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Comparison of time taken from initial presentation to histological diagnosis of Glioblastoma Multiforme (GBM) in Birmingham, United Kingdom and Strasbourg, France

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ABSTRACT

Background: The aim of this study was to investigate possible delays in referral time for Glioblastoma multiforme (GBM) patients diagnosed at two similar neurosurgical centres (in Birmingham, UK and Strasbourg, France) and their impact on survival. Differences in the referral patterns for GBM patients within these healthcare systems may affect subsequent management and are potential targets to optimise the care of patients with GBM.

Methods: Medical case notes of 105 GBM patients in Birmingham and 81 in Strasbourg, admitted during October 2006 and April 2008, were reviewed. Data regarding demographic details, route of admission, presenting symptoms, date of initial presentation to a medical professional and dates of the first CT or MRI scan, first neurosurgical intervention, histological diagnosis and mortality was recorded.

Results: The median time taken from initial presentation to first neurosurgical intervention was lower in Birmingham compared to Strasbourg (13 vs. 21 days, respectively; p = 0.026). Similarly, the time taken from initial presentation to histological diagnosis was lower in Birmingham (15 vs. 24 days, respectively; p = 0.011). However, survival was poorer in Birmingham than Strasbourg (p = 0.001) and age (HR = 1.029; 95%CI 1.010–1.048; p = 0.003) and time from initial presentation to neurosurgical intervention (HR = 0.993; 95%CI 0.988–0.998; p = 0.011) were predictors of mortality in these groups.

Conclusion: Patients in Birmingham are diagnosed with GBM more rapidly than those in Strasbourg but they have poorer survival. Differences in disease severity may partially account for the observed results and further large scale work is required to support this study.

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1. Introduction

In the United Kingdom (UK), around 4400 people are newly diagnosed with a brain tumour each year and over 80% of these are classified as gliomas [1]. Glioblastoma Multiforme (GBM or WHO grade IV astrocytoma) is the most common type of primary brain tumour in the UK, and generally has a poor prognosis due to its tendency to disseminate throughout the brain [2–4]. Early diagnosis and treatment of GBM may be influenced by the structure of healthcare systems and exploring reasons for possible delays in referral is essential to optimise patient care [5].

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In the UK, the Patient Care Pathway for suspected cancer is outlined by a Government advisory body, known as the National Institute for Health and Clinical Excellence (NICE). The NICE guidelines state that patients may present with symptoms including headache to their General Practitioner (GP) or to the local emergency department with more acute neurological signs and symptoms such as seizures. Investigations to confirm a suspected brain tumour more specifically CT or MRI scans are usually performed and patients are typically admitted and transferred to the local neurosurgical centre. If neurosurgical intervention is considered, a stereotactic biopsy may be taken and/or immediate debulking of the tumour by the neurosurgeon. The case is then discussed at the neurosurgery multidisciplinary team meeting and the patient is subsequently made aware of their diagnosis [6].

In 2000, the UK Government devised the National Health Service (NHS) Cancer Plan to improve access to specialist services and improve cancer care. These new guidelines aimed to reduce waiting times for diagnosis and treatment by ensuring that no patient

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had to wait longer than two months from an urgent GP referral for a suspected cancer to the beginning of treatment unless there was a valid clinical reason or patient choice dictated otherwise [7]. Furthermore time taken from diagnosis to first definitive treatment was set to one month [8]. However, the efficacy of these guidelines is debatable when considering the most recent data from the EURO-CARE study, which showed that the UK was amongst the lowest in a European 'league table' of cancer survival [9,10].

In France, which was one of the highest ranking European countries for cancer survival rates in Western Europe, the referral system is similar to the UK given that patients initially present to their GP or to an emergency department at their local hospital (regional or university hospital). Patients who present to the GP can be referred to the local hospital (public or private) for further investigation including CT or MRI scans. If neurosurgical intervention is required then patients are referred to the nearest hospital with neurosurgical facilities for intracranial biopsy or surgery. After the operation patients are mainly followed up at the nearest hospital with a neuro-oncology centre for adjuvant therapies including radiotherapy and chemotherapy.

The aim of this study is to investigate whether there is a difference in the time taken from the point at which a patient first presents with neurological signs and symptoms to a healthcare professional to when a histological (i.e. definitive) diagnosis of GBM has been obtained, in the UK compared to France, and its impact on survival. In view of the results of the EUROCARE study, we hypothesised that GBM patients in France are referred faster and receive treatment more quickly than in the UK and consequently survive longer. Analysis of potential delays in referral time to specialist neurosurgical centres may allude to new ways of improving the care and management of patients with GBM.

2. Methods

In this retrospective study, we reviewed the medical case notes of patients with a histological diagnosis of GBM at two neurosurgical centres, each serving a similar sized population of approximately two million people in Birmingham, UK and Strasbourg, France. The study sample was identified using databases from the neuropathology departments at both tertiary centres. Patients diagnosed with GBM between October 2006 and April 2008 were included in the study, and any patients that progressed from low grade astrocytomas to GBM and also patients who received private health care were excluded. The histological diagnosis of GBM was made by senior pathologists based on the WHO Classification of central nervous system tumours at both centres.

Information regarding patient demographic details, presenting symptoms, route of referral, date of initial presentation to a medical professional and dates of their first computed tomography (CT) or magnetic resonance imaging (MRI) scan, first neurosurgical intervention and histological diagnosis was obtained for comparison between the two centres. Patients classified as emergency admissions included those who were admitted via the local emergency department or referred by another general hospital for emergency specialist neurosurgical intervention. Other routes of referral analysed were local GP and other specialist referrals, for example, by neurologists and ophthalmologists. Specialist neurosurgical intervention included a stereotactic biopsy and/or debulking of the brain lesion. The frequency of each presenting symptom was analysed in all emergency admissions and all GP referrals at both centres.

The median (and mean) time taken from initial presentation to first scan, first neurosurgical intervention and histological diagnosis was calculated for both centres, as well as the time taken from first neurosurgical intervention to histological diagnosis. The time taken from initial presentation to histological diagnosis was used to

Table 1Demographic details and route of referral for GBM patients in Birmingham, UK and Strasbourg, France.

	Birmingham [n=105]	Strasbourg [n=81]	p-Value
Demographics			
Gender (% male)	61.0	61.3	0.967
Age (mean ± SEM, years)	62.1 ± 1.2	60.5 ± 1.6	0.414
Route of referral n (%)			
Emergency hospital admission	90 (85.7)	24(32.0)	<0.001*
General Practitioner referral	14(13.3)	43 (57.3)	<0.001*
Other specialist referral	1(1.0)	8(10.7)	0.020^{*}
Unknown	= ' '	6(7.4)	-

SEM is the standard error of the mean.

determine to overall difference in referral time between Birmingham and Strasbourg. These time periods were also analysed for each presenting symptoms, as well as all emergency admissions and all GP referrals at both centres. Patient mortality including inpatient and outpatient deaths was calculated using the date of first admission and date of death. This study was approved as a clinical audit by the Local Research and Development Department. Confidentiality of information was maintained at all times in accordance with the UK Data Protection Act.

2.1. Data analysis

Data was analysed using SPSS version 15.0 (SPSS Inc. Chicago, IL). Chi-square analysis was used to investigate differences in routes of referral. The Mann–Whitney *U*-test was used to analyse the median time taken from initial presentation to the first scan, first neurosurgical intervention or histological diagnosis for GBM patients in Birmingham and Strasbourg. Kaplan–Meier survival and forward Cox regression analysis was used to examine differences in survival between the two neurosurgical centres and to determine the predictors of mortality amongst these groups.

3. Results

The demographic details and the route of referral of patients in the study are shown in Table 1. Of the 186 patients, 105 (56.5%) were diagnosed with GBM in the UK and 81 (43.5%) in France during the study period. There were no significant differences in the gender distribution and mean ages of the two groups of patients. Patients in the UK were more frequently admitted as emergency cases presenting to the local emergency department or referred from other hospitals compared to Strasbourg (90 vs. 24, p < 0.001 patients respectively). Patients in Strasbourg were more likely to be referred for neurosurgical evaluation by the GP or other specialists (43 vs. 14; p < 0.001; 8 vs. 1, p = 0.020 patients respectively).

The presenting symptoms of GBM patients in our study are summarised in Table 2. The symptoms that were more common in GBM patients from Birmingham were headache (p = 0.046), gait disturbance (p = 0.007), memory deficit (p < 0.001) and monoparesis (p = 0.004). A larger proportion of GBM patients in Birmingham had more than one presenting symptom (p < 0.001). Interestingly, hemiplegia was reported to be more frequent in patients diagnosed in Strasbourg (p = 0.001). Comparison of all emergency admissions revealed that only monoparesis was more common in this group of patients in Birmingham than Strasbourg (26 vs. 2 patients respectively, p < 0.045).

Table 3 outlines the median and mean time periods from initial presentation to a healthcare professional to the first CT or MRI scan, first neurosurgical intervention and histological diagnosis for GBM in patients from Birmingham and Strasbourg. The median

^{*} Statistical significance of *p* < 0.05.

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