Referral guidelines for suspected central nervous system or brain tumours

A J Larner

If the evidence base for referral guidelines is unfavourable they should be abandoned

The proposition that the early diagnosis of brain tumours is desirable is one with which few, if any, neurologists would disagree. Concerns about delayed diagnosis are also a common theme among patients.¹ Although consensus may be lacking about optimal treatment in certain situations such as low-grade glioma, early identification at the least permits monitoring, and at best may improve prognosis. However, the best method for the early identification of central nervous system (CNS) tumours remains uncertain, as the possible presentations are diverse and overlap with many other neurological conditions.

In 1997, the UK government issued a white paper entitled *The New NHS – Modern, Dependable* (Department of Health, HMSO), which guaranteed that everyone with suspected cancer would be able to see a specialist within 2 weeks of their general (primary care) practitioner deciding that they needed to be seen urgently and requesting an appointment. Initially implemented for breast cancer, the 2-week policy (also known as the 2-week standard, 2-week rule or 2-week wait) was later implemented for many other tumour types, including CNS or brain cancers. In *Referral guidelines for suspected cancer*, published by the UK Department of Health (DoH) in 2000, the indications for urgent referral were specified (box).²

It is probable that few neurologists would dissent from these indications, although acknowledging the breadth of neurological conditions potentially encompassed by them: the predictive value of many of these presenting symptoms in primary care is unknown. The document acknowledged the need to achieve a balance between setting the threshold for referral too high, hence missing patients with tumours (ie, low sensitivity), or too low, and hence including many people without tumours (ie, low specificity). From the medicolegal perspective, it was acknowledged that the guidelines were not mandatory

(true of any forms of guidance) but represented “best available evidence”. How have they fared in clinical practice?

The need for audit and review of the DoH guidelines was acknowledged from the outset; it was envisaged that “monitoring ... in practice will generate a vast amount of new information which should be used to revise the guidelines in the future”.² A retrospective audit of the “cancer fast track” guidelines for CNS or brain cancer covering a 9-month period in 2000–2001, immediately after their implementation, was undertaken in a tertiary referral centre (Queen’s Medical Centre, Nottingham) and a district general hospital (Derbyshire Royal Infirmary, Derby). It identified 43 referrals (ca 5/month; no denominator was provided to allow calculation of the proportion of all referrals). A significant number (13/43 = 29%) did not conform to the guideline criteria (box), and the “hit rate” for CNS or brain tumour identification was low (4/43 = 9%). The commonest diagnoses seen were chronic daily headache (10), epilepsy (5) and migraine (3). Concurrently, at least 69 patients with CNS or brain tumours were identified in the same geographical region independent of the 2-week system. These data prompted a call for early reassessment of the 2-week policy in neurology.^{3,4}

The disappointing findings of the Nottingham and Derby audit might simply reflect the time necessary for general practitioners to become familiar with new guidelines, with which they are swamped.⁵ As no subsequent examination of the CNS or brain cancer guidelines has been identified, a further audit was undertaken to assess how they have become integrated into clinical practice 4 years after implementation. This was a prospective audit, over an 18-month period (2 August 2004–1 February 2006 inclusive), in one district general hospital (Halton) in northwest England. Because of the time constraints imposed by the guidelines, referral letters were not seen by the

neurologist before the booking of out-patient appointments. Of 482 new patient referrals seen by one consultant neurologist, 10 (2.1%; 95% confidence interval (CI) = 0.8% to 3.3%), were referred under the auspices of the 2-week policy (M:F = 3:7, age range 36–72 years, median 46 years). Nine patients had headache; one had limb pain and weakness secondary to a longstanding back injury, the general practitioner querying a diagnosis of multiple sclerosis. No patient conformed to the referral criteria (box). Final diagnoses in the patients with headache, using internationally agreed diagnostic criteria,⁶ were chronic tension-type headache (n = 5), chronic migraine (n = 1), drug overuse headache (n = 2) and frequent tension-type headache (n = 1). The other patient had no clinical or investigative evidence of multiple sclerosis. Hence, compared with the previous audit,^{3,4} this study found a lower rate of referral under the guidelines (<1/month v >4/month); a higher proportion of referrals not conforming to guideline criteria (100% v 29%); and a lower “hit rate” of CNS or brain tumour identification (0% v 9%). This audit might therefore be taken to suggest that there is no evidence for the efficacy of the guidelines in identifying CNS or brain tumours in this location, despite the time elapsed for general practitioners to become familiar with them.

The parochial nature of these two audits precludes easy extrapolation to the national situation; there may be (unreported) localities where the 2-week policy for CNS or brain cancer works extremely well, and the National Institute for Clinical Excellence, which is undertaking the revision of the guidelines for publication in 2006, may be party to “a vast amount of new information”. To inform any judgements on the guidelines, it would be desirable to expand the evidence base with large audits, ideally prospective, which allow the calculation of sensitivity, specificity, positive and negative predictive values, as for any diagnostic test. Furthermore, it would be desirable to show that cancers identified through this scheme were not only treated more quickly but also had a better outcome than those identified by standard routes.

In the absence of additional data specific to CNS or brain cancer, experience using the 2-week referral guidelines in other areas of medicine might be examined to ascertain whether the problems are generic, or specific to neurological practice. The published data relate mostly to gastrointestinal, breast and urological cancers. For example, a study of the first year’s workings

Box: Brain tumours—guidelines for urgent referral

- Subacute progressive neurological deficit developing over days to weeks (eg, weakness, sensory loss, dysphasia and ataxia)
- New onset seizures characterised by one or more of the following:
 - focal seizures
 - prolonged postictal focal deficit (>1 hour)
 - status epilepticus
 - associated interictal focal deficit
- Patients with headache, vomiting and papillo-oedema
- Cranial nerve palsy (eg, diplopia, visual failure, including optician-defined visual field loss, unilateral sensorineural deafness)
- Consider urgent referral for patients with non-migrainous headaches of recent onset, present for at least one month, when accompanied by features suggestive of raised intracranial pressure (eg, woken by headache, vomiting and drowsiness)

of the 2-week policy in a gastrointestinal unit, including >700 referrals, found that 17% of upper gastrointestinal and 16% of colorectal referrals had a malignancy; 22% and 28% of referrals were inappropriate according to the referral guidelines; and 64% and 62% of malignancies seen over the year presented outside of the scheme. In the mean time, routine outpatient waiting time rose from a median of 9.3 to 15.6 weeks, despite ad hoc clinics being set up to meet the extra demand.⁷ These findings were largely replicated in other centres.^{8–9} Patients referred to one fast track colorectal clinic had more advanced disease than standard referrals, which may have prognostic implications.⁹ Cancer detection rate dropped from 22% to 19% after introduction of the referral guidelines in a Fast Access Breast Clinic at a district general hospital, whereas waiting time for non-urgent appointments doubled from 4 to 8 weeks.¹⁰ A study of several UK breast units found that a quarter of the referrals did not comply with guidelines, and 36% of cancers were not referred through the scheme.¹¹ Tumours discovered in patients referred to a urology clinic under the 2-week rule because of raised prostate specific antigen were beyond cure.¹²

What lessons may be learnt from the UK experience of “cancer fast track” referral guidelines? The cancer detection rate of the guidelines is generally low; often, more malignancies are picked up outside of the guidelines. This may

partly reflect the breadth of the criteria, as the predictive values of individual features for the diagnosis of cancer vary widely. Narrower referral criteria might retain high sensitivity while reducing the pressures that inevitably come to bear on fast track services,¹³ often requiring a substantial reorganisation of local clinical resources, with increased waiting times for referrals deemed non-urgent being one ineluctable consequence. The emphasis of the referral guidelines on time from general practitioner referral to hospital appointment may be inappropriate: studies in gastrointestinal and urology clinics have shown that time lags before referral and after outpatient appointment but before treatment are the major causes of delay.^{14–15}

Returning specifically to the guidelines for CNS or brain cancers, the available data are sparse but, such as they are, seem to endorse the view that the 2-week system works “not too well”.¹⁶ As the guidelines are ambiguous, being not sufficiently explicit, they are open to misuse or abuse. Perceived long waiting times for neurology outpatient appointments may contribute to this, as may the lack of specific educational interventions about the purpose of the guidelines and lack of “ownership”. As headache seems to be the most common reason for referral under these auspices, greater general practitioner awareness of extant guidelines for the management of headache in primary care¹⁷ may be of greater value in patient management.

However well-intentioned or laudable the original aim, if the evidence base for CNS or brain cancer referral guidelines is unfavourable, then they should be abandoned, as is the case for any other test or treatment that does not work.

J Neurol Neurosurg Psychiatry 2006;**77**:1305–1306.

doi: 10.1136/jnnp.2005.077453

Correspondence to: A J Larner, Walton Centre for Neurology and Neurosurgery, Lower Lane, Fazakerley, Liverpool L9 7LJ, UK; a.larner@thewaltoncentre.nhs.uk

Competing interests: None declared.

REFERENCES

- 1 Davies E, Clarke C. Early symptoms of brain tumours. *J Neurol Neurosurg Psychiatry* 2005;**76**:1205–6.
- 2 Department of Health (DoH). Referral guidelines for suspected cancer, 2000. www.dh.gov.uk/assetRoot/04/01/44/21/04014421.pdf (accessed 4 Sep 2006).
- 3 Wills AJ, Pengiran Tengah DNSA. Audit of 2 week urgent referrals for CNS/brain tumours (abstract). *J Neurol Neurosurg Psychiatry* 2002;**72**:136.
- 4 Pengiran Tengah DNSA, Byrne PO, Wills AJ. Urgent 2-week referrals for CNS/brain tumours: a retrospective audit. *Clin Oncol* 2003;**15**:7–9.
- 5 Medendum Group Publishing. *Guidelines: summarising clinical guidelines for primary care*, Vol 25. Berkhamsted: Medendum Group Publishing, 2005. www.eguidelines.co.uk (accessed 4 Sep 2006).
- 6 International Headache Society Classification Subcommittee. The international classification of headache disorders, second edition. *Cephalalgia* 2004;**24**(Suppl 1):1–160.
- 7 Boulton-Jones JR, Gamble S, Robinson MH, et al. The impact of the two-week wait scheme for suspected gastrointestinal cancers. *Clin Med* 2003;**3**:483–4.
- 8 Spencer H, Sakellariou V, Ullah S, et al. Gastrointestinal cancer and the “two week wait”. *Clin Med* 2004;**4**:383.
- 9 Chohan DPK, Goodwin K, Wilkinson S, et al. How has the “two-week wait” rule affected the presentation of colorectal cancer? *Colorectal Dis* 2005;**7**:450–3.
- 10 Khawaja AR, Allan SM. Has the breast cancer “two week wait” guarantee for assessment made any difference? *Eur J Surg Oncol* 2000;**26**:536–9.
- 11 Sauven P. Two week rule for cancer referrals: specialists, not GPs, may be best qualified to assess urgency. *BMJ* 2001;**323**:864–5.
- 12 Allen D, Popert R, O'Brien T. The two-week-wait cancer initiative in urology: useful modernization? *J R Soc Med* 2004;**97**:279–81.
- 13 Kapoor N, Bassi A, Sturgess R, et al. Predictive value of alarm features in a rapid access upper gastrointestinal cancer service. *Gut* 2005;**54**:40–5.
- 14 Flashman K, O'Leary DP, Senapati A, et al. The Department of Health's two week standard for bowel cancer: is it working? *Gut* 2004;**53**:387–91.
- 15 Subramonian KR, Puranik S, Mufti GR. How will the two-weeks-wait rule affect delays in the management of urological cancers? *J R Soc Med* 2003;**96**:398–9.
- 16 Jones R, Rubin G, Hungin P. Is the two week rule for cancer referrals working? Not too well. *BMJ* 2001;**322**:1555–6.
- 17 Larner AJ. Guidelines for the management of headache in primary care: are they being used? *J Headache Pain* 2005;**6**:420–1.