morbidity before diagnosis was reflected in the duration and/or severity of symptoms and in the often harrowing accounts given by parents at interview. Of the children with papilloedema two remained permanently blind in spite of a good tumour prognosis.

Discussion

We found considerable delays in the diagnosis of brain tumours in children. The early and repeated presentation of children to health professionals suggest that parental concern is a good indicator of the need for further assessment. Headaches in children with brain tumours are variable in quality and can deviate considerably from the pattern of early morning headaches associated with vomiting. Changes in personality and behaviour were common and may direct attention from the underlying problem.

Important features of this study are the high participation rate and the representative nature of the sample. It includes a wide range of tumour histopathologies and there is no significant difference in age and sex distribution from that reported by previous studies. The study is unique in using a parental interview to supplement information gathered from medical records. Nevertheless retrospective studies which interview parents at various intervals after diagnosis have the potential to be biased. However, analysis revealed that the pattern of answers was unrelated to time from diagnosis and concurred significantly with information from medical records. The psychological checklist for the 0–2 year olds has not been validated but was specific for the types of symptoms reported as being associated with brain tumours in this age group.

A striking finding is the variability in presentation. Only 31% of cases presented to the neurosurgical unit with the classical triad of headache, vomiting, and papilloedema. Early morning headaches occurred in only 27% of children and only a third of headaches were always associated with vomiting. The prevalence of psychological and behavioural presenting symptoms is higher than reported in previous studies. There was an age difference in the nature of psychological difficulties: in younger children these were behavioural while older children experienced more emotional problems.

Results indicate that delay can occur at every stage and in every age group. Only seven children presented initially with vomiting accompanied by headache and were immediately referred for neuroimaging by their general

Table 4 Changes in personality and behaviour in six months before diagnosis; figures are number (%)

0–2 Years (n=9)		*2–5 Years (n=13)*		*5–16 Years (n=31)*	
Became sleepy	6 (67)	Eating habits	12 (92)	Anxious	24 (77)
Irritable	5 (56)	Temper tantrums	10 (77)	Mood swings	21 (68)
Disrupted sleep pattern	4 (44)	Sleeping pattern	8 (62)	Poor concentration	20 (65)
Cried more than usual	4 (44)	Speech problems	7 (54)	Solitary behaviour	19 (61)
Demanded more attention	4 (44)	Management problems	6 (46)	Irritable	17 (55)
		Encopresis	4 (31)	Appeared unhappy	17 (55)

practitioner. In the majority prompt referrals were incidental, for example, resulting from a routine paediatric consultation or investigation after head injury. The interval between symptom onset and diagnosis was shortest for children aged 0–2 years despite there being no significant difference in the histopathology, grade, or location of tumours, or parental persistence (number of consultations before diagnosis) across age groups.

The reasons for delay in diagnosis in the remainder of the children appear multifaceted. Headaches appear to present particular diagnostic difficulty. Migraine was an initial diagnosis in 19% of children in the study (half of all those who presented with headache) compared with a prevalence in the school population of about 10%.[10] The mean interval from symptom onset to tumour diagnosis in this group was 31·5 weeks and 92% had headaches which increased in frequency and severity and progressed to nocturnal awakening – characteristics which should trigger referral for neuroimaging.[3]

Change in psychological functioning was the first symptom in over half the children and resulted in a delay in diagnosis. Behavioural difficulties in young children and emotional difficulties in older children are common in the normal population, and a number of parents had not acted on them until their child developed physical symptoms.

Parental interviews indicated that sometimes poor communication between professionals contributed to the delay in diagnosis. Some parents had not been told of a deterioration in their child's school performance until after the correct diagnosis was made. A significant number reported that medical professionals looked at the presenting symptoms of each consultation in isolation. It appears from clinical data and parental interview that it is the overall pattern of symptoms rather than individual episodes which indicates the need for further investigation. There were also difficulties between parents and professionals, and some parents felt that they were being a nuisance or 'neurotic'.

In conclusion, our findings suggest that sustained parental concern about symptoms suggestive of an intracranial neoplasm should lead to an early referral. Careful note taking, review of recent consultations, and improved communication between general practitioners and other professionals including opticians, psychologists, and teachers should provide an improved picture of the child's functioning and contribute to earlier diagnosis. School health services could provide a mechanism whereby any anxieties that teachers have about children are investigated and information passed on to parents and general practitioners.

The International Headache Society has produced criteria for the diagnosis of migraine. Despite variability in the presentation of childhood headaches these criteria have generally been found to be an adequate diagnostic tool.[10] Severe recurrent headaches not meeting these criteria require careful monitoring. Psychological and behavioural changes are often a factor in the presentation of childhood brain tumours, and although these are fairly typical of childhood and teenage years, the possibility of an organic aetiology must be appropriately pursued[11] before assuming a psychogenic basis.

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