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PP2. LONG-TERM FOLLOW-UP OF POLYMYALGIA RHEUMATICA PATIENTS TREATED WITH METHOTREXATE AND STEROIDS

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Introduction: We have recently demonstrated that combination therapy with prednisone and methotrexate (MTX) is effective as steroid-sparing treatment for patients with newly diagnosed polymyalgia rheumatica (PMR) [1]. This schedule reduces the incidence of flare-ups and the amount of prednisone required to maintain remission. However, no substantial reduction was found in the incidence of steroid-related side effects in the MTX-treated patients, despite the lower cumulative dose of prednisone they received. Possible explanations are the narrow difference in the cumulative dose of prednisone between groups, and the low incidence of side effects in this relatively “healthy” group of PMR patients, a common problem of controlled trials. Another possibility is the short follow-up. To test this last hypothesis, we decided to review the charts of the participating patients and to visit them again after a mean period of 5 years after completion of the original study.

Patients and methods: Four of the original five rheumatologic tertiary referral centres, covering 61 of the original 72 (84.7%) patients, agreed to participate in the study. Patients were contacted by phone and asked to visit the clinic. If the patient was dead, a close relative was interviewed and information was collected on his/her previous health conditions and cause of death through a standardized questionnaire.

Results: Data were obtained from 47/61 (77%) of the original patients. Five patients (10.6%) had died because of cerebrovascular accident, myocardial infarction, congestive heart failure (2 patients), or unknown cause. Two of the 23 MTX-treated patients (8.7%) had died in comparison with 3/24 (12.5%) controls. Exacerbations and relapses of PMR were seen in 4/23 (17.4%) MTX-treated patients in comparison with 10/24 (41.7%) controls (p = 0.11 by Fisher’s exact test). Five out of 23 (21.7%) MTX-treated patients were still on steroids 5 years after completion of the study in comparison with 11/24 (45.8%) controls (p = 0.009 by Fisher’s exact test). Twenty-five patients (88%) had died in comparison with 3/24 (12.5%) controls. Exacerbations and relapses of PMR were seen in 4/23 (17.4%) MTX-treated patients in comparison with 10/24 (41.7%) controls (p = 0.11 by Fisher’s exact test). Five out of 23 (21.7%) MTX-treated patients were still on steroids 5 years after completion of the study in comparison with 11/24 (45.8%) controls (p = 0.009 by Fisher’s exact test).

Potential side effects of steroid treatment were relatively rare. No differences were observed in their incidence, with a mean of 1.9 side effects for MTX-treated patients and 2.6 for controls. The analysis of single steroid-related side effects gave similar results.

Conclusions: In this long-term evaluation of the effect of MTX supplementation for PMR patients, there was a tendency toward less residual disease activity over 5 years in MTX-treated patients. However, complications of steroid treatment were rare in both groups without a significant difference between them. To assess whether MTX-supplementation therapy could spare some side-effects of steroids, a prospective evaluation of unselected patients is probably more appropriate.


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PP3. ERDHEIM-CHESTER DISEASE: YET ANOTHER MIMIC OF POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS?

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Background: Erdheim-Chester Disease is a rare non-langerhans cell histiocytosis. First described in the 10th Century, there are only 60 cases in the literature. It can present with bone pain, visual field loss, pituitary failure and lower limb claudication. Prognosis is approximately two years from diagnosis.

We present the case of a 67 year old man whose symptoms were considered classical of polymyalgia rheumatica. He responded to steroid therapy initially but re-presented with eye symptoms thought to be caused by giant cell arteritis.

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POSTER PRESENTATIONS
Methods: He had initially presented to a rheumatologist three years earlier with generalised myalgia, stiffness and cramps, associated with marked acute phase response and iron-deficiency anaemia. A diagnosis of polymyalgia rheumatica was made and an oral steroid was commenced with some improvement. Gastrointestinal and haematological investigations did not identify any pathology to account for the anaemia.

He re-presented with left-sided visual field loss associated once again with an acute phase response and was treated with high dose steroids pending temporal artery biopsy, which was negative.

On presentation to us, he had marked xanthelasma and xanthomatous lesions over his cheeks. Systems examination including musculoskeletal examination was unremarkable. His blood tests once again revealed a marked acute phase response and, of note, normal fasting serum lipid concentrations.

Results: Plain radiography of his long bones revealed widespread sclerotic lesions. His bone scan showed symmetrical uptake in the meta- and diaphyses of his long bones. Bone biopsy revealed sclerotic bone laden with foamy macrophages, which stained CD68-positive but negative for s-100 and CD1a. A diagnosis of Erdheim-Chester Disease was made.

MRI revealed retro-orbital infiltrates causing optic nerve compression. Parotid and renal involvement were seen on CT imaging of the abdomen. PET scan only showed disease behind the left eye and in the long bones. Local radiotherapy to both orbits was performed to protect his vision. Systemic therapy was commenced initially with intravenous steroid and pulsed cyclophosphamide. Treatment continues with lower dose oral steroid and infliximab. His symptoms have improved, his inflammatory markers have reduces and he has not developed any cardio-respiratory involvement at this stage.

Conclusions: This case illustrates a rare mimic of polymyalgia and giant cell arteritis, though the lack of complete response of steroid, the xanthomata and sclerotic bone all suggest an alternative cause.

PET scanning was used for the first time and helped tailor therapy to metabolically active sites of disease.

We propose that anti-TNF agents are appropriate therapy to control progression of this disease.

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PP4. THE DIFFICULTIES IN THE DEVELOPMENT OF HISTOLOGICAL SCORING FOR INFLAMED TEMPORAL ARTERY IN GIANT CELL ARTERITIS

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Background: The major complication of GCA is vision loss. A recent audit showed a high percentage of visual loss (29%) in biopsy patients. Cytokine patterns in temporal artery biopsy specimens (TAB) such as high interferon-gamma have reported correlation with clinical features of ischaemia. It will be useful to differential patients at higher risk for ischaemic events early, to prevent complications such as vision loss. We undertook this study to determine whether a light microscopic histological score of TAB could reliably quantify the inflammatory response and different histological patterns in GCA.

Methods: A scoring system to quantify inflammatory response in TAB was evolved from a UK-Swedish collaboration. TAB were scored as mild (1), moderate (2), Severe (3) for the following: general degree of inflammation, extent of inflammatory invasion with regard to wall layers and the circumference, presence and the extent of multinucleate giant cells, intimal thickening, fibrinous exudation and neovascularisation. Twenty five TAB from biopsy positive GCA were scored twice after a 4-week interval by a consultant histopathologist. The slides were then exchanged between the 2 centres and underwent similar review by the other histopathologist. The histopathologist were blinded to each other’s scores, their own scores as well as clinical data. Intra and inter-observer reliability was assessed using kappa statistics.

Results: Intra-observer reliability showed moderate (k = 0.59, 95% CI 0.51–0.66) and good (k = 0.77, 95% CI 0.71–0.84) agreement for the two observer reliability showed poor agreement (k = 0.16, 95% CI 0.12–0.20). Of the seven parameters of inflammation only intimal thickening produced fair or better inter-observer agreement (k = 0.34, 95% CI 0.19–0.48). The agreement for giant cell infiltration was no better than would be expected by chance (k = 0.02, 95% CI –0.11 to –0.07). The table shows the percentage of TAB with moderate/severe involvement (scores 2 or 3).

Conclusions: The overall histological scores showed poor inter-observer and intra-observer reliability in GCA. Evaluation of giant cells and neo-vascularisation showed highest variability. We suggest that future histological studies agree the definitions of such abnormalities in a prior consensus training phase.

Histological score (%) with moderate/severe involvement:

<table>
<thead>
<tr>
<th></th>
<th>Inflam</th>
<th>Layer</th>
<th>Circu</th>
<th>Giant cells</th>
<th>Intimal prolif</th>
<th>Fib</th>
<th>Exu</th>
<th>Neovas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observer 1a</td>
<td>68.6</td>
<td>84.2</td>
<td>88.1</td>
<td>35.3</td>
<td>84.3</td>
<td>31.3</td>
<td>25.4</td>
<td></td>
</tr>
<tr>
<td>Observer 1b</td>
<td>66.6</td>
<td>86.2</td>
<td>90.1</td>
<td>40.9</td>
<td>84.2</td>
<td>37.2</td>
<td>41.2</td>
<td></td>
</tr>
<tr>
<td>Observer 2a</td>
<td>92.1</td>
<td>100</td>
<td>98</td>
<td>21.4</td>
<td>84.2</td>
<td>21.5</td>
<td>50.9</td>
<td></td>
</tr>
<tr>
<td>Observer 2b</td>
<td>92.1</td>
<td>100</td>
<td>99.9</td>
<td>19.6</td>
<td>84.2</td>
<td>23.4</td>
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PP5. POLYMYALGIA RHEUMATICA (PMR) CAN RECUR YEARS AFTER DISCONTINUATION OF STEROID THERAPY

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Background: Although relapses of PMR are well recognized, overt recurrences of the disease have been but glancingly acknowledged. (Relapse is herewith defined as increased disease activity, including worsened symptoms and rises in the acute phase reactants, occurring in the face of ongoing treatment; recurrence is defined as increased disease activity after cessation of treatment.)

Methods: 12 patients with recurrences of PMR years after discontinuation of steroid therapy were culled from my clinical practice of 30 years. In order to insure separation from mere relapsing disease, I have included only patients off treatment for at least 2 years. All patients had PMR per the Healey criteria (Semin Arthritis Rheum 1984;13;322–8) at the time of initial diagnosis and of subsequent recurrence(s). 3 patients with ESRs <40 who fulfilled these criteria were included. No patient was positive for rheumatoid factor, and none developed erosive disease during the periods of follow-up.

Results: 12 patient are described, 8 female and 4 male, ranging in age at the time of initial diagnosis from 53 to 78 years (mean 64.1 years). The period of follow-up ranged from 7.3 to 25.1 years (mean 14.3 years). The duration of initial steroid therapy ranged from to 1 to 11.1 years (mean 3.4 years). At the time steroids were discontinued, patients were asymptomatic, and sedimentation rates had normalized. The duration between discontinuation of steroid therapy and its resumption for recurring disease was 2.0 to 14.7 years (mean 6.1 years). 3 patients had more than one recurrence, as defined above. 5 recurrences were accompanied by peripheral arthritis. 1 case of giant cell arteritis occurred.