

P8. INFLAMMATORY AUTOIMMUNE DISEASES OF THE ELDERLY POPULATION (IADE): A PROSPECTIVE LONGITUDINAL COHORT STUDY

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Background: The elderly population is susceptible to autoimmune inflammatory diseases due to ageing of the immune system. Senescence-associated inflammation has been connected to a two- to four-fold increase in the levels of acute-phase reactants, such as CRP and IL-6. PMR is the most common source of joint/muscle pain and inflammation in individuals older than 50 years with an incidence rate reported to be as high as 112.6 per 100 000 at >50 years. It is often challenging to make a definite diagnosis, and especially the distinction between PMR, GCA, RA, crystal arthropathies and SpA can be difficult. Recently, the new classification criteria for PMR have been published as a result of collaboration between the ACR and the European League Against Rheumatism. The criteria raised a question about an overlap between PMR and other types of inflammatory joint/muscle pain in the elderly and suggested further validation in the primary care setting. The aim of this study is to explore the clinical overlap and difference of inflammatory autoimmunity in the elderly people (IADE).

Methods: This is a prospective, observational, longitudinal, cohort study. Three hundred patients and 100 disease controls with non-inflammatory conditions (e.g. OA, frozen shoulder) will be recruited in the participating centres within secondary and primary care settings. The primary aim will be to assess patients above the age of 50 years with new onset inflammatory, autoimmune diseases (RA, SpAs, PMR, GCA and crystal arthropathies) presenting with pain in shoulders and hips, arthritis and increased inflammatory markers. A secondary objective is to validate the ACR/EULAR provisional classification criteria in PMR, the ACR/EULAR classification criteria in RA and Assessment of Spondyloarthritis (ASAS) criteria for SpA in this population. Ultrasound of the shoulders, hips, knees, hands and feet as well as temporal, axillary and carotid arteries will be performed in all cases with systematic acquisition of images by standardized methods. Fat-suppressed MRI of the spine and sacroiliac joints will be undertaken where there is high likelihood of axial SpA. In addition, biomaterial (serum, plasma and DNA) will be collected to perform cytokine, biomarker studies and genetic analyses aiming to elucidate the pathogenetic mechanism of the IADE. The recruitment period will be 12 months. The patients will be reviewed after 4 weeks, 26 weeks, 12 months and the final control will be at 24 months after recruitment.

Discussion: This study has been designed to assess the clinical overlap and differences of IADE, specifically exploring common and divergent clinical features of PMR, GCA, RA, SpA and crystal arthropathies compared with non-inflammatory conditions such as OA.

P9. GIANT CELL ARTERITIS—OVER DIAGNOSED?

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Background: GCA is the most common vasculitis in the western world. It typically affects individuals >55 years of age and has significant morbidity from its pathology and its treatment. There are no recent (after 2001) estimates of the occurrence in the UK. The aim of this study was to estimate the occurrence of GCA in the UK.

Methods: All temporal artery biopsies performed at the Norfolk and Norwich University hospital between 2003 and 2012 were reviewed. Cases of GCA were included only after careful case notes review with

all cases fulfilling 1990 ACR criteria. The general practice (GP) location was noted for each of the included cases. The GP location was grouped into standard local authority boundaries. In cases where the individual practice population lay on a local authority boundary, the practice was classified into the local authority area which held the majority of the registered patients. The population denominator was calculated from national census data.

Results: There were 601 temporal biopsies performed at the NNUH between the years 2003 and 2012. Subsequently 267 individuals were diagnosed with GCA (44%); 206 were biopsy positive cases (77.2%). The mean age at diagnosis was 75.4 years; 187 were women (70%). Patients with biopsy positive GCA were significantly older (mean difference 2.4 years CI 0.1, 4.7, $P < 0.05$) and had a statistically significantly higher ESR (mean difference 12 mm/h, CI 4, 21, $P = 0.005$) compared with individuals with biopsy negative disease. Incidence was calculated for the last 6 years of the study since robust data recording allowed for assured inclusion of cases of GCA with negative biopsy. There were 219 cases of GCA (61 biopsy negative—27.9%) diagnosed in this period (2007–2012). Seven cases of GCA came from practices within the local authority area of Great Yarmouth and one case from elsewhere. These were excluded from the analysis. Of the remaining 211 cases of GCA came from 72 general practices in five local authority areas. The incidence rate per 100 000 was 13.9 (95% CI 10.7, 25.3) in people aged >50 years.

Conclusion: The results reveal and estimate of 13.9 per 100 000 people aged >50 years. This is much lower than the estimate from the GPRD study carried out in 2001. Within the GPRD study only three out of a selection of 45 cases that were reviewed had a positive temporal artery biopsy (6.7%) and 10 cases (22.2%) were diagnosed and managed in primary care alone. Assuming an incidence for our study is similar to that of the GPRD then in Norfolk perhaps as many as 50% of cases of GCA are managed in the community without undergoing biopsy before embarking on toxic corticosteroid treatment.

P10. REVIEW OF THE EXPERT PANEL METHODOLOGY IN THE DIAGNOSTIC AND CLASSIFICATION CRITERIA FOR VASCULITIS STUDY: A PILOT STUDY

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Background: The Diagnostic and Classification Criteria for Vasculitis (DCVAS) Study is a multinational observational study to develop diagnostic criteria and to update classification criteria for the primary systemic vasculitides. By 2015 the database will include clinical, laboratory and radiology data from over 2000 patients with vasculitis and 1500 comparator patients who present with features similar to vasculitis. To avoid the inherent circularity of using the submitting physician diagnosis as the gold standard, a reference diagnosis for each patient will be established using a combination of expert panel opinion and data-driven methods (e.g. machine learning algorithms). The aim of this analysis was to evaluate the methodology by which the expert panel will assess individual patient data to establish the reference diagnosis.

Methods: By November 2012, 1662 patients had been recruited; 391 had complete 6 month follow-up data. Forty cases were randomly extracted and developed into clinical vignettes. The clinical vignettes were assessed for diagnoses by 6 independent experts using an online platform. Ten patients were assessed by all experts and the other 30 were each assessed by two of the six experts, randomly chosen. The experts first chose between primary vasculitis, secondary vasculitis, or other illness; then the respective major class (small-, medium- or large-vessel vasculitis, or no predominant size vasculitis); and then the subtype or the specific disease for each category. For each answer a level of certainty (unlikely, possible, probable, definitive or unknown) was provided. The diagnoses of the expert panel and the submitting physician were compared.

Results: The 40 clinical vignettes represented 26 women and 14 men, with mean age of 62.5 ± 20.3 years (range 20–86 years). Data from all 120 clinical vignette reviews were available for analysis. Treating clinicians submitted a diagnosis of primary vasculitis in 32 patients (17 small-vessel, 1 medium-vessel, 13 large-vessel and 1 with no predominant size); secondary vasculitis in 2 and other illness in 6. The expert panel agreed with the submitted diagnosis of primary vasculitis in 97% of the cases (definite 54%, probable 35% and possible 8%). However, only 78% of the submitted patients with primary vasculitis were classified as having the same sub-type of vasculitis when compared with the expert panel diagnosis (9% could not be sub-typed within the correct major class of vasculitis, 9% classified the cases with another sub-type of the same major class, 3% chose another major class or diagnosis and 2% selected the unknown option). There was an intraclass correlation coefficient of 0.82 (CI 0.57, 0.95) in the 10 CVs assessed by the 6 experts, indicating low variability between evaluators.

Conclusion: An expert panel agreed with the individual submitting physician regarding a diagnosis of some form of primary vasculitis in nearly all cases, but disagreement about the exact form of vasculitis occurred in 22% of cases. Physician-based opinion may be more reliable for defining general categories of vasculitis than for defining specific subtypes. This exercise highlights the potential for diagnostic bias when using physician-opinion to define the gold standard diagnosis.

P11. UPDATE ON INCIDENCE OF GIANT CELL ARTERITIS IN THE CURRENT ERA OF ADVANCED DIAGNOSTIC IMAGING

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Background: GCA is the most common type of vasculitis which occurs especially in women who are older than 70 years of age and of northern European origin. Magnetic resonance angiogram (MRA), CT angiogram (CTA) and PET are increasingly being used as non-invasive tools to diagnose extracranial involvement of the large vessels in patients with suspected GCA. We aimed to assess the incidence of GCA in the current era of advanced diagnostic imaging, 2005–2009 compared with previous decades.

Methods: Using the resources of Rochester Epidemiology Project (REP), incident cases of GCA in Olmsted County, Minnesota, USA between 1 January 2005 and 31 December 2009 were identified. Overall incidence was compared with 1970–2004 and imaging use compared with 1 January 2000 and 31 December 2004 from the same population. GCA was defined according to the 1990 ACR classification criteria and physician diagnosis. Patients >50 years of age with elevation of ESR or CRP and CTA, MRA or PET scan evidence of large vessel vasculitis involving the ascending aorta and/or its branches were also included. Asymptomatic patients with incidental findings of aortitis on pathology following aortic aneurysm repair or aortic valve replacement were not included. Incidence of GCA per 100 000 population was calculated after adjusting for age and sex to the 1980 US white population aged ≥ 50 years.

Results: We identified 39 patients with GCA in 2005–2009 and 35 patients in 2000–2004. Mean age of patients was 77.1 years [standard deviation (s.d.) 8.8] in the 2005–2009 cohort and 79.3 years (s.d. 7.4) in the 2000–2004 cohort ($P=0.28$). The majority of the patients were women: 77% in 2005–2009 and 83% in 2000–2004 ($P=0.53$). Temporal artery biopsy (TAB) was positive in 28 of 39 patients (76%) in 2005–2009 and in 28 of 35 (82%) in 2000–2004 ($P=0.49$). 5 of 11 patients in 2005–2009 cohort and 2 of 7 patients in 2000–2004 cohort with negative TAB were included based on the radiological criteria. Among these 5 patients in the 2005–2009 cohort, CTA was used in 2; MRA in 1; PET scan in 2 patients; and MRA was used in the patient in the 2000–2004 cohort. The overall age- and sex-adjusted incidence rate in 2005–2009 was 19.5 per 100 000 population (95% CI 13.2, 25.8). This is nearly identical to the estimated incidence of GCA in all years from 1970 through 2004, which ranged from 18.8 to 28.5 per 100 000.

Conclusion: Imaging techniques such as CTA, MRA and PET are more commonly used in recent years for diagnosing GCA involving the ascending aorta and/or its major branches in suspected GCA when negative TAB. In spite of use of advanced imaging, the overall incidence of GCA has not changed significantly in recent years.

P12. INCREASED RHO KINASE (ROCK) ACTIVITY IN TEMPORAL ARTERIAL BIOPSIES FROM PATIENTS WITH GIANT CELL ARTERITIS

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Background: ROCKs are implicated in the pathogenesis of many vascular diseases. ROCK activation is associated with Th17 differentiation and production of Th17-associated cytokines, IL-17 and IL-21. Th17 cells and related cytokines are present in increased levels in active GCA. ROCK activity in GCA is unknown. The aim of this study was to assess ROCK activity in temporal artery biopsy (TAB) specimens in GCA vs controls.

Methods: All TAB performed at a tertiary care centre over a 5-year period were identified. Charts were reviewed for clinical information. Subjects were categorized according to 1990 ACR criteria and TAB status into three groups: GCA with positive TAB, GCA with negative TAB and age- and sex-matched controls. Paraffin-embedded temporal artery specimens were stained for phospho-ezrin/radixin/moesin (pERM), a surrogate of ROCK activity, using immunohistochemical stain. pERM stained slides were reviewed by a pathologist blinded to clinical status. Three separate areas (endothelium, adventitia and vaso vasorum) were scored for intensity of staining on a scale of 0–2 for total possible composite score of 6. Primary outcome was biopsy pERM intensity score in subjects with GCA compared with controls.

Results: Nineteen subjects with GCA had positive TAB, 17 subjects had GCA with negative TAB and 18 age-sex-matched controls were analysed. Mean age was 77.9 ± 9.1 years and 81.4% were female with no differences in baseline demographics between the 3 groups (Table 1). Compared with controls, GCA subjects with either positive or negative TAB had significantly higher pERM intensity scores ($P=0.0159$). Adjusting for diabetes, hypertension, prednisone and statin use, GCA subjects still had higher pERM intensity scores (OR 7.3; 95%CI 1.9, 25.9, $P=0.0046$). Comparing GCA with negative TAB with controls, high pERM score had sensitivity of 90.4% and negative predictive value of 90.9%.

Conclusion: Subjects with GCA had more intense pERM staining in TAB specimens compared with age- sex-matched controls regardless of whether TAB was positive or negative, suggesting increased ROCK activity in GCA. High pERM staining score had a sensitivity higher than the sensitivity of routine TAB histopathology itself, suggesting it may be a useful adjunctive diagnostic tool in patients with negative TAB. The ROCK pathway warrants further investigation in GCA as it may be of both diagnostic and therapeutic significance.

TABLE 1 Demographics of the groups

| | GCA (n = 36) | | Control (n = 18) | P value |
|----------------------------------|--------------------------|--------------------------|------------------|---------|
| | Biopsy positive (n = 19) | Biopsy negative (n = 17) | | |
| Age, mean (s.d.), years | 78.4 (9.2) | 76.6 (7.9) | 78.4 (10.5) | 0.81 |
| Female, n (%) | 14 (74) | 16 (94) | 13 (72) | 0.2 |
| Prednisone dose, mean (s.d.), mg | 55.6 (17.9) | 50.6 (17.1) | 47.2 (27.2) | 0.5 |
| Hypertension, n (%) | 8 (44) | 10 (59) | 12 (67) | 0.39 |
| Diabetes, n (%) | 1 (6) | 6 (35) | 4 (22) | 0.11 |
| Statin, n (%) | 5 (28) | 8 (47) | 11 (61) | 0.13 |
| pERM intensity score | | | | 0.0159 |
| ≤4 | 4 (21) | 1 (6) | 10 (56) | |
| >4 | 15 (79) | 16 (94) | 8 (44) | |

P13. THE ACR/EULAR CLASSIFICATION CRITERIA IN HUNGARIAN POLYMYALGIA RHEUMATICA PATIENTS

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Background: New classification criteria (2012) have been developed by the ACR/EULAR PMR study group. Diagnostic value of the new ACR/EULAR classification criteria has been studied in new onset Hungarian PMR patients.

Methods: All PMR patients were clinically evaluated including laboratory determinations and US examinations. New onset PMR