Chronic periaortitis

R. N. Jois, K. Gaffney, T. Marshall and D. G. I. Scott

Chronic periaortitis commonly involves the infrarenal portion of the abdominal aorta. Idiopathic retroperitoneal fibrosis, inflammatory abdominal aortic aneurysm and perianeurysmal retroperitoneal fibrosis are its various clinical presentations. They present as a non-specific systemic inflammatory disorder and may lead to ureteric obstruction and consequent renal failure. An exaggerated inflammatory response to advanced atherosclerosis has been thought to be the main pathogenetic process. Autoimmunity has also been proposed as a contributing factor. Contrast-enhanced CT scanning is the diagnostic test of choice. Steroids and immunosuppressive agents are successfully used in the treatment of idiopathic retroperitoneal fibrosis and selected cases of inflammatory abdominal aortic aneurysm, and surgery is used in others. Early diagnosis is important in order to reduce morbidity from complications such as renal failure and mortality from aortic rupture.

Key words: Chronic periaortitis, Idiopathic retroperitoneal fibrosis, Inflammatory aneurysm of abdominal aorta.

The term chronic periaortitis encompasses idiopathic retroperitoneal fibrosis (IRF), inflammatory abdominal aortic aneurysm (IAAA) and perianeurysmal retroperitoneal fibrosis [1, 2]. Although these disorders differ in their clinical presentation, their histopathological characteristics are identical: advanced atherosclerosis of the abdominal aorta, chronic inflammatory infiltrates in the aortic adventitia, medial thinning in dilated or undilated aorta with varying degree of periaortic fibrosis, and extension to involve adjacent structures [2]. The classical presentation is with back/abdominal pain, fever, malaise, weight loss, anaemia of chronic disease and raised inflammatory markers.

IRF is characterized by periaortic fibrosis, which, causes non-specific symptoms and leads to obstruction of the ureters and sometimes adjacent abdominal structures [3, 4]. IAAA is characterized by the triad of back/abdominal pain, pulsatile abdominal aortic aneurysm (surrounded by fibrotic tissue) and an elevated ESR [5, 6]. Perianeurysmal retroperitoneal fibrosis has features of both these conditions and presents with fibrosis around atherosclerotic aortic aneurysm, which may result in ureteric blockage [7].

It is important to recognize chronic periaortitis early in its course in order to attempt to prevent the severe secondary complications of renal failure (due to ureteric obstruction) and the potentially fatal consequence of aortic rupture. Our understanding of the pathogenesis and approach to treatment has been greatly facilitated by advances in imaging techniques in recent years.

Inflammation and autoimmunity have been proposed as the pathogenetic processes leading to chronic periaortitis. The pioneering work of Mitchinson [1], Parums et al [2, 8, 9], Ramshaw et al. [10, 11], Koch et al. [12], Pennell et al. [6], Sterpetti et al. [13] and Rose and Dent [14] has helped to establish the fact that inflammation is the major pathogenetic process in periaortitis. Inflammation is not seen in the aortic adventitia unless there is advanced atherosclerosis, and the intensity ranges from mild in athero-sclerosis to more extensive in periaortitis. In these studies, aortic histology in both subclinical and clinical periaortitis showed dense chronic inflammatory infiltrates in the adventitia, often with lymphoid follicle formation and active germinal centres. There were no differences in histology between IAAA and IRF apart from an increased aortic diameter in the former. The aortic adventitial infiltrate differed from those described solely in the atheroma itself and comprised predominantly B-lymphocytes and plasma cells that were in turn surrounded by CD4-positive T lymphocytes. Similar lymphocyte populations, periaortic inflammation and fibrosis have been demonstrated in histology specimens of IRF, mediastinal fibrosis and IAAA [1, 8, 9, 15, 16]. Also, HLA-DR expression has been found to be abundant here [10, 11]. These observations have led to the unifying concept of chronic periaortitis as proposed by Mitchinson [1], which is characterized by chronic inflammation in the presence of advanced atherosclerosis, resulting in a spectrum of clinical disorders that include IRF and IAAA. Further work by Ramshaw and Parums [17] showed increased expression of intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VAM-1) in the aortic adventitial infiltrates. This increased with the severity of chronic inflammation. These observations support the concept of initiation and progression of a B-cell-dominant inflammatory process in chronic periaortitis.

Autoimmunity to a component of atherosclerotic plaque, viz. oxidized low-density lipoprotein (LDL) and ceroid, has been proposed as the antigenic stimulus in the initiation of the inflammatory process. This has been supported by the finding of IgG in the plasma cells of the adventitia and in close apposition to extracellular ceroid in the necrotic base of atherosclerotic plaques [18]. Also, serum antibodies to oxidized LDL and ceroid have been shown to be more common in chronic periartitis than healthy young controls [19]. Recent studies have looked into the role of tumour necrosis factor-α and its converting enzyme in aneurysm formation [20]. In a recent review, Vaglio et al. [21] reported vasculitis with fibrinoid necrosis involving the aortic vasa vasorum and the small and medium retroperitoneal vessels, suggesting that chronic periartitis could be a systemic autoimmune disease, perhaps involving a vasculitic process of small and medium vessels. This supports previous studies, which reported a prevalence of small- and medium-vessel vasculitis in 10–80% [3, 22]. The association of various autoimmune diseases, such as systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis..
than 5 cm.

sidered if the aneurysm reaches a maximum diameter of more
(ultrasound scan every 6 months). Elective surgery will be con-
10 mg/day. He is under regular review with aneurysm surveillance
fell to 10 mm/h and CRP to less than 7 mg/dl after 10 days of
showed a 4.3 cm aneurysm of the infrarenal abdominal aorta and
surrounding the aorta and common iliac aneurysm. These appear-
there was a ‘rind’ of abnormal material of soft tissue density
aneurysmal dilatation of both common iliac arteries. In addition,
indings were normal: renal, liver and bone profile, serum and urine
electrophoresis. ANA, ANCA and serological testing for syphilis
were negative. Chest and spine radiographs, radioisotope bone
scan, echocardiogram and CT scan of the chest were normal. She
did not attend for the initial follow-up.

Two months later she presented again with recurrent episodes
of severe diffuse abdominal pain. CT scan of the abdomen revealed
a mantle of soft tissue encircling the aorta for a length of 3 cm
starting at the origin of left renal artery. These changes were
consistent with periaortic fibrosis (limited retroperitoneal fibrosis).
No enlarged lymph nodes were seen and other abdominal organs
appeared normal. Magnetic resonance imaging (MRI) of the
chest showed thickening of the wall of the arch and the upper
descending aorta, with a moderately intense signal on T2 and STIR
images, suggesting mediastinal fibrosis. She was commenced on
prednisolone 30 mg daily. During the next 2 months her back/
abdominal pain settled, phonation improved and ESR fell to
30 mm/h. A repeat MRI scan 4 months later showed a reduction
in the periaortic soft tissue around the abdominal aorta and not
much change in the chest when compared with previous imaging.
No new lesions were seen. Two months later she was readmitted
to hospital with severe lumbar back pain. On examination, lumbar
movements were restricted and ESR was 100 mm/h. The presen-
tation was thought to be consistent with a relapse of her condition.
Prednisolone was increased to 60 mg daily. On the same day she
developed massive abdominal distension and a cardiac arrest.

Postmortem examination revealed extensive retroperitoneal
haemorrhage due to ruptured abdominal aorta. There was focal
dilatation of the abdominal aorta with gross thickening of the
aorta and periaortic tissues. The luminal surface was creamy and
granular with advanced atherosclerosis. The rupture site was 4 cm
distal to the renal arteries, with adherent thrombus and significant
thinning of the aortic wall. Patchy involvement of the descending
thoracic aorta was also seen, with focal dilatation and adherent
thrombus to the external wall suggestive of previous tearing.
This and the previous MRI scan appearance were thought to account
for the previous history of thoracic pain and recurrent laryngeal
nervous palsy. The renal artery lumen was narrowed by more than
50% due to the atherosclerosis.

Case 3

A 56-yr-old lady presented with thoracic back pain with gradual
onset that had started one year previously. She also had malaise,
weight loss of 5 kg and recent-onset hoarse voice. She had
necrotic anaemia of 10 g/dl and an ESR of 100 mm/h. Clinical
examination revealed left vocal cord palsy. The following investi-
gations were normal: renal, liver and bone profile, serum and urine
electrophoresis. ANA, ANCA and serological testing for syphilis
were negative. Chest and spine radiographs, radioisotope bone
scan, echocardiogram and CT scan of the chest were normal. She
did not attend for the initial follow-up.

Two months later she presented again with recurrent episodes
of severe diffuse abdominal pain. CT scan of the abdomen revealed
a mantle of soft tissue encircling the aorta for a length of 3 cm
starting at the origin of left renal artery. These changes were
consistent with periaortic fibrosis (limited retroperitoneal fibrosis).
No enlarged lymph nodes were seen and other abdominal organs
appeared normal. Magnetic resonance imaging (MRI) of the
chest showed thickening of the wall of the arch and the upper
descending aorta, with a moderately intense signal on T2 and STIR
images, suggesting mediastinal fibrosis. She was commenced on
prednisolone 30 mg daily. During the next 2 months her back/
abdominal pain settled, phonation improved and ESR fell to
30 mm/h. A repeat MRI scan 4 months later showed a reduction
in the periaortic soft tissue around the abdominal aorta and not
much change in the chest when compared with previous imaging.
No new lesions were seen. Two months later she was readmitted
to hospital with severe lumbar back pain. On examination, lumbar
movements were restricted and ESR was 100 mm/h. The presen-
tation was thought to be consistent with a relapse of her condition.
Prednisolone was increased to 60 mg daily. On the same day she
developed massive abdominal distension and a cardiac arrest.

Postmortem examination revealed extensive retroperitoneal
haemorrhage due to ruptured abdominal aorta. There was focal
dilatation of the abdominal aorta with gross thickening of the
aorta and periaortic tissues. The luminal surface was creamy and
granular with advanced atherosclerosis. The rupture site was 4 cm
distal to the renal arteries, with adherent thrombus and significant
thinning of the aortic wall. Patchy involvement of the descending
thoracic aorta was also seen, with focal dilatation and adherent
thrombus to the external wall suggestive of previous tearing.
This and the previous MRI scan appearance were thought to account
for the previous history of thoracic pain and recurrent laryngeal
nervous palsy. The renal artery lumen was narrowed by more than
50% due to the atherosclerosis.

Case 1

A 67-yr-old man presented with a 6-week history of intermittent
low back pain, worse at night, and disturbing sleep. He had lost
2 kg weight in the previous month. He was a lifelong smoker.
Clinical examination was normal.

Investigations showed raised ESR of 45 mm/h and CRP of
67 mg/dl (normally <7 mg/dl). Full blood count, renal function,
liver and bone profile, serum and urine electrophoresis, and immu-
noglobulins were all in the normal range. Serum cholesterol was
5.4 mmol/l. X-rays of the lumbar spine and chest were normal.

Clinical examination was normal.

2 kg weight in the previous month. He was a lifelong smoker.

A magnetic resonance scan of the lumbar spine was undertaken
to exclude discitis and metastases. This showed that the abdominal
aorta was dilated and abnormal. A contrast-enhanced CT scan
showed a 4.3 cm aneurysm of the infrarenal abdominal aorta and
aneurysmal dilatation of both common iliac arteries. In addition,
there was a ‘rind’ of abnormal material of soft tissue density
surrounding the aorta and common iliac aneurysm. These appear-
ances were consistent with inflammatory aneurysm of the distal
abdominal aorta (Fig. 1). Additional investigations, including
ANA, ANCA and serological testing for syphilis, were negative.

He was treated with prednisolone 40 mg daily, resulting in
complete resolution of back pain over the next few days. The ESR
fell to 10 mm/h and CRP to less than 7 mg/dl after 10 days of	reatment. Methotrexate was added to help steroid reduction to
10 mg/day. He is under regular review with aneurysm surveillance
(ultrasound scan every 6 months). Elective surgery will be con-
sidered if the aneurysm reaches a maximum diameter of more
than 5 cm.

Case 2

A 67-yr-old man presented with thoracic back pain with gradual
onset that had started one year previously. She also had malaise,
weight loss of 5 kg and recent-onset hoarse voice. She had
necrotic anaemia of 10 g/dl and an ESR of 100 mm/h. Clinical
examination revealed left vocal cord palsy. The following investi-
gations were normal: renal, liver and bone profile, serum and urine
electrophoresis. ANA, ANCA and serological testing for syphilis
were negative. Chest and spine radiographs, radioisotope bone
scan, echocardiogram and CT scan of the chest were normal. She
did not attend for the initial follow-up.

Two months later she presented again with recurrent episodes
of severe diffuse abdominal pain. CT scan of the abdomen revealed
a mantle of soft tissue encircling the aorta for a length of 3 cm
starting at the origin of left renal artery. These changes were
consistent with periaortic fibrosis (limited retroperitoneal fibrosis).
No enlarged lymph nodes were seen and other abdominal organs
appeared normal. Magnetic resonance imaging (MRI) of the
chest showed thickening of the wall of the arch and the upper
descending aorta, with a moderately intense signal on T2 and STIR
images, suggesting mediastinal fibrosis. She was commenced on
prednisolone 30 mg daily. During the next 2 months her back/
abdominal pain settled, phonation improved and ESR fell to
30 mm/h. A repeat MRI scan 4 months later showed a reduction
in the periaortic soft tissue around the abdominal aorta and not
much change in the chest when compared with previous imaging.
No new lesions were seen. Two months later she was readmitted
to hospital with severe lumbar back pain. On examination, lumbar
movements were restricted and ESR was 100 mm/h. The presen-
tation was thought to be consistent with a relapse of her condition.
Prednisolone was increased to 60 mg daily. On the same day she
developed massive abdominal distension and a cardiac arrest.

Postmortem examination revealed extensive retroperitoneal
haemorrhage due to ruptured abdominal aorta. There was focal
dilatation of the abdominal aorta with gross thickening of the
aorta and periaortic tissues. The luminal surface was creamy and
granular with advanced atherosclerosis. The rupture site was 4 cm
distal to the renal arteries, with adherent thrombus and significant
thinning of the aortic wall. Patchy involvement of the descending
thoracic aorta was also seen, with focal dilatation and adherent
thrombus to the external wall suggestive of previous tearing.
This and the previous MRI scan appearance were thought to account
for the previous history of thoracic pain and recurrent laryngeal
nervous palsy. The renal artery lumen was narrowed by more than
50% due to the atherosclerosis.

Case 3

A 71-yr-old lady presented with a history of recurrent dull diffuse
abdominal pain, retrosternal heartburn, malaise and weight loss
over 3 months. She was a lifelong smoker. She also had a hoarse
voice and laryngeal examination confirmed left total vocal cord
palsy. Blood count, renal function and liver and bone profile
were normal and ESR was 106 mm/h. Endoscopic examination
of the bowel was normal. Chest X-ray revealed two soft-tissue
opacities peripherally in the left lower zone. CT scanning of
the chest was carried out to exclude malignancy. This showed
periaortic fibrosis around the root of the great vessels arising
from the aortic arch, consistent with fibrosing mediastinitis. The
periaortitis also extended into the abdomen distal to the left renal
artery (Figs 2a and 3a). There were multiple peripheral tiny
intrapulmonary nodules, possibly pulmonary hyalinizing granu-
oma. Thoracoscopic biopsy of the periaortic tissue was done to
exclude malignancy and this showed chronic inflammatory inflit-
rate and fibrosis. This presentation was consistent with the diag-
nosis of idiopathic mediastinal fibrosis and retroperitoneal fibrosis
(chronic periaortitis). ANA, ANCA and serological testing for

Fig. 1. Rind of abnormal periaortic tissue (arrow).
syphilis were negative. Temporal artery biopsy showed no evidence of arteritis. She was started on prednisolone 1 mg/kg, which resulted in complete resolution of the abdominal pain and malaise. The ESR normalized to 15 mm/h by 5 months after steroid treatment. A repeat CT scan showed resolution of the periaortic fibrotic cuff (Figs 2b and 3b) and the pulmonary nodules. Low-dose prednisolone was continued. Two years later, her abdominal pain recurred and ESR was elevated at 30 mm/h. This responded to an increased dose of prednisolone and addition of azathioprine. A repeat CT scan showed no recurrence of periaortic fibrosis. She has had a subsequent recurrence of mediastinal fibrosis and this has also responded to a temporary increase in the dose of steroids.

Discussion

Epidemiology

Albarran, a French urologist, was the first to describe IRF in 1905 [32]. Ormand’s description in 1948 established it as a definite clinical entity [33]. The term IRF may be misleading since it is no longer considered idiopathic but secondary to advanced atherosclerosis, and is probably an autoimmune process. The estimated annual incidence is 0.2–0.5 per 100,000, with no ethnic difference. Middle aged to elderly men are more commonly affected (male to female ratio, 2:1 to 3:1).

The first description of IAAA was by Walker et al. in 1972 [34]. The triad of thickened aneurysm wall, extensive perianeurysmal and retroperitoneal fibrosis and dense adhesions of adjacent abdominal organs defines IAAA. IAAA represent 3–10% of abdominal aortic aneurysms. It occurs predominantly in men (male to female ratio from 6:1 to 30:1). The mean age at presentation is 62–68 yr, which is 5–10 yr younger than in patients with non-inflammatory abdominal aortic aneurysm [13, 14, 28, 29, 34, 35].

Clinical features

Dull diffuse back/abdominal/flank pain is the commonest symptom (80%). Fever, weight loss, anorexia, vomiting, malaise, claudication, testicular pain and ureteral colic have also been described [4, 5, 36, 37]. A palpable tender pulsatile abdominal aneurysm is seen in 15–30% of IAAA cases [5, 29, 35]. In contrast, between 8 and 18% of patients with non-inflammatory aortic aneurysms are symptomatic [13, 29]. Our patients in all three cases had similar presentation.

Ureteral obstruction leading to unilateral or bilateral hydronephrosis and consequent renal insufficiency is the commonest organ involvement in IRF [29, 36–40]. This can be the presenting complaint, and therefore IRF is often seen more in urology practice. Ureteric obstruction is commonly due to oedema and inflammation rather than fibrosis. This observation is supported by the fact that the obstruction can improve rapidly with steroid therapy. In IAAA, fibrous periaortic tissue results in entrapment of the ureters (53%) [41] and may in turn cause obstructive uropathy in 10–21% of patients [13, 42, 43].
tion has been reported in 18–21% of patients [29, 41]. Venous thromboembolism, true or pseudointestinal obstruction and spinal cord compression are rare associations due to spread of fibrosis [6, 29, 40, 44]. Reidel’s thyroiditis [4], sclerosing cholangitis [45], pulmonary hyalinizing granuloma (seen here in case 3) [46] and retro-orbital fibrosis [47] have also been described as rare associations.

A similar chronic inflammatory process can occur around the thoracic aorta and in continuity through the diaphragm. This has been described as idiopathic mediastinal fibrosis [16] and was also seen in our patients (cases 2 and 3).

Retroperitoneal fibrosis can also occur secondary to metastatic disease, lymphoma, sarcoma and carcinoid. The incidence of malignant disease has been reported to be around 7.9% in cases clinically resembling IRF [48, 49]. Hence, a biopsy of the fibrotic tissue may be necessary to rule out malignancy. Use of drugs, including methysgeride, pergolide, bromocriptine, beta-blockers, methyldopa, hydralazine, can result in retroperitoneal fibrosis, which is reversible on discontinuation of the offending drug.

Arterial aneurysms in other sites have been reported in IAAA—internal iliac arteries [43%], thoraco-abdominal aorta [13%] and the femoral artery [13%]. Systemic hypertension, peripheral vascular disease, diabetes mellitus and coronary artery disease are more frequently associated with chronic periaortitis.

Diagnosis

An elevated ESR is seen in 80–90% of the patients. Normocytic, normochromic anaemia and worsening renal function are common. The definitive diagnostic test is contrast-enhanced CT scanning or MRI. These demonstrate the periaortic soft tissue mass as a ring of abnormal tissue around the aorta, with a varying extent of spread, and the aorta is aneurysmal in IAAA. CT-guided biopsy is usually adequate to exclude malignancy in IFFF, though open multiple deep biopsies may occasionally be required. Ino et al. [50] reported sensitivity of 83.3%, specificity of 99.7% and accuracy of 93.7% for the diagnosis of IAAA using CT scanning, which was particularly helpful in our patients. CT scanning is also helpful in diagnosing complications such as hydrophrosis, aorto-enteric fistula and infected iliac artery aneurysms.

The accuracy of ultrasound in detecting the periaortic cuff is low, and Pennell et al. reported a positive diagnosis in only 13.5% of their patients [6].

Gadolinium-enhanced MRI is also a good diagnostic tool [51]. The inflammatory cuff is enhanced homogeneously following contrast administration.

Excretory urography may suggest the diagnosis by demonstrating ureteral entrapment in IRF, but this is seldom needed.

Treatment

Medical. The role of steroids in chronic periaortitis is controversial. They have been used along with surgery with good results [52]. The presence of inflammatory cells in the fibrous tissue forms the basis for steroid use. Complete resolution of back/abdominal pain, regression of the sedimentation rate and histological features. Early diagnosis and inflammatory aortic aneurysms.

Surgery. Ureterolysis (freeing the ureter from fibrous adhesions) without lateral transposition and wrapping them with omentum is the procedure of choice for patients with hydronephrosis in IRF. Ureteral stents are also used. Concomitant steroid use is advised [4, 5, 13, 35].

Operative repair of the aneurysm is the definitive treatment for IAAA. Surgery is recommended when the aneurysm is greater than 5 cm in maximal transverse diameter. The risk of rupture in an aneurysm measuring 4–5 cm is around 25% and postrupture mortality is more than 75%. Aneurysmal exclusion is the principle behind surgery and is aimed at reduction of the inflammatory response and prevention of rupture. With improved surgical techniques, the operative mortality for elective aneurysm repair is as low as 0.9–5% [70] and survival is similar to that of the non-inflammatory type [71]. Open repair has been the traditional method, though more recently a transfemoral endoluminal technique using endoprosthesis has been tried successfully [72, 73].

Resolution of periaortic fibrotic tissue after surgery for IAAA is still debated. Some investigators have reported complete resolution whilst others have noted partial regression and even persistence of the inflammatory cuff [74–76]. New low-grade periaortic fibrosis has been reported after endovascular repair in a small number of patients [76]. Stella et al. [41] noted that postoperative improvement was significantly more marked in cases characterized by higher preoperative inflammatory indices in the aneurysmal wall.

<table>
<thead>
<tr>
<th>Rheumatology</th>
<th>Key messages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic periaortitis is a common pathogenetic concept for retroperitoneal fibrosis and inflammatory aortic aneurysms. The underlying idea of an inflammatory reaction to advanced atherosclerosis has evolved on the basis of common clinical and histological features. Early diagnosis may be important in reducing the mortality associated with chronic periaortitis.</td>
<td></td>
</tr>
</tbody>
</table>

The authors have declared no conflicts of interest.
References


