Fast track pathway reduces sight loss in giant cell arteritis: results of a longitudinal observational cohort study

P. Patil[1,2], M. Williams[1], W.W. Maw[1], K. Achilleos[1], S. Elsideeg[1], C. Dejaco[1,3], F. Borg[1], S. Gupta[4], B. Dasgupta[1]

[1]Southend University Hospital, Essex, UK; [2]Aditya Birla Memorial Hospital, Pune, India; [3]Medical University Graz, Austria; [4]Castle Point and Rochford Clinical Commissioning Group, Essex, UK.

Pravin Patil, MD, MRCP
Mark Williams, MRCP
Win Win Maw, MRCP
Katrina Achilleos, MRCP
Sunhoury Elsideeg, MD
Christian Dejaco, MD
Frances Borg, MRCP
Sunil Gupta, MRCP
Bhaskar Dasgupta, MD, FRCP

Please address correspondence to:
Bhaskar Dasgupta,
Southend University Hospital,
Prittlewell Chase,
Westcliff-on-sea,
Essex SS0 0RY, United Kingdom.
E-mail: bhaskar.dasgupta@southend.nhs.uk

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ABSTRACT

Objectives. *To investigate the effectiveness of a fast track pathway (FTP) on sight loss in patients with suspected giant cell arteritis (GCA).*

Methods. *A longitudinal observational cohort study was conducted in the secondary care rheumatology department. One hundred and thirty-five newly referred suspected GCA patients seen via the FTP (Jan. 2012-Dec. 2013) were compared to 81 patients seen through the conventional referral and review system (Jan. 2009-Dec. 2011).*

Results. *The FTP resulted in significant reduction in irreversible sight loss from 37.0% (as seen in the historical cohort 2009-2011) to 9.0 % (2012-2013, OR 0.17, p=0.001). Adjustment for clinical and demographic parameters including known risk factors for GCA associated blindness did not significantly change the primary result (OR 0.08, p=0.001). FTP resulted in a reduction of time from symptom onset to diagnosis, particularly by reduction of time from general practitioner's (GP) referral to the rheumatology review (79% of FTP patients were seen within one working day compared to 64.6 % in the conventional pathway, p=0.023). The FTP has seen a reduction in number of GP appointments.*

Conclusions. *There was a significant reduction of permanent sight loss with a fast track GCA pathway. The effect may be due to multiple factors including better GP education and reduction in delayed diagnosis. These results need verification at other sites.*

Introduction

Giant cell arteritis (GCA) is associated with irreversible vision loss in 15–25% of cases. This almost always occurs prior to glucocorticoid (GC) therapy (1). Hence early recognition along with the institution of high dose GCs is paramount (2). Patients with ischaemic symptoms, such as diplopia, transient visual loss, or jaw/tongue claudication, are at particularly high risk (3).

However, twenty-four percent of GCA cases may not have headaches and systemic, ischaemic or polymyalgic symptoms can predominate (4, 5). There may be multiple referral routes in the absence of agreed pathways and standards of care (5).

We present outcomes from a fast-track pathway (FTP) for GCA, implemented in Southend University Hospital and its catchment area. FTP was introduced to secure early referrals, standardised assessment, rapid review and treatment of patients with suspected disease.

The pathway focused on primary care and Accident & Emergency (A&E) that regularly receive GCA referrals. It was publicised to GPs with reminders every 3 months through regular time-to-learn sessions. PMRGCAuk and the regional Essex Group helped publicise the pathway through newsletters, meetings and advice line.

Methods

We conducted a retrospective analysis of a longitudinal cohort of suspected GCA patients. All patients with suspected GCA (Jan. 2012-Dec. 2013) were enrolled into FTP. We serve a catchment area with a population of about 350,000 with some referrals from outside of our catchment area. Data from FTP cases was compared with a cohort of suspected GCA patients seen in the conventional pathway since January 2009. We collected data regarding demographics, referral date, symptom onset, date of first medical and hospital visit, clinical features at presentation, visual symptoms and complications, temporal artery biopsy and treatment. We reviewed case records from all suspected GCA patients and data available

from the hospital medical information systems. Informed patient consent was obtained given the retrospective analysis of an anonymised database.

For patients with features of GCA without ischaemic symptoms, the referrer would start high dose oral GC (prednisolone 40–60 mg daily) and contact rheumatology team urgently (6) for review in GCA clinic within a working day. Temporal/axillary artery ultrasound and biopsy would follow within a week. Patients with features of GCA and ischaemic symptoms were referred to the A&E for assessment by on call medical Registrar with urgent advice from Ophthalmology and Rheumatology. After exclusion of other serious pathology patient would receive intravenous infusion of methylprednisolone (500 mg daily for 3 days) followed by investigations as stated above.

All patients would be reviewed 2 weeks following initial assessment. The final judgment was made by a single rheumatologist in the light of clinical features, results of laboratory investigations and biopsy results plus response to GC.

Statistical analysis

Statistical analysis was performed using SPSS (version 20.0). The Kolmogorov-Smirnov test was used to check the normality of metric data. For data with parametric distribution, the mean (± standard deviation) is shown and we applied the Student's *t*-tests for comparisons. For data with non-parametric distribution, we indicated the median (range) and used the Mann-Whitney U-test. Proportions were analysed by the chi-square test or Fisher's exact test as appropriate. Multivariate backward logistic regression analysis (maximum likelihood method, significance level for exclusion of parameters 0.1) was conducted to investigate the possible influence of age, sex, hypertension, headache, scalp tenderness, temporal swelling, reduced pulsation, jaw claudication, tongue pain/necrosis, eye pain, PMR, limb claudication, constitutional symptoms, ESR, haemoglobin, positive histology on the association between fast-track/conventional pathway and the risk of visual loss. CRP was not included because of high co-linearity with ESR. The following sensitivity analyses were performed: (1) construction of an inclusive model forcing parameters that differed between patients referred by conventional pathway and fast track into the model, (2) an inclusive model forcing parameters that differed between patients with and without sight loss in univariate analysis into the model, (3) exclusion of cases producing lowest/highest Degrees of freedom beta coefficients from the logistic regression (DFBETAs) or (4) largest Cook values.

Table I. Clinical characteristics of GCA patients diagnosed through fast track compared to conventional pathway.

Clinical feature	GCA-conventional (n=46)	GCA-fast track (n=67)	*p*-value
Age (years)†	75.4 (±7.6)	74.1 (±7.6)	>0.2
Female¥	33 (71.7)	52 (77.6)	>0.2
Transient visual symptoms¥	11 (23.9)	9 (13.4)	0.15
Positive TA biopsy¥	27/45 (60.0)	19/48 (39.6)	0.049
Hypertension¥	26 (56.5)	40 (59.7)	>0.2
Headache¥	40 (87.0)	63 (94.0)	0.19
Scalp tenderness¥	35 (76.1)	52 (77.6)	>0.2
Temporal swelling¥	12 (26.1)	27 (40.3)	0.12
Reduced pulsation¥	6 (13.0)	29 (43.3)	0.001
Jaw claudication¥	26 (56.5)	44 (65.7)	>0.2
Tongue pain¥	1 (2.2)	0	>0.2
Tongue necrosis¥	1 (2.2)	0	>0.2
Eye pain¥	1 (2.2)	1 (1.5)	>0.2
PMR symptoms¥	16 (34.8)	28 (41.8)	>0.2
Limb claudication¥	0	25 (37.3)	<0.001
Constitutional symptoms¥	27 (58.7)	48 (71.6)	0.15
ESR [mm/1st hour]†	48.0 (±24.0)	37.0 (±24.3)	0.022
CRP [mg/L]‡	60.0 (2.0-329.0)	35.0 (1.0-286.0)	0.018
Haemoglobin [g/L]†	11.7 (±1.6)	12.0 (±1.8)	>0.2
Symptom to diagnosis [days]*	21 (1-196)	17.5 (0-206)	>0.2

†mean (standard deviation), ‡median (range), ¥n (percentage) *of positive biopsies.

Results and effects of change

Clinical characteristics of patients in conventional and fast track pathway

GCA was diagnosed in 46 out of 81 (56.8%) patients referred by the conventional pathway (8 in 2009, 19 in 2010 and 19 in 2011) and in 67 out of 135 (49.6%, $p>0.2$) in the FTP (33 in 2012 and 24 in 2013). All patients diagnosed with GCA fulfilled ACR classification criteria (7). GCA patients in the conventional pathway had a higher percentage of a positive temporal artery biopsies and higher acute phase reactant levels (Table I). Patients seen through the FTP had higher incidence of reduced pulsation and limb claudication. There were no differences in oral GC initial dosages [median 60 mg/day (range 15–60) conventional *vs*. 60 mg/day (30–80) FTP; $p>0.2$] and patients on GC for other reasons [n=2 for PMR and n=1 for arthritis in conventional (total 6.5%) *vs*. n=5 for PMR (7.5%) in FTP; $p>0.2$] between the 2 groups, whereas more patients received IV methyl prednisolone pulse in the conventional pathway [n=14 (30.4%) conventional *vs*. n=11 (16.4%) FTP; $p=0.078$].

Characteristics of patients with and without permanent visual impairment

Permanent visual impairment was observed in 23 (20.4%) patients (8). As shown in Table II patients with sight loss were older, were more commonly men, suffered more frequently from hypertension and had a higher positive biopsy rate than patients without sight loss. Further, visual impairment was linked with a lower frequency of headaches, transient visual symptoms, scalp tenderness and limb claudication. Two patients with visual impairment had tongue pain/tongue necrosis. The mean ESR level was higher and haemoglobin levels were lower in patients with sight loss.

Table II. Characteristics of GCA patients with and without sight loss.

Clinical feature	GCA-no sight loss (n=90)	GCA-sight loss (n=23)	*p*-value
Age (years)†	75.1 (±8.5)	80.8 (±6.9)	0.003
Female¥	71 (78.8)	14 (60.9)	0.059
Transient visual symptoms¥	20 (22.2)	0	0.013
Positive TA biopsy¥	27/70 (38.6)	19/23 (82.6)	<0.001
Hypertension¥	49 (54.4)	17 (73.9)	0.091
Headache¥	87 (96.7)	16 (69.6)	<0.001
Scalp tenderness¥	74 (82.2)	13 (56.5)	0.009
Temporal swelling¥	32 (35.6)	7 (30.4)	>0.2
Reduced pulsation¥	27 (30.0)	8 (34.8)	>0.2
Jaw claudication¥	57 (63.3)	13 (56.5)	>0.2
Tongue pain¥	0	1 (4.3)	
Tongue necrosis¥	0	1 (4.3)	0.019
Eye pain¥	2 (2.2)	0	>0.2
PMR symptoms¥	37 (41.1)	7 (30.4)	>0.2
Limb claudication¥	23 (25.6)	2 (8.7)	0.082
Constitutional symptoms¥	60 (66.7)	15 (65.2)	>0.2
ESR [mm/1st hour]†	39.2 (±24.4)	51.2 (±24.0)	0.044
CRP [mg/L]‡	39.0 (1.0-329.0)	56.5 (4.0-213.0)	0.115
Haemoglobin [g/L]†	12.1 (±1.7)	11.2 (±1.6)	0.029
	Types of sight loss		
Sight loss	GCA-conventional (n=17)	GCA-fast track (n=6)	
Partial, monocular¥	6 (35.3)	1 (16.7)	
Complete, monocular¥	8 (47.1)	5 (83.3)	
Partial, bi-ocular¥	0	0	
Complete, bi-ocular¥	3 (17.6)	0	
	Referring specialist		
Specialty	GCA-conventional (n=46)	GCA-fast track (n=67)	
General practitioner	18 (39.1)	52 (77.6)	*p*<0.001
Ophthalmologist	6 (13.0)	2 (3.0)	
Acute medical unit	7 (15.2)	4 (6.0)	
Accident & Emergency	10 (21.7)	4 (6.0)	
Self-referral	2 (4.3)	2 (3.0)	
Other	3 (6.5)	3 (4.5)	

†mean (standard deviation), ‡median (range), ¥n (percentage), *of positive biopsies.

Fifteen (93.8%) out of 16 patients with sight loss in whom temporal artery ultrasonography was performed had a positive result whereas 54/78 (69.2%, *p*=0.043) patients with uncomplicated GCA were ultrasound positive. Ultrasonography was not performed regularly in the conventional group.

GC pulse therapy was given more commonly to patients with sight loss [n=12 (52.2%) *vs*. 13 (14.4%), *p*<0.001] whereas the median oral GC dose was the same in both groups [sight loss: 60 mg/day (40–80) *vs*. no sight loss: 60 (15–70)]. No patient treated with GC for other reasons than GCA suffered visual impairment.

Effect of fast track clinic on the incidence of sight loss

The number and types of sight loss in the conventional and FTP are shown in Table II. Permanent visual impairment was more commonly observed in conventional compared to FTP [n=17 (37.0%) *vs*. n=6 (9.0%), OR 0.17 (95% CI 0.06-0.47) *p*=0.001 in univariate analysis]. Only in 2 patients central artery occlusion was seen. In all other patients AION was the cause of sight loss.

Multivariate regression analysis showed that co-variables significantly associated with visual impairment were age [OR 1.16, (95%CI 1.04-1.27), *p*=0.005], male sex [OR 3.49 (95%CI 0.82-14.8), *p*=0.090], scalp tenderness [OR 0.13 (95%CI 0.03-054), *p*=0.005] and haemoglobin [OR 0.64 (95%CI 0.4–1.01), *p*=0.053]. However, none of these factors significantly altered the association between FTP and sight loss [OR 0.08 (95% CI 0.02–0.34), *p*=0.001]. Sensitivity analyses (data not shown) also did not change the primary result.

Effect of fast track clinic on referral routes and symptom to diagnosis time

A numerical (but statistically not significant 17.5 days (range 0–206) *vs*. 21.0 days (1–196) related to GCA patients only, and 17.5 (0–1095) *vs*. 20 (0-196) related to all patients) reduction of time from symptom onset to diagnosis was achieved by FTP. In particular, we observed a reduction of time from GPs' referral to rheumatology review as the majority of FTP patients were seen within one working day (79.0% compared to 64.6% in the conventional pathway, *p*=0.023; related to GCA patients only: 85.6% *vs*. 71.1%, *p*=0.087 for all patients).

Table II demonstrates the multiple routes of GCA referrals seen conventionally versus as seen with FTP. With implementation of FTP there was increase in direct referrals from GP (77.6% compared to 39.1% in conventional pathway, *p*<0.001 for GCA patients and 86.0% *vs*. 37.7%, *p*<0.001 for all patients) and at the same time reduction in referrals from other front line specialties.

Discussion

To our knowledge, this is the first report of a FTP for GCA with a significant reduction of permanent sight loss in FTP cohort. The contributory factors include reduction of time from referral to rheumatology review, elimination of multiple referral routes (Table II), increased public awareness of the disease and increasing knowledge of GPs.

The rate of GCA related visual complications could be significantly reduced with implementation of FTP. We recommend wider adoption of this model and the concept of 'symptom to steroid

time' as a performance measure alongside increase in public and professional awareness and 'one-stop shop' rapid access clinics for GCA.

A paradoxical finding in our study was that patients with permanent visual impairment, less commonly had headaches, scalp tenderness and transient visual symptoms than those without sight loss. Another study of 237 GCA patients showed a higher average age at the diagnosis and lower values of ESR and CRP in patients with ocular involvement than patients without visual impairment (9). This suggests that GCA is diagnosed earlier when well-known hallmark symptoms are present. Our educational sessions particularly concentrate on recognising atypical GCA such as presentation without headaches and/or with constitutional symptoms, polymyalgia and jaw pain.

The number of positive temporal artery biopsies is lower than reported in previous studies. This may relate to high numbers of large-vessel GCA patient as well as increased case recognition and referrals. FTP allowed earlier detection of mimicking pathologies and restricted long-term GC exposure to patients with confirmed disease.

Limitations

Our study compares FTP patients with a historical cohort. Historical cohorts have been used to justify service development in areas such as early arthritis (10), cardiovascular and cerebrovascular ischaemia. Adjustment for demographic and clinical parameters (including all known risk factors for blindness) in the multiple regression analyses did not affect our primary conclusion about the protective effects of FTP on sight loss. The alternative trial where patients with suspected GCA are randomised either to conventional or FTP would be unethical in light of our findings and accepted guidelines.

It is possible that in conventional pathway more patients with severe disease were seen especially those with visual manifestations. Another possibility is that FTP patients were referred earlier with non-visual symptoms. We would like to encourage early referrals in GCA based on lessons learned from rheumatoid arthritis management. In the past, damage (erosions) and severity (nodules, rheumatoid factor) were essential descriptions of rheumatoid disease. This has changed to detection and treatment of early perhaps milder disease to adhere to the therapeutic window for disease modification (11). The disease remains the same but the outcomes change with our approach to its treatment (12) (13). Similarly, the evidence from ischaemic stroke management indicates that implementing a clinical pathway is particularly effective in changing professional behaviours in the desired direction and significantly lowers mortality (14).

Conclusions

In this study adoption of FTP resulted in significant reduction in permanent sight loss. The results and conclusions from our study need verification at other sites and over longer observation periods. However, we feel that our experience with FTP warrants further consideration as the model of care that can reduce ischaemic injury in GCA.

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