Immunosuppressive treatment of chronic periaortitis: a retrospective study of 20 patients with chronic periaortitis and a review of the literature

K Warnatz, A G Keskin, M Uhl, C Scholz, A Katzenwadel, P Vaith, H H Peter, U A Walker

**Background:** Retroperitoneal fibrosis (RPF) and inflammatory aneurysm of the abdominal aorta (IAAA) are regarded as two manifestations of the same disease, termed “chronic periaortitis”.

**Objective:** To determine the optimal therapeutic and diagnostic approaches to IAAA.

**Methods:** The outcome of medical immunosuppressive and surgical treatment of 20 patients was examined. Measurements of the C reactive protein (CRP) were compared with contrast enhanced imaging studies in the follow up of the patients.

**Results:** The diameter of the periaortic mantle and its contrast enhancement improved in 13/15 (87%) patients given immunosuppressive treatment for a period of more than 6 months. Strong contrast enhancement was associated with a substantial rise in CRP, but no correlation between the CRP value and thickness of the fibrotic mass was found, even at intraindividual follow up.

**Conclusions:** Immunosuppressive treatment should be included in the first line treatment of patients with RPF and should be maintained long term. Imaging studies are better than CRP measurements in the evaluation of response to treatment.

**Patients and Methods**

The electronic patient records of our hospital were searched for the following keywords: “Ormond’s disease”, “retroperitoneal fibrosis”, or “inflammatory aneurysm of the abdominal aorta”.

Data were collected retrospectively from patient charts, a questionnaire, and by direct questioning when possible. The following information was obtained: symptoms, laboratory measurements (white blood cell count, CRP, creatinine), the findings in imaging studies at the time of diagnosis and at follow up, as well as the prior medical history. MRI was performed in 12 patients with a Siemens Sonata 1.5 T (Erlangen, Germany) using standard body coil or body array coils running the following sequences: spin echo T1 weighted, transversal slices before and after administration of a contrast medium (0.1 mmol/kg gadolinium-DTPA; Magnsevit, Schering AG, Berlin), slice thickness 8 mm; fast spin echo T2 weighted, transversal and sagittal slices, slice thickness 8 mm, as well as fat suppressed, T2 weighted inversion recovery sequence, slice thickness 10 mm, transversal slices.

Alternatively, a spiral multislice CT scanner (Volume Zoom; Siemens, Erlangen) was the standard machine for scanning the abdomen in eight patients. Reconstructed slice thickness of the transversal slices was 5 mm. In all patients, 100–120 ml contrast medium (Imeron; Altana AG, Konstanz) was injected intravenously during the scan procedure to obtain a good vessel contrast. The thickness of the periaortic mantle, its longitudinal extension, and contrast enhancement were scored by a single experienced radiologist, who was unaware of the temporal sequence of the images. Partial

**Abbreviations:** AZA, azathioprine; CRP, C reactive protein; CT, computed tomography; CYC, cyclophosphamide; DJ, double J; IAAA, inflammatory aneurysm of the abdominal aorta; MMF, mycophenolate mofetil; MRI, magnetic resonance imaging; OCS, oral corticosteroids; RPF, retroperitoneal fibrosis
Table 1 Clinical data of 15 patients with retroperitoneal fibrosis (RPF) and five with inflammatory aneurysm of the abdominal aorta (IAAA)

<table>
<thead>
<tr>
<th>ID</th>
<th>Diagnosis</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Cardiovascular risk factors</th>
<th>Prior or current comorbidity</th>
<th>Symptoms at presentation</th>
<th>Imaging at diagnosis</th>
<th>Vascular involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RPF</td>
<td>50</td>
<td>M</td>
<td>AH, CHOL, 30 PY</td>
<td>CHD, calan diverticulosis</td>
<td>Abdominal and low back pain, WL</td>
<td>CT 10 90 – – –</td>
<td>– – –</td>
</tr>
<tr>
<td>2</td>
<td>RPF</td>
<td>45</td>
<td>F</td>
<td>CHOL, 50 PY</td>
<td>None</td>
<td>Low back pain</td>
<td>MRI 20 91 ++ –</td>
<td>+ –</td>
</tr>
<tr>
<td>3</td>
<td>RPF</td>
<td>30</td>
<td>M</td>
<td>AH, CHOL</td>
<td>Hodgkin’s lymphoma, latent hypothyroidism</td>
<td>Poor documentation</td>
<td>MRI 10 104 + + +</td>
<td>+ + +</td>
</tr>
<tr>
<td>4</td>
<td>RPF</td>
<td>48</td>
<td>F</td>
<td>AH, 10 PY</td>
<td>CHD, Riedel’s thyroiditis</td>
<td>Ciguria, otherwise poor documentation</td>
<td>– – – + + +</td>
<td>– + +</td>
</tr>
<tr>
<td>5</td>
<td>RPF</td>
<td>37</td>
<td>M</td>
<td>AH, 30 PY</td>
<td>Pancreatitis, gastric ulcer, Hashimoto’s thyroiditis, diabetes mellitus</td>
<td>Low back and flank pain</td>
<td>MRI 10 100 + + +</td>
<td>+ + +</td>
</tr>
<tr>
<td>6</td>
<td>RPF</td>
<td>37</td>
<td>M</td>
<td>CHOL, 21 PY</td>
<td>Leucocytoclastic vasculitis</td>
<td>Flank pain, WL</td>
<td>MRI 20 140 ++ +</td>
<td>+ ++</td>
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<tr>
<td>7</td>
<td>RPF</td>
<td>63</td>
<td>M</td>
<td>AH, CHOL, 40 PY</td>
<td>CHD, pharyngeal carcinoma</td>
<td>Low back pain, WL</td>
<td>CT 10 90 ND ++ +</td>
<td>+ ++</td>
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<tr>
<td>8</td>
<td>RPF</td>
<td>49</td>
<td>F</td>
<td>40 PY</td>
<td>PAOD, COLD, malignant melanoma</td>
<td>Abdominal pain, WL</td>
<td>MRI 20 66 ++ +</td>
<td>+ +</td>
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<td>9</td>
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<td>38</td>
<td>M</td>
<td>AH, CHOL, 25 PY</td>
<td>CHD, PAOD, glomerulosclerosis, slipped disk sacculitis</td>
<td>Abdominal and flank pain, WL</td>
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<td>+ + +</td>
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<tr>
<td>10</td>
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<td>F</td>
<td>CHOL, 30 PY</td>
<td>COLD, sigma diverticulosis</td>
<td>Abdominal and low back pain, night sweats, WL</td>
<td>MRI 12 144 – – +</td>
<td>+ +</td>
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<td>11</td>
<td>RPF</td>
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<td>M</td>
<td>AH, CHOL, 40 PY</td>
<td>CHD, PAOD, COLD</td>
<td>Abdominal and low back pain, WL</td>
<td>MRI 10 91 – – +</td>
<td>+ +</td>
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<td>12</td>
<td>RPF</td>
<td>71</td>
<td>M</td>
<td>AH, 30 PY</td>
<td>CHD, PAOD, hyperthyroidism</td>
<td>Renal failure</td>
<td>– – – – + + –</td>
<td>– –</td>
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<td>13</td>
<td>RPF</td>
<td>43</td>
<td>M</td>
<td>AH, CHOL, 20 PY</td>
<td>PAOD</td>
<td>Low back pain, night sweats, WL</td>
<td>MRI 5 100 ++ ++</td>
<td>+ ++</td>
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<td>41</td>
<td>M</td>
<td>AH, 40 PY</td>
<td>Prostate hyperplasia</td>
<td>Low back pain</td>
<td>MRI 8 48 – – +</td>
<td>– –</td>
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<tr>
<td>15</td>
<td>RPF</td>
<td>54</td>
<td>F</td>
<td>AH, 30 PY</td>
<td>Osteoporotic vertebral fracture</td>
<td>Abdominal and low back pain, WL</td>
<td>CT 10 110 + – +</td>
<td>+ –</td>
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<td>16</td>
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<td>61</td>
<td>M</td>
<td>AH, CHOL, 80 PY</td>
<td>CHD, PAOD, pulmonary adenocarcinoma</td>
<td>Poor documentation</td>
<td>CT 2 96 – – +</td>
<td>+ +</td>
</tr>
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<td>IAAA</td>
<td>60</td>
<td>M</td>
<td>AH, CHOL, 40 PY</td>
<td>CHD, PAOD, previous spondylitis</td>
<td>Abdominal and flank pain, night sweats, WL</td>
<td>CT 15 140 – – +</td>
<td>+ +</td>
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<tr>
<td>18</td>
<td>IAAA</td>
<td>58</td>
<td>M</td>
<td>CHOL, 40 PY</td>
<td>Previous mycobacterial spondylitis</td>
<td>Low back pain</td>
<td>– – – – + + –</td>
<td>– –</td>
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<td>19</td>
<td>IAAA</td>
<td>69</td>
<td>M</td>
<td>AH, 40 PY</td>
<td>CHD</td>
<td>Poor documentation</td>
<td>CT 40 84 – – +</td>
<td>+ +</td>
</tr>
<tr>
<td>20</td>
<td>IAAA</td>
<td>61</td>
<td>M</td>
<td>CHOL</td>
<td>CHD, PAOD, duodenal ulcer</td>
<td>Low back and flank pain</td>
<td>– – – – + + –</td>
<td>– –</td>
</tr>
</tbody>
</table>

AH, arterial hypertension; CHOL, hypercholesterolaemia; PY, smoking in pack years; CHD, coronary heart disease; PAOD, peripheral arterial obstructive disease; COLD, chronic obstructive lung disease; WL, weight loss; CE, contrast enhancement of the periaortic mantle: absent ‘–’, detectable ‘(+’), intermediate ‘++’ and strong ‘+++’; ND, not done; UTO, urinary tract obstruction: absent ‘–’, unilateral ‘+’ or bilateral ‘++’. Vascular involvement is defined as involvement of renal or iliac vessels or the vena cava inferior. No images were available for retrospective analysis in patients 4, 12, 18, and 20.
remission was defined as improvement, and full remission as normalisation of the respective variable.

For statistical calculation of the association between the increase in CRP and contrast enhancement, Kruskal-Wallis one way analysis of variation on ranks was used with subsequent multiple comparisons.

RESULTS

Demographics and medical history

Twenty two patients with chronic periaortitis were identified during the past 12 years and were seen by the department for urology, vascular surgery, nephrology, or rheumatology. The diagnosis of chronic periaortitis was confirmed in 20 patients (14 male, 6 female patients; table 1), based on either histology (12 patients) and/or typical radiological findings. Two patients were excluded from further analysis owing to retroperitoneal dissemination of malignant cells (cholangiocarcinoma and bladder cancer) with survival of less than 6 months after diagnosis.

The average age at the time of diagnosis of chronic periaortitis was 51 years (range 30–71). Fifteen patients manifested with isolated RPF and five with IAAA. The median ages of the patients presenting with RPF and with IAAA were 49 years (range 30–71) and 62 years (range 58–69), respectively. The average time of follow up was 39 months (range 5–75). Table 1 gives the medical history of the patients studied. Cardiovascular risk factors were common both in patients with IAAA and those with RPF. Fifteen (75%) patients had a history of arterial hypertension, 13 (65%) presented with hypercholesterolemia, and 18 (90%) were heavy cigarette smokers, with an average of 35 pack years (range 10–80). Coronary heart disease was diagnosed in 10 (50%) patients and peripheral arterial obstructive disease in 8 (40%). Autoimmune disorders were recorded in 4 (20%) patients and included thyroiditis, leukocytoclastic vasculitis, and sacroiliitis.

Symptoms and laboratory findings at the initial presentation

Fifteen of 16 (94%) patients were referred with pain. In 11/16 (69%) patients, the pain was localised in the lower back, in 7/16 (44%) in the abdomen, and in 5/16 (31%) in the flanks. Weight loss was documented in 9/16 (56%) patients, either before diagnosis, or during the further course of the disease. One patient presented with renal failure, and two with Leriche’s syndrome. Laboratory evidence of renal insufficiency (diagnosed as serum creatinine = 97 μmol/l at two consecutive visits) was detectable in 40% of patients. Microhaematuria was present in 30% of subjects. The CRP (normal range <5 mg/l) was initially increased in 10/13 (77%) subjects and the erythrocyte sedimentation rate (Westergren’s method) was >20 mm/1st h in 14/16 (87.5%). Only 10% of patients presented with leucocytosis.

Imaging

Initial ultrasound examination disclosed signs of urinary tract obstruction in 13 (65%) subjects (five bilateral and eight unilateral). MRI or contrast enhanced CT scans typically showed a fibrotic mass surrounding the infrarenal aorta, but
excluding its posterior wall (fig 1). The average (SD) thickness and longitudinal extension of the periaortic mantle were 14.3 (8.5) mm and 99.8 (25) mm, respectively.

Involvement of the renal arteries was detected in 38% of images and compression of the vena cava in 75% (without corresponding clinical symptoms). Contrast enhancement of the lesion was present in only 56% of the initial images. Radiological follow up was not possible in six patients, either because only one imaging session was performed (n = 2) or because images could not be retrieved (n = 4). No correlation was found between the CRP value and the thickness of the fibrotic mass, even at intraindividual follow up (data not shown). Strong enhancement of gadolinium in the lesions was associated with high CRP values, whereas no such association was detected between slight or absent enhancement and CRP (fig 2).

### Treatment

Treatment consisted of surgical intervention without immunosuppression (5 patients), immunosuppression only (11 patients), or a combination of both (4 patients) (table 2). Ureteral obstruction was relieved by intrarenal stenting with a double J catheter (DJ).

Immunosuppressive drugs were used in 15 patients and reduced the diameter of the periaortic mantle in 13 (87%) of them (figs 1 and 3). This reduction took many months of treatment in most patients (fig 3). Notably, 50% of the initial 14 DJ were permanently removed during immunosuppression and none of our patients needed intraperitoneal displacement of the ureter after immunosuppression was included in the first line treatment. CRP values normalised in 55% of those patients in whom it had initially increased and improved in the others. Contrast enhancement improved in all patients with strong uptake.

The initial regimen consisted of cyclophosphamide (CYC) in nearly 50%. Usually 6 (range 5–9) intravenous CYC pulses were given (mean cumulative dose 5.9 g, range 4.3–8.0) and patients were then switched to either azathioprine (AZA, 2–3 mg/kg/day) or oral corticosteroids (OCS) maintenance treatment. Eight patients received AZA. All of them responded, but three had to be switched because of new onset leucopenia or anaemia. Ciclosporin A was used twice and had to be discontinued in one patient because of new onset hypertension. Three patients (two receiving mycophenolate mofetil (MMF) and one receiving OCS monotherapy) progressed with the initial immunosuppression.

Five patients were treated only surgically. Aortic repair was performed in three patients with IAAA (patients 16, 17, and 20) and ureterolysis in two patients with isolated RPF (patients 4 and 12). One of the patients with IAAA received an intraluminal stent and two a synthetic graft. Two patients were lost to follow up and the third is in partial remission as measured by renal function and inflammatory variables. In both patients with isolated RPF, postoperative removal of DJ catheters is reported, but both were subsequently lost to follow up.

Two patients with IAAA received immunosuppressive treatment. One patient (patient 18) was treated postoperatively and went into full remission. In the other patient...
(No 19), who received initially successful OCS monotherapy, a renal artery obstruction had to be stented after 3 years. After intravenous CYC followed by AZA this patient is now in partial remission and receives low dose OCS alone.

**DISCUSSION**

We retrospectively examined the medical outcome of 20 patients with chronic periaortitis receiving surgical and/or immunosuppressive treatment.

As reported previously, chronic periaortitis was diagnosed mostly in the fifth decade of life,6–10 with non-specific and ill-defined flank, back, or abdominal pain.6–10 Fever was uncommon. Smoking has been recently described as a risk factor11 and was prevalent in 90% of our patients with IAAA and RPF. We were unable to assess other risk factors, such as asbestos exposure,11 in our retrospective analysis but noted a coincidence with other autoimmune disorders.7,12–14

There are no specific laboratory tests for chronic periaortitis. CRP or BSG are initially increased with very varying (and at times only very low) frequency.5,10–13 In our series, the CRP level was increased mostly in patients with strongly contrast enhancing lesions, but was not associated with the diameter of the periaortic mantle. Although the CRP often (but not unequivocally) normalised before the gadolinium uptake and the diameter of the periaortic mantle, normal CRP values did not exclude worsening imaging parameters. These facts suggest that the CRP is not a reliable marker for excluding chronic periaortitis and for monitoring disease activity.

Imaging has a major role in the diagnosis and should be performed in patients with unexplained back, flank, or abdominal pain. Although ultrasound is useful for detecting urinary tract obstruction or aortic aneurysms, it is limited in describing the extent of RPF, or in distinguishing between inflammatory and non-inflammatory AAA.14–16 Contrast enhanced MRI and CT permit more detailed imaging of chronic periaortitis, but it is unclear which technique is better.17–18 MRI may be preferred because of its ability to obtain sagittal as well as coronal images, and because it avoids exposure to x rays and iodinated contrast medium.

Since the first publication of successful treatment with OCS in 195819 several reports have suggested that immunosuppressive treatment is effective.20–22 In our study, disease activity was eventually controlled by immunosuppression in 13/15 (87%) of patients, although modifications were often required. Mild to moderate cases were treated with AZA (2 mg/kg body weight) plus OCS, whereas severe or refractory disease was treated with cyclosporin A (2 mg/kg body weight) for 6 months, followed by AZA. All patients treated with CYC went into remission and seem to decrease the concomitant periaortal inflammation,14,15 but the data seem to permit a careful observation of the spontaneous postoperative course after aneurysm repair. Preoperative steroids were, on the one hand, recommended to reduce the inflammatory mass15 and, on the other, advised against23 because of a presumed risk of intraoperative aortic rupture. Postoperative immunosuppression, however, may benefit some patients as suggested by our experience.

We conclude that immunosuppressive treatment is an effective and well tolerated treatment for RPF and should therefore be included in the early management of disease. Response to treatment may be protracted and should be monitored with imaging studies.

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