Thromboangiitis obliterans or Buerger’s disease: challenges for the rheumatologist

X. Puechal and J.-N. Fiessinger

Introduction

Thromboangiitis obliterans (TAO) or Buerger’s disease is characterized by occlusive segmental and often multiple inflammatory lesions of medium-sized and small arteries and superficial veins. In the characteristic acute phase lesion, in association with occlusive cellular thrombosis, the acute inflammation involving all layers of the vessel wall led TAO to be classified as a vasculitis. In addition to these variable and non-specific pathological findings, TAO can be distinguished from other types of vasculitis based on its tendency to occur in young male subjects, its close association with tobacco consumption, the rarity of systemic signs and symptoms, a highly cellular thrombus with relative sparing of the blood vessel wall, the absence of elevated acute-phase reactants and of immunological markers. Complete cessation of smoking remains the cornerstone of therapy, but blockade with antagonists of cannabinoid or endothelin receptors and the use of gene- or cell-based therapy to induce therapeutic angiogenesis have opened up new possibilities for treatment.

Epidemiology and pathogenesis

In the absence of specific diagnostic criteria, it is difficult to determine the prevalence of TAO. Although this disease is found worldwide, it seems to have a higher prevalence in the Middle East, Asia and the Far East than in Europe or North America. TAO accounts for 0.5–5% of patients hospitalized for arterial occlusive disease in Europe [1–4] and up to 16% of such patients in Japan [5]. TAO affects all races [6]. A genetic predisposition has been proposed based on the higher incidence of this disease in Ashkenazi than in non-Ashkenazi Jews in Israel [7]. Either no association with an HLA antigen is observed [8], or conflicting results are obtained, with all series published to date being small and results being related to country of origin [9–12].

TAO was initially thought to affect almost exclusively men, since less than 1% of those affected were women [6]. In the most recent studies, the proportion of female TAO patients varies between 11% and 23% [4, 8, 13, 14]. This increase may be due to an increase in smoking among women.

The young age of the patients is another key characteristic of TAO among the vasculitides [15–17]. The symptoms almost always begin before the age of 40 yrs.

The link with smoking is one of the most original features of TAO. Almost all the patients affected are smokers, most of them heavy smokers [8, 18]. Once the disease has become established, stopping smoking is the only way to prevent progressive flare-ups. Taking up smoking again, even years later, may trigger a new flare-up of the disease [8, 14]. This strong association suggests that tobacco plays a role in the pathogenesis of the disease or, at least, that tobacco is a highly contributive factor. It has been suggested that something, yet undefined, in nicotine may be involved. All types of tobacco and cigarette paper have been implicated and a few cases have been described among users of smokeless tobacco [19]. Less than 5% of TAO patients are non-smokers. These cases might be triggered by cold, frostbite, traumatism of the extremities or even abuse of sympathomimetic drugs [3, 7, 20–22]. Cases of juvenile arteritis with atherosclerotic lesions have been related to the use of Cannabis saliva or C. indica [23]. The role of cannabis was recently reconsidered, resulting in the description of a specific cannabis arteritis [24]. Clinically cannabis arteritis is very similar to Buerger’s disease and the reported differences in pathological lesions are not very convincing [25]. While nearly all patients with TAO use tobacco in some forms, the role of cannabis remains
more controversial and these habits should be considered as factors strongly contributory to TAO.

An impaired endothelium-dependent vasorelaxation in the peripheral vasculature, even in the non-diseased limbs, has been shown in patients with TAO [26]. Mild perturbations in clotting have been described but there is no evidence to suggest that hypercoagulability or fibrinolytic abnormalities play a major role [27].

Various investigations have also been carried out with the aim of identifying an autoimmune mechanism responsible for TAO [2, 28–32]. Hypersensitivity to type I [2, 28] and III [2] collagen associated with the presence of anti-collagen [2] or anti-elastin [30, 32] antibodies has been shown. These abnormalities have proved to be non-specific and have not been confirmed. They may also occur secondarily to inflammatory modifications rather than being the cause of the vascular lesions [31]. Increased levels of anti-endothelial cell antibodies have been reported in patients with active disease [33], but the specificity of such findings remains to be established.

Clinical features

TAO generally begins in young male smokers with hand or foot ischaemia due to distal small arteries and veins involvement of the limbs.

Ischaemia of the lower limbs

The commonest presenting symptoms are ischaemic manifestations of the lower limbs [3, 8, 14, 21]. Claudication in the arch of the foot is an early sign and is suggestive of, or even specific to TAO [34]. This condition is a manifestation of infrapopliteal vessel occlusive disease. In 70–80% of cases [4, 14], the diagnosis is not made until the critical ischaemia phase, with rest pain and ischaemic ulcerations of the toes or feet. Rest pain generally occurs on the foot, causing continuous pain and obliging patients to sleep with their legs dangling downwards. The intensity of this pain often contrasts with the apparently limited, almost benign appearance of the ischaemic trophic lesions (Fig. 1). Superinfection often occurs and the lesions progress towards necrosis and distal gangrene.

Involvement of the upper limbs

Ischaemia of the upper limbs is clinically evident in 40–50% of patients, but may be detected in 63% of patients by Allen’s test [14] and in 91% of patients by arteriogram of the hand and forearm [35]. In the Allen’s test, the examiner places the thumbs to occlude the radial and ulnar arteries of one hand of the patient. The patient opens the fist and the examiner then releases pressure distal to the wrist is patent, there is prompt return to colour to the hand (positive test). The manoeuvre is repeated with the pressure from the radial artery but not the ulnar artery. If the radial artery distal to the wrist is patent, there is prompt return to colour to the hand (negative test). If the artery is occluded, the hand will remain pale (positive test). The manoeuvre is repeated with the pressure released from the ulnar artery but not the radial artery. Raynaud’s phenomenon, generally unilateral, is observed in about half of all patients. Typically, ischaemia is expressed clinically as unilateral or asymmetric symptoms on exercise or digital trophic troubles.

Superficial thrombophlebitis

Superficial thrombophlebitis is observed in 40–60% of cases. Deep vein thrombophlebitis is unusual and suggestive of an alternative diagnosis, such as Behcet’s disease. This superficial thrombophlebitis is migratory and recurrent and affects the arms and legs. Migrating phlebitis (phlebitis saltans) in young patients is therefore highly suggestive of TAO [20, 21].

Systemic signs and symptoms

Systemic signs and symptoms are very rare in patients with TAO [36, 37], with the exception of rheumatic manifestations. Visceral damage has been reported mostly in old publications for isolated cases without all the diagnostic criteria. The diagnosis of an exceptional form of TAO should be made only with the greatest reservation in cases of all the diagnostic criteria. In some of these cases, visceral artery damage results more likely from atherosclerosis, favoured by or associated with TAO [38]. Thus, when TAO occurs in an unusual location, diagnosis should be made only after the identification of typical inflammatory vascular lesions on histopathological examinations [39].

TAO may begin with joint manifestations [40–46]. Such presentations occur in 12.5% of patients, in the pre-occlusive phase [44]. Patients present recurrent episodes of arthritis of the large joints, with transient, migratory single-joint episodes accompanied by local signs of inflammation. The wrists and knees are the most frequently involved joints. The duration of signs and symptoms ranges from 2 to 14 days. The arthritis is non-erosive. Joint problems precede the diagnosis of TAO by about 10 yrs on average [44]. To recognize TAO at this stage is a challenge for the rheumatologist. A diagnosis of TAO should be considered in otherwise healthy young smokers with intermittent or palindromic rheumatism and distal pulses should be palpated regularly because the first ischaemic signs may not appear until 10 yrs later [44]. Arthritis disappears definitively with the appearance of ischaemic signs. A few cases of undifferentiated HLA B27 spondylarthropathies have also been reported in patients with TAO [44]. Nevertheless, in cases in which intermittent joint manifestations are observed before the appearance of ischaemic signs, auto-immune diseases and other types of vasculitis should be first ruled out. At this stage, the most relevant differential diagnoses include palindromic rheumatism, rheumatoid arthritis, spondylarthropathies, crystal-induced arthropathies, lupus, Behcet’s disease, sarcoidosis, Wegener granulomatosis, micropolyangitis and polyarteritis nodosa. A search for the cardinal signs of auto-immune diseases, elevated acute-phase reactants and specific immunological tests generally leads to diagnosis. Apart from these articular manifestations, before the diagnosis of TAO is made, another challenge is represented by the painful ischaemic symptoms and the inflammatory reactions associated with superficial thrombophlebitis [44]. These symptoms are sometimes accompanied by nocturnal pain and swelling due to stasis oedema. They often lead to the patient consulting the rheumatologist [44]. Abnormal...
distal pulses are not always recognized and an initial erroneous diagnosis is often made that refers to a loco-regional or periarticular problem [44]. Exceptional cases of central nervous system involvement have been reported in TAO [47–49]. Transient ischaemic attacks or ischaemic stroke may occur [49]. Post-mortem histological examinations have demonstrated inflammation of the small and medium-sized arteries of the leptomeninges or even of the meninges or veins.

Intestinal involvement is rare in cases of TAO [50–59]. It may occur at any time in the course of the disease and may even be inaugural. Digestive ischaemia may manifest as abdominal pain, diarrhoea, weight loss or melaena. Intestinal perforation and mesenteric infarction may occur. Recent thromboses have been documented with inflammation of the vessel walls of the small intestine [50, 54–56], the colon [52, 58], or the entire intestine [51, 57, 59], with no atheromatous lesions.

Coronary involvement is also extremely rare if it exists [60, 61]. Cases of myocardial infarction have been linked to TAO [62, 63]. In addition to vascular problems, cases of nephropathy due to mesangial IgA deposition have been reported [64].

Investigations

The diagnosis of TAO is rendered difficult by the lack of specific clinical, radiological and biological features [65, 66], the rarity of histopathological evidence of inflammatory vascular lesions [67] and the lack of diagnostic criteria validated or accepted internationally. The diagnosis is therefore made at the end of investigations aiming to eliminate differential diagnoses and to search for other signs of the disease. The distal nature of the thromboangitis and the involvement of the upper limbs are two major arguments for differentiating TAO from atherosclerotic arteriopathies.

Non-invasive vascular evaluation

Ultrasound investigation is used to check for a lack of atherosclerotic lesions and can identify the distal sites of symptomatic arterial occlusion and other sites of lesions. Measurement of toe systolic pressure and of transcutaneous oxygen pressure can be used to confirm the ankle–toe gradient and the severity of ischaemia.

Angiography

The angiographic patterns of TAO are not pathognomonic to this disease [3, 66, 68], but angiography remains an essential step in the diagnosis of TAO. It shows that TAO virtually always occurs in more than one limb, often in all four, even if not clinically involved [18, 35]. The most important diagnostic criterion is the smooth and regular, non-atherosclerotic nature of the artery wall both at the site of, and also proximally to arterial occlusions [3, 16, 67]. Some aspects are evocative but inconsistent and not specific such as corkscrew collaterals. The arteriographic findings may be identical to those of auto-immune diseases. The small and medium-sized arteries are affected in a segmental and often bilateral manner. In the legs, infrapopliteal lesions predominate, affecting one or several vascular beds, but particularly the anterior and posterior tibial arteries (Fig. 2). In the arms, the lesions primarily concern the radial and cubital arteries, together with the palmar arcades and the digital arteries [35].

Laboratory findings

TAO can neither be evoked nor be diagnosed on the basis of biological examinations. Indeed, it is the normal and negative nature of all biological explorations that is remarkable and can be used to eliminate other conditions. Acute-phase reactants are normal or slightly elevated in the absence of extensive trophic lesions. In cases of distal arteriopathy, Buerger’s disease may be excluded in patients with diabetes mellitus [39], whereas modest hyperlipidaemia remains compatible with the diagnosis [38]. Complete blood count is needed to exclude a myeloproliferative syndrome. Screening for hypercoagulability is negative [38]. Buerger’s disease has rarely been reported to be associated with the presence of anticoagulant antibodies [69, 70]. The relationship between the two entities is unclear [69, 71]. A deficit in protein C or protein S, or even in anti-thrombin III may be associated with venous or arterial occlusion and leads to rejection of the diagnosis of TAO. Creatinaemia and studies of urinary sedimentation and proteinuria demonstrate the absence of renal damage suggestive of autoimmune diseases. Searches for rheumatoid factor, anti-nuclear antibodies, anti-centromere antibodies, anti-SCL-70 antibodies and ANCA are necessary, but should be negative, as should tests for hypocomplementaemia, cryoglobulinaemia, hepatitis B and C.

Pathological findings

TAO is an inflammatory disease of the arteries and veins characterized by highly cellular and inflammatory occlusive thrombus, primarily of the distal extremities. The disease affects the small- and medium-sized (1–5 mm diameter) arteries and veins in a segmental and plurifocal manner. However, in contrast to all of the major arteritides, no fibrinoid necrosis of the arterial wall is observed and the architecture wall of the vascular wall is preserved. This feature distinguishes TAO from other types of systemic vasculitis and from arteriosclerosis, in which there is usually striking disruption of the internal elastic lamina and the media [39]. The lesions are not specific and vary according to the duration of the disease (Fig. 3). In the acute phase, arterial and venous lesions are characterized by an association of thrombosis and inflammation. Thromboses are often occlusive and sometimes display moderate, non-specific inflammatory infiltrate, consisting mostly of polymorphonuclear leucocytes, mononuclear cells and rare multinucleated giant cells. In the artery, infiltration is mostly observed in the intima and the thrombus [72]. Macrophages expressing HLA-DR and dendritic cells are preferentially located in the intima [72] and may present antigens brought by the blood stream to CD4+ T lymphocytes predominating in the infiltrate [73]. Linear deposits of immunoglobulins and complement are found along the length of the internal elastic lamina [72], which, like the media, is respected. The appearance of panvasculitis described by Buerger [15], in which inflammatory infiltrate extends to all the layers of the vessel wall without mutilation, is rarely observed in the arteries. In the late phase, the thrombus is...
organized and the vessel is occluded and retracted, with adventitious and periarterial fibrosis. Biopsy of a subcutaneous nodule can be used to confirm the presence of superficial thrombophlebitis at the mostly acute phase, with the same occlusive thrombotic lesions and various degrees of inflammation extending to the entire venous wall (Fig. 4).

**Diagnostic criteria**

Several diagnostic criteria have been proposed [2, 14, 16, 38, 74–78], almost all of which take into account exclusion criteria and signs consistent with the diagnosis. None has been validated. Mozes’s criteria [2, 16], as modified by Fiessinger [38], included women and a major exclusion criterion based on popliteal artery entrapment syndrome (Table 1). Adar’s group recently proposed a point-based scoring system that improves the specificity of diagnosis [77]. The probability of TAO is calculated as the arithmetic sum of points and the possible inclusion of patients with exclusion criteria developing after diagnosis requires regular re-evaluation of the initial diagnosis.

**Table 1. Diagnostic criteria for Buerger’s disease [2, 16, 38] (a definitive diagnosis of Buerger’s disease is retained in young smokers with distal lower limb ischaemia)**

<table>
<thead>
<tr>
<th>With at least two of the following three symptoms</th>
<th>After the exclusion of following</th>
</tr>
</thead>
<tbody>
<tr>
<td>– Superficial thrombophlebitis</td>
<td>– Diabetes mellitus</td>
</tr>
<tr>
<td>– Arterial upper limb involvement</td>
<td>– Atheromatous lesions</td>
</tr>
<tr>
<td>– Raynaud’s phenomenon</td>
<td>– Potential source of embolism</td>
</tr>
<tr>
<td></td>
<td>– Entrapment syndrome</td>
</tr>
<tr>
<td></td>
<td>– Auto-immune diseases</td>
</tr>
<tr>
<td></td>
<td>– Myeloproliferative syndrome</td>
</tr>
<tr>
<td></td>
<td>– Hypercoagulability states</td>
</tr>
</tbody>
</table>

The presence of any one of these symptoms renders the diagnosis probable.

**Table 2. Prevalence of amputations in patients with thromboangiitis obliterans, based on the most recently reported series [4, 14, 81, 82, 85–87]**

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Number of patients</th>
<th>Mean follow-up period (yrs)</th>
<th>Minor amputations (%)</th>
<th>Major amputationsa (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olin et al. [14]</td>
<td>1990</td>
<td>89</td>
<td>7.6</td>
<td>17</td>
<td>10</td>
<td>27</td>
</tr>
<tr>
<td>Dehaine et al. [4]</td>
<td>1995</td>
<td>74</td>
<td>3.5</td>
<td>20</td>
<td>7</td>
<td>27</td>
</tr>
<tr>
<td>Shimematsu et al. [86]</td>
<td>1999</td>
<td>287</td>
<td>19</td>
<td>16.7</td>
<td>10.5</td>
<td>27.2</td>
</tr>
<tr>
<td>Sasaki et al. [85]</td>
<td>2000</td>
<td>850</td>
<td>10</td>
<td></td>
<td></td>
<td>25.2</td>
</tr>
<tr>
<td>Cooper et al. [82]</td>
<td>2004</td>
<td>111</td>
<td>5</td>
<td>11</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Bozkurt et al. [87]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ohta et al. [81]</td>
<td>2004</td>
<td>110</td>
<td>10.6</td>
<td>30.9</td>
<td>11.8</td>
<td>42.7</td>
</tr>
<tr>
<td>Ates et al. [79]</td>
<td>2006</td>
<td>344</td>
<td>11.6</td>
<td>39.5</td>
<td>5.5</td>
<td>45</td>
</tr>
</tbody>
</table>

aMajor amputation is defined as amputation above or below the knee or of the hand.

**Outcome and prognosis**

The clinical course of TAO is characterized by acute exacerbations separated by phases of remission that may last several years. The trophic lesions progress during flare-ups, either by being more proximal or by affecting a limb that was not previous affected. The need for repeated amputations is an indication of the severity of the disease. The life expectancy of patients with TAO is classically normal [8, 74], with a survival rate of almost 90% [79] or 95% at 10 yrs [80] and 85% at up to 25 yrs [81]. However, Cooper et al. [82] reported excessive late mortality in their study of 111 patients with a mean follow-up of 15 yrs.

Tobacco plays a key role in the progression and prognosis of the disease. Flare-ups resolve and ulcers heal only after the patient has stopped smoking [21]. The occurrence of new ischaemic lesions is generally linked to the patient continuing to smoke or starting to smoke again [4, 8, 14, 21, 83]. In the series of patients reported by Schatz et al., only 5% of the patients who stopped smoking continued to present progressive disease, vs 100% of those who continued to smoke [83]. Similarly, Mills et al. reported an absence of progression in all patients who managed to stop smoking [8]. In the study by Ohta and Shionoya [84], half the patients who continued to smoke displayed progressive disease.

The risk of amputation is highly correlated with continuing to smoke. The amputation rate varies from 42% to 5% at the Cleveland Clinic Foundation according to tobacco use; this...
difference is highly significant and clinically relevant [14]. In Japan, an analysis of 850 patients identified in a national study showed that the risk of amputation was 2.73 times higher (95% CI: 1.86–4.01) in patients who continued to smoke [85]. The prevalence of amputations in more recently published series is concordant (Table 2). At the end of a 5-y follow-up period, one quarter of patients are likely to have had an amputation. After 10 yrs, the risk of amputation is up to 45% [79, 84–86]. The risk of major amputation (above or below the knee or even the hand) remains high, at between 4.4% and 11.8% [4, 14, 81, 82, 85–87].

**Treatment**

**Conservative therapy**

The major role played by smoking in the development, progression and prognosis of TAO accounts for giving up smoking being indispensable to the therapeutic management of patients with TAO. All possible means should be used to encourage patients to give up the use of tobacco, in all its forms, completely and definitively [39]. Patient education is important, but only 43–70% of cases manage to give up smoking [38, 39]. Patients should be reassured that if they manage to give up smoking completely, the disease will go into remission and amputation will be avoided [39]. Psychological help may be useful in certain cases [88]. Selective cannabinoid receptor antagonists, such as rimonabant, which shows promise as a treatment for helping patients to stop smoking, open up interesting new treatment perspectives for this disease strongly related to tobacco use [89, 90].

Local care is the other main component of therapeutic management [38]. The aim is to obtain cleansing of the wound with the creation of sufficient new tissue to enable healing. Except for discontinuation of tobacco, there is no other definitive treatment. Care should be taken to prevent mechanical or heat trauma. Calcium inhibitors are frequently recommended [8, 14], although there is no proof that they are actually effective. Similarly, although there is no documented coagulation abnormality and no clinical evidence that anticoagulation therapy may be beneficial [38, 69], some teams use it. Non-steroidal anti-inflammatory drugs are the treatment of choice for superficial venous thromboses [38]. The generation of hypervolemia has been proposed but there is no evidence that expanding plasma volume improves blood flow to the ischaemic limb [38]. Epidural spinal cord stimulation has been proposed in patients with rest pain or trophic problems [91, 92], but the value of this method remains to be demonstrated [93].

Prostacycline derivatives have been evaluated in case-control studies [75, 94, 95] and have been shown to be more effective than placebo [75, 94]. Fifteen patients with TAO treated by continuous perfusion for 72 h with epoprostenol (PG12) showed an improvement in pain and trophic troubles (with respect to the placebo group) that continued for 6 weeks [94]. In another randomized study, 152 patients with Buerger’s disease presenting pain at rest, with or without trophic problems, received a daily perfusion of iloprost or placebo plus aspirin [75]. After 21–28 days of perfusion, the trophic lesions had healed or the pain had disappeared in 85% of the patients on iloprost and 17% of the patients on aspirin. At 6 months, 88% of the patients treated with iloprost had responded to treatment, vs only 21% of those treated with aspirin. Furthermore, amputation was required in 18% of the patients in the aspirin group and only 6% of the patients in the iloprost group. The results of a European study, which compared two doses of oral iloprost with a placebo, were less impressive [95]. No significant difference was found between groups for the primary end point, which was total healing of lesions, at any of the time points considered. Low-dose iloprost was significantly more effective than placebo for relieving pain at rest without the need for an analgesic, at the end of follow-up. High-dose iloprost was not significantly more effective than placebo.

An increase in the level of endothelin-1, a potent vasoconstrictor, was reported in patients with clinical exacerbations of Buerger’s disease in one small study [96]. However, in a recent personal randomized study in 10 patients with Buerger’s disease, the acute infusion of tezosentan gave no greater haemodynamic change than placebo.

**Surgical treatment**

Revascularization treatment is rarely possible due to the diffusion of vascular damage and the distal nature of the disease. In cases in which distal target vessel has been available and bypass surgery carried out, the results have depended on the patient giving up smoking [97] and have often been disappointing [8, 14, 87, 98]. Sympathectomy has been much used but the results obtained are difficult to evaluate and not very convincing. Some experts consider that sympathectomy may help in cases of distal trophic lesions, as a last resort before amputation, or carried out at the same time as amputation [38, 39, 79, 87]. Other surgical techniques remain to be evaluated: use of a nutrient flap, atypical bypass surgery, omental transfer or tibial intramedullary Kirschner-wire to stimulate angiogenesis.

**Experimental therapy**

A new area was opened up with the use of gene transfer to induce therapeutic angiogenesis in TAO [99]. In 1998, Isner et al. published preliminary encouraging results in patients receiving intramuscular injections of vascular endothelial growth factor (VEGF). A recent open-labelled, dose-escalating, phase 1 clinical trial evaluated the safety of such intramuscular VEGF gene transfer, using naked plasmid DNA in seven patients with TAO [100]. The injections were well tolerated. Ischaemic ulcers healed or improved in four of six patients. Five of seven patients showed an increase in collateral vessels around the injection sites.

Preclinical studies have shown that implantation of bone marrow mononuclear cells, including endothelial progenitor cells, into ischaemic limbs, increases collateral vessel formation. In 2002, Tateishi-Yayuma et al. [101] published impressive results for patients with critical ischaemia treated by the autologous transplantation of bone marrow cells. This therapy showed some success in pain relief in patients with Buerger’s disease [102]. Autologous whole bone marrow stem cell transplantation was very recently performed by fenestration of the tibia in 27 patients with Buerger’s disease [103]. Over a mean follow-up period of 19 months, 13 of 17 affected limbs with non-healing ulcers healed. Post-operative angiograms showed some degree of collateral development. Another preliminary report in four patients with TAO has recently suggested that stem cell therapy using umbilical cord blood-derived multipotent stem cells may be useful in healing the necrotic skin lesions and relieving pain [104].

**Conclusions**

TAO remains a systemic vasculitis strangely linked to smoking, which determines its occurrence, progression and prognosis by currently unknown mechanisms. Except for discontinuation of tobacco use, there is no other definitive therapy. Selective cannabinoid receptor antagonists have shown promise for helping patients to stop smoking. Prostacycline analogues may help patients with critical limb ischaemia. Recent innovative genetic and cell-based therapeutic approaches have been proposed to induce angiogenesis but they require evaluation in randomized controlled trials to confirm their beneficial effects in patients with TAO.
Thromboangiitis obliterans or Buerger’s disease

Key message

- Thromboangiitis obliterans (Buerger’s disease) is a vasculitis in young mostly male smokers that affects the small and medium-sized arteries and veins of the limbs. It often poses a diagnostic challenge and may begin with intermittent arthritis. Complete cessation of smoking remains the cornerstone of therapy. The emergence of new biological agents and gene- or cell-based therapy may provide significant tools for management of this systemic vasculitis.

The authors have declared no conflict of interest.

References


79. Ates A, Yekeler I, Ceviz M, et al. One of the most frequently vascular diseases in northeastern of Turkey: Thromboangiitis obliterans or Buerger’s disease (experience with 344 cases). Int J Cardiol 2006;111:147–53.


94. Nizankowski R, Krolikowski W, Bielatowicz J, Szczeklik A. Prostacyclin for ischemia ulcers in peripheral arterial disease. A