Thieme

Arterial leg pain

Arteriell bedingte Beinschmerzen

Author
Christoph Kalka

Affiliations
Innere Medizin I, Marienhospital Brühl

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Correspondence
PD Dr. Christoph Kalka
E-Mail: dr.christoph.kalka@marienhospital-bruehl.de

ABSTRACT

Arterial diseases of the lower extremities are part of the daily medical practice. Given the frequency and variety of symptoms of leg discomfort, appreciation for vascular disorders is demanded as some syndromes are associated with an increased morbidity and mortality. Unfortunately, not few of these patients undergo long lasting investigations for orthopedic or neurological issues making awareness of arterial disorders a high priority. Apart from atherosclerotic peripheral artery disease (PAD), non-atherosclerotic arterial causes of lower limb discomfort include a heterogenous group of uncommon conditions. Important for the outcome is to identify an arterial disorder, to evaluate the degree of the perfusion deficit, to determine the risk of losing the limb and to commence adequate management of the disease.

ZUSAMMENFASSUNG

In der differentialdiagnostischen Abwägung von Beinschmerzen spielen arterielle Gefäßerkrankungen eine wichtige Rolle. Nicht selten allerdings werden in der täglichen Arztpraxis zunächst orthopädische und neurologische Ursachen in Erwägung gezogen. Ein Grund ist sicher die facettenreiche Symptomatik und die Heterogenität arterieller Durchblutungsstörungen.
Obwohl arteriell bedingte Schmerzen der Beine überwiegend arteriosklerotischer Genese sind, sollte das Vorliegen nicht-arteriosklerotischer Ursachen wie die Embolie, die Gefäßdissektion, Kompressionssyndrome und inflammatorische Erkrankungen immer in Erwägung gezogen werden. Prognoseentscheidend ist das Erkennen einer arteriell bedingten Problematik, die Abschätzung des Schweregrades der Durchblutungsstörung und dadurch auch des Amputationsrisikos der Extremität sowie ein zügiges Management.

Vascular pain in the leg

Both arterial and venous diseases are an integral part of routine medical practice, and not only for specialists in vascular diseases. Patients present with a wide variety of symptoms in the legs, which means that careful consideration of the differential diagnosis is important.

Differential diagnosis of arterial vascular diseases

Disorders of the arterial circulation cause a reduction in the oxygen supply to the tissues. In the lower limbs, this leads to ischaemic muscle pain, particularly when there is an increased energy demand on exercise. Peripheral arterial disease (PAD), the most common arterial vascular disease, is therefore a disease that classically first manifests during movement, i. e. with muscle work. As the disor-

der of perfusion and nutrition advances, the energy requirement can no longer be met even without muscle activity, which results in pain at rest.

In principle, exercise-related pain is always distal to the affected vascular territory [1]. For example, occlusion of the distal abdominal aorta and the pelvic arteries gives rise to pain below the pelvis, i. e. in the muscles of the buttocks and thighs. Classical intermittent claudication presents as unpleasant cramps in the calf on walking, with rapid relief on standing still. If the lower leg arteries are affected, then the result is claudication in the foot. This last condition rarely causes symptoms, however, as the distal distribution type of claudication is usually found in people who are in the late stages of diabetes and therefore have reduced pain sensation due to neuropathy.

The symptoms described are the expression of chronic circulatory problems. As a rule, the work-up and differential diagnosis is not urgent. In contrast, the acute forms of PAD dramatically restrict the circulation of the leg and have to be diagnosed and treated as quickly as possible in order to prevent impending amputation. If a vessel is suddenly occluded without sufficient collateral circulation, the result is extremely painful and serious.

Differential diagnosis of arterial occlusion in the leg – **ACUTE**

- Pallid white limb
- Ischaemic pain at rest (during the night)
- Clear difference in colour between the two limbs
- Increased pain on elevating the leg
- Pain improved by lowering the leg

Differential diagnosis: mainly neurological causes with paralysis or irritation of nerve roots, such as acute radicular or pseudoradicular lesions, herniated discs, or sciatica. A change in position by raising or lowering the leg does not usually alter the symptoms in these neurological conditions but extension or flexion has a marked impact.

Differential diagnosis of arterial occlusion in the leg – **CHRONIC**

- Somewhat pale to clearly livid limb, less difference in colour between the two legs
- Pain only on walking
- Pain relief from standing still

Differential diagnosis: mainly orthopaedic conditions with symptoms that occur on weight-bearing or standing or after walking only a short distance of a few metres. In contrast to patients with arterial perfusion problems, patients with orthopaedic conditions prefer to sit down.

The causes of arterial leg pain

Arteriosclerotic leg pain

Those affected are usually over the age of 50, although juvenile forms of arteriosclerosis are also possible. There is often systemic disease with manifestations of the arteriosclerotic vascular changes in all regions: peripheral, cerebrovascular, coronary, and abdominal. With multiple affected sites, the five-year mortality from the time of onset is about 30 % [2–4].

Classically, there is exercise-induced leg pain after walking a reproducible distance, with rapid recovery at rest. Unlike the situation with spinal claudication due to spinal stenosis, when patients prefer to sit down, it is usually only necessary for patients with PAD to stop moving and stand still. It should be remembered that many patients with PAD are asymptomatic, without any difference in overall mortality.

The major risk factors for arteriosclerosis are smoking, hypertension, hyperlipidaemia and diabetes. The unmet need for pharmacotherapy in patients with PAD with respect to risk factors and concomitant diseases remains problematic.

The most important aspects of the diagnostic work-up are a thorough history and clinical examination with pulse status, inspection of the skin and determination of the occlusion pressure or ankle-brachial index (ABI). An ABI < 0.9 indicates the presence of PAD.

Further diagnostic investigation includes treadmill testing and duplex ultrasonography, which should always be carried out before radiological investigations.

All patients with a confirmed diagnosis of PAD have to have baseline treatment with optimal medication to treat the cardiovascular risk factors and the prescription of walking exercise training, which is most effective in the form of structured vascular sporting activities. In addition, invasive therapeutic procedures such as catheter interventions or surgical revascularisation with thromboendarterectomy or bypass grafting are available. The decision on appropriate treatment should be made in view of the clinical status and with interdisciplinary input whenever possible. These measures may be considered for the purpose of improving quality of life but they must always be implemented to prevent amputation whenever there is critical ischaemia of the limb. Amputation must never be performed without thorough vascular investigation and angiography.

Acute arterial occlusion

Acute arterial occlusion of the lower limbs is caused by a complete embolic or thrombotic blockage of an artery. It is the most common angiological emergency [5]. When the collateral arterial supply is inadequate, acute ischaemia results and this can have organ- or life-threatening effects.

Clinically, there is a dramatic event with the sudden onset of intense pain distal to the site of occlusion, with pallor, coldness, and disorders of motor function and sensation.

Acute PAD has an annual incidence of about 7–14/100 000 population and is associated with very high morbidity and mortality, despite innovative diagnostic investigations and treatment. The risk of amputation in the first 30 days from the start of acute leg ischaemia is between 10 % and 30 %. The mortality rate in the same period after the event is 15–30 %.

Acute PAD is mainly due to emboli (70–80 %) and less often to acute local arterial thrombosis (20–30 %). 80–90 % of arterial emboli come from the heart.

Source of cardiogenic emboli

- Atrial fibrillation (70 %)
- Heart valve lesions
- Acute myocardial infarction
- Heart wall aneurysms
- Endocarditis
- Left-heart tumours

- Atrial myxoma
- Prosthetic heart valves
- Dilated cardiomyopathy
- Paradoxical arterial emboli via a patent foramen ovale.

Source of extracardiac emboli

- Aneurysms of the aortoiliac and femoropopliteal regions
- Cholesterol emboli
- Arteriosclerotic plaques
- Compression syndrome
- Catheter emboli or iatrogenic vascular injury
- Tumours (lung cancer, pulmonary metastases, angiosarcoma)
- Foreign bodies

Acute arterial thrombosis arises mainly in previously damaged vessels, as acute-on-chronic events, for example due to ruptured plaque. In addition, dissection, trauma, vasculitis, postoperative vascular damage, paraneoplastic syndrome, and medications may be the cause of acute arterial thrombosis.

The extent of the symptoms of acute arterial occlusion depends on its nature, location, and possible collateral circulation. In the case of complete embolic arterial occlusion, compensatory mechanisms via a pre-existing collateral system are usually lacking. The clinical picture shows typical signs and symptoms (the six Ps, according to Pratt). When an acute thrombotic occlusion arises in pre-existing peripheral arterial disease, the symptoms usually develop more slowly and are less serious thanks to the collateral vessels that have already formed.

Complete limb ischaemia, according to Pratt (the six Ps):

1. Pain: sudden intense pain like the lash of a whip
2. Pulselessness: absence of pulses
3. Paleness: pallor of the skin
4. Paraesthesia: disorder of sensation
5. Paralysis: paralysis of the muscles to about a hand width below the occlusion
6. Prostration: shock

The first three signs and symptoms (sudden pain, pulselessness, paleness) are the most clinically reliable.

An incomplete ischaemic syndrome often has an acute thrombotic origin. Clinically, there is pallor and loss of pulses distal to the arterial occlusion. Cooling of the affected limb is often delayed. The bluish colour of the ischaemic limb indicates cessation of flow in the capillary bed with peripheral cyanosis and characterises severe limb ischaemia. If sensation and motor function are additionally affected, there is complete ischaemia. The window of opportunity before the imminent loss of the limb is then less than six hours.

Complications when reperfusion is too late are the tourniquet or reperfusion syndrome with muscle oedema and myoglobinaemia and/or myoglobinuria, acidosis with hyperkalaemia, loss of volume, and acute kidney injury with crush syndrome and disseminated intravascular coagulation.

A rapid diagnosis from a precise history, clinical examination and diagnostic imaging is therefore of crucial prognostic importance. Once the diagnosis has been made, measures to restore the disrupted arterial circulation should be initiated immediately.

The extent of organ damage depends on how long the particular tissue can tolerate ischaemia. In the case of skin, muscles, and nerves the figures are 12, 6 to 8, and 2 to 4 hours respectively. Asking about the time of onset of the limb pain and pre-existing diseases sheds light on the age and origin of the arterial occlusion.

Optimal management depends on the first doctor to see the patient recognising that it is an emergency and immediately referring the patient to a hospital with the necessary diagnostic and therapeutic services.

Non-invasive diagnostic procedures consisting of Doppler pressure measurements, continuous wave Doppler, and duplex ultrasound provide a rapid objective assessment of the perfusion disorder.

Determination of the ankle-brachial index (ABI) with the help of Doppler pressure measurements provides information on the extent to which the acute peripheral arterial occlusive event is compensated (normal ABI > 0.9). A pathological ABI < 0.6 and blood pressure in the posterior and anterior tibial arteries of < 50 mmHg at the ankle indicate critical limb ischaemia. Distal to the acute arterial occlusion, either no Doppler signal or a monophasic signal with a widened curve and increased end-diastolic blood flow is recorded. The echogenicity of the lumen in the region of the occlusion is variable.

Duplex ultrasound offers many advantages over other imaging techniques: Besides determining the site of the occlusion and the haemodynamics, it can also show completely or incompletely thrombosed arterial aneurysms as the possible cause of the occlusion. It should be regarded as the key diagnostic procedure.

Intra-arterial digital subtraction angiography (DSA), MRI or CT angiography with contrast medium may be used, depending on the informational value, the location, vascular preload, and availability. Acute arterial occlusion is characterised on angiography by an abrupt cut-off of the column of contrast medium. It shows the characteristic rounded upwardly convex filling defect at the proximal end of the embolus. In contrast to acute thrombotic arterial occlusion, there are usually no well-developed collateral vessels.

The advantage of immediate DSA is that therapeutic measures such as embolectomy or local intra-arterial lysis can be performed in the same session.

With interdisciplinary cooperation, angiologists, radiologists, and vascular surgeons should decide on the therapeutic strategy promptly and put it into action. The specific therapeutic measures depend on the aetiology of the acute arterial occlusion and the presence of complete or incomplete ischaemia (▶ **table 1**).

In Rutherford class I of acute limb ischaemia, targeted procedures to open the vascular lumen can be carried out on the day following the acute event, after general therapeutic measures and anticoagulation have been initiated.

In Rutherford classes II and III, all diagnostic and therapeutic measures have to be carried out urgently.

Immediate measures:

- Inform the vascular surgeons, keep the patient nil by mouth
- Lower the affected limb (higher perfusion pressure)
- Cushion the affected leg (cotton wool wrap)
- Do not apply cold packs or heat – no pressure

▶ **Tab. 1** Classification of acute limb ischaemia (according to Rutherford).

class	clinical picture/prognosis	sensation	motor function	Doppler signal	
				arterial	venous
I. viable	not immediately threatened	maintained	not disrupted	audible	audible
II. threatened	salvageable				
a. marginally	if promptly treated	minimal or none	not disrupted	rarely audible	audible
b. immediately	with immediate revascularisation	more than toes, associated rest pain	limited	inaudible	audible
III. irreversible	major tissue loss or permanent nerve damage inevitable	anaesthetic	paralysis	inaudible	inaudible

- Painkillers, iv analgesics (opioids); do not give intramuscular injections, so that possible lytic therapy is not compromised
- Immediate intravenous anticoagulation with 10 000 IU unfractionated heparin (prevention of further emboli or thrombus formation)

Revascularisation procedures

Basically, emergency surgical treatment is indicated when complete ischaemia is present with an acute occlusion of one of the major limb arteries proximal to the groin. Arterial occlusion distal to the inguinal ligament is suitable for a combined approach with catheter intervention and local lysis. In the case of acute PAD with incomplete ischaemia, combined treatment methods such as local catheter-assisted lytic therapy come into consideration.

Endoluminal therapy of an acute limb ischaemia encompasses several techniques that can be used alone or in combination with local fibrinolytic therapy. The thromboembolic material causing the occlusion is first broken up and then removed. Recognised efficient procedures for mechanical thrombectomy are aspiration thromboembolectomy, mechanical fragmentation catheter systems, and hydrodynamic catheter systems.

Leriche syndrome

Leriche syndrome is due to a complete occlusion of the abdominal aorta between the origin of the renal arteries and the aortic bifurcation. A distinction is made between acute Leriche syndrome, with sudden occlusion of the infrarenal aorta presenting as an emergency, and chronic occlusion [6].

The cause of acute distal aortic occlusion is usually cardiac embolism and more rarely arterial thrombosis of the aorta. In 90 % of cases, the cause of chronic occlusive disease of the aorta is progressive arteriosclerosis.

Acute Leriche syndrome gives rise to a severe circulatory disorder of the entire lower limb and occasionally also the pelvic organs, with life-threatening consequences. Acute kidney injury (rhabdomyolysis) or spinal ischaemia (involvement of the lumbar arteries) may also occur, as well as faecal and urinary incontinence.

Chronic aortic occlusive disease presents as peripheral arterial disease with intermittent claudication affecting especially the hips, thighs, and buttocks, and there is sometimes pain at rest. Some 50–80 % of men with Leriche syndrome have erectile dysfunction.

On clinical examination, there are no palpable pulses in the lower limbs and they cannot be detected with Doppler scanning. Duplex ultrasound shows that there is no flow in the leg arteries. Thrombus or the abrupt cessation of the flow signal in the aorta can be demonstrated by B-mode and duplex ultrasound. With chronic aortic occlusion, the Doppler signals are monophasic and there is a poststenotic flow profile in the leg arteries. In addition, occlusion of the aorta can be confirmed radiologically by means of conventional angiography, CT angiography or MRI angiography.

Immediate surgical treatment is essential in the case of acute Leriche syndrome. The window of opportunity is only 6–10 hours. With fresh thrombosis/embolism, the first-line procedure is a transfemoral thrombectomy. If this is not possible, an aortobiiliac or aortobifemoral bypass graft has to be inserted. Even with a successful operation, however, this syndrome has a high mortality as patients are usually in a poor general condition before surgery, with decompensated heart failure or a severe coagulation disorder.

Depending on its stage, chronic aortic occlusive disease can be treated conservatively with medication, minimally invasive endovascular intervention with stenting if necessary, or surgically by aortobiiliac or aortobifemoral bypass grafting.

Aortic dissection

Classical aortic dissection is characterised by the detachment of the intima and the development of a false lumen. In most cases, the inner layer detaches in the direction of the blood flow. There are subsequently two patent lumens separated from each other by a dissection membrane.

The Stanford classification distinguishes type A aortic dissection, with involvement of the ascending aorta, from type B aortic dissection, in which the initial tear lies distal to the take-off of the left subclavian artery and, by definition, the ascending aorta is not affected [7]. Involvement of aortic branches or progression into the iliofemoral vessels leads to ischaemia of the lower limbs (19 %). The differential diagnosis of acute aortic dissection should also be considered in patients with unexplained syncope (13 %), chest pain (61 %) or back pain (53 %), abdominal pain (30 %), stroke (4.7 %), and also with acute heart failure (6.6 %). A difference between the pulses on the two sides (15 %) or signs of malperfusion should give particular pause for thought.

Patients with conservatively treated type B aortic dissection have a 30-day mortality of about 10 %, while patients with complications have a mortality rate of about 20 % on the second day and about 30 % after one month. Advanced age, shock and malperfusion are predisposing factors for increased early mortality.

Patients with uncomplicated acute type B aortic dissections have to be closely monitored in the ICU. Their blood pressure must be kept under control. Rapid interventional or, in rare cases, surgical treatment may be needed for acute complications of type B aortic dissection.

The risk of rupture is less with type B lesions and more time is available for diagnostic investigations. Transoesophageal echocardiography (TEE) using Doppler ultrasound can often differentiate between the true and the false lumen. Computed tomography or magnetic resonance imaging can identify the take-off of the vessels and the precise extent of the dissection.

In the acute stage, the results of surgery are no better than conservative treatment with medication, so at first there is no primary indication for an operation. Surgery or an interventional procedure is indicated if chest pain persists, signifying progressive expansion of the dissection; if there is evidence of a silent rupture; and with displacement of essential branches of the abdominal aorta.

Thromboangiitis obliterans (Buerger's disease)

Thromboangiitis obliterans (TAO) is a segmental inflammatory disease of small and medium-sized arteries, veins and nerves. It usually affects people under the age of 50, mainly men who are cigarette smokers [8] . TAO differs from arteriosclerotic arterial occlusive disease in its typical segmental vascular involvement with unremarkable large arteries, (simultaneous) involvement of the upper limb, an association with thrombophlebitis, and the lack of classical cardiovascular risk factors apart from nicotine abuse.

TAO is a clinical diagnosis. As a rule, the symptoms affect more than two limbs; the absence of typical intermittent claudication is characteristic. The main symptoms consist of intense pain at rest, ulceration and gangrene in the fingers or toes, Raynaud's phenomenon, and inflammatory changes without any evidence of arteriosclerosis or the presence of cardiovascular diseases.

Physical examination should include a thorough check on the pulse status and an Allen test on the upper extremities, which are often asymptomatic. The circulation of the hand is checked by the function of the radial and ulnar arteries. Laboratory tests serve to exclude inflammatory conditions in the differential diagnosis. Diagnostic imaging in the form of CT or MRI angiography is used to assess the involvement of the vessels. Angiography shows the segmental arterial occlusion and the typical corkscrew-like collaterals, although these are not pathognomonic.

Basic treatment is for the patient to stop smoking immediately and completely, passive as well as active. Optimal local wound care and pain therapy are also important. Intravenous therapy with vasoactive prostaglandins such as alprostadil or iloprost for at least 14 days can be added. Several studies have shown a positive effect on ulcer healing and pain relief. Surgical or endovascular procedures do not achieve convincing long-term results and have high early or late occlusion rates and low primary and secondary patency rates. Further therapeutic options include lumbar sympatholysis, treatment with the endothelin receptor antagonist bosentan and phosphodiesterase-V inhibitors, although the evidence for all these approaches is poor. The experimental use of stem cells and the transmission of angiogenesis-stimulating factors are showing promising results, as is extracorporeal therapy with immunoadsorption. Several studies have shown these approaches to provide rapid pain relief for the patients, improve ulcer healing, and achieve a high rate of return to work.

Although the life expectancy of affected patients seems to be unaltered or hardly changed because there is no organ involvement, the amputation rate during the course of this disease is high, with figures of 27–75 % in the period from 5 to 11 years.

Compression syndromes

Compression syndromes result from the permanent irritation of neurovascular structures at sites of preformed anatomical constriction from muscles or ligaments [9]. Secondary factors such as growth, muscle training, elongation of blood vessels, or accidents may cause intimal lesions, wall dissection, aneurysm formation, and degenerative occlusion through repetitive vascular injury.

In the lower limbs, the popliteal artery can be constricted by aberrant muscle origins (popliteal artery entrapment) causing the clinical picture of intermittent claudication, paraesthesia, and cold feet after exercise to develop. Progressive limb ischemia is rare but may result from advanced arterial degeneration and poststenotic aneurysmal dilatation of the artery. Although an anatomical entrapment seems to be quite common, clinical evidence of compression syndrome is found in only a few cases.

In addition to the routine clinical examination, active plantar flexion of the foot is performed as a provocation manoeuvre. In positive cases, this provocation leads to a decrease in pulse intensity over the arteries at the ankle. Measurements of abnormal pulse volumes or a loss of continuous wave Doppler signals reinforce the provisional diagnosis. Arterial duplex ultrasound may likewise show the abnormal flow under provocation.

Further investigation with CT or MRI angiography allows an assessment of the anatomical conditions.

Treatment consists of surgical release of the constriction by resection or translocation of the compromised anatomical elements.

Cystic adventitial degeneration

Cystic adventitial degeneration primarily affects the popliteal artery but has also been described in the external iliac artery and the femoral artery. The classical symptom is leg pain that is unusual in lingering for up to 20 minutes after exercise has ceased. It is due to compression of the lumen by a cystic collection of mucinous material within the adventitia of the artery [10]. The clinical picture of this disease may wax and wane, with long periods when there are no symptoms and then the sudden reappearance of leg pain. The precise origin of cystic adventitial degeneration is still unknown, although repetitive trauma, systemic disease, and a persistent embryonic synovial track have all been suggested.

A positive Ishikawa sign with disappearance of the foot pulses on passive knee flexion is supplemented by MRI. Angiography is not worthwhile, as it will not show the structures actually causing the compression.

Endovascular catheter-assisted therapy has been shown to be ineffective. Measures such as ultrasound-guided puncture of the cystic structures, surgical resection preferably with a vein graft, or adventitial resection are to the fore. Patients should have good long-term care from a vascular specialist because of the high recurrence rate.

Raynaud's syndrome

Phenomena such as attacks of vasospasm in the fingers and toes, usually bilateral pain, and the triphasic colour change in the skin from blue to white and then red (tricolour phenomenon) characterise Raynaud's syndrome [11]. A distinction can be made between primary and secondary Raynaud's syndrome. In the latter, there is always an underlying disease, such as a collagenosis or other systemic disease. Symmetrical involvement and the lack of skin lesions suggest primary Raynaud's – the thumb is usually spared. A positive history of Raynaud-associated diseases such as lupus erythematosus, scleroderma or rheumatoid arthritis, asymmetrical involvement of the digits, a high erythrocyte sedimentation rate (ESR), and raised antinuclear antibodies (ANA) are consistent with secondary Raynaud's.

Clinical diagnostic investigations include functional tests to exclude perfusion disorders in the hand, such as the Allen test and the fist closing test (with arms lifted, the fist is closed and opened for two minutes; the palm of the hand and inner aspect of the fingers are then examined for protracted pallor) and duplex ultrasound to assess blood vessel morphology and locate any stenosis or occlusion. In addition, a standardised, documented and quantified provocation test is used. This dynamic perfusion measurement belongs with plethysmography, capillary microscopy, and thermography.

Physical measures such as ceramic-impregnated gloves and pocket hand warmers are used as prophylaxis against the cold. Potential co-initiators such as smoking, β-blockers and ergotamines should be avoided. Calcium antagonists may be used in a therapeutic trial.

The intravenous prostaglandins alprostadil and iloprost may be used in severe cases, especially when there are skin lesions. Phosphodiesterase inhibitors such as sildenafil or tadalafil may be considered for long-term treatment, as well as endothelin antagonists (bosentan).

Vasculitis

Vasculitis represents a heterogeneous group of inflammatory systemic diseases that are characterised by the inflammatory infiltration and necrosis of blood vessels [12]. Involvement of the limbs with pain in the legs as the clinical correlate is seen in Takayasu arteritis, and less commonly in giant cell arteritis and polyarteritis nodosa.

Takayasu arteritis

Takayasu arteritis (also known as aortic arch syndrome or pulseless disease) almost exclusively affects women between the ages of 20 and 30. It is a rare disease with an annual incidence of two to three cases per million and shows great regional variation.

The disease mainly involves the major elastic arteries that branch from the aorta. Granulomas form in the vessel walls, which subsequently form scar tissue and narrow the vessels. The increased blood pressure may cause aneurysms to develop, especially in the arteries near the heart. The results may be a fatal stroke or heart attack. The initial symptoms are non-specific such as a general feeling of malaise with headache, night sweats, weight loss, recurrent fever, myalgia, arthralgia or arthritis. Other signs, which can be attributed to the occlusion of the blood vessels, occur much later. Depending on the vessel that is affected, there may be circulatory disorders in the hands, the heart or the brain. Signs of disease progression include circulatory disorders in the upper body (difference in blood pressure between the right and left sides), involvement of the carotid arteries (40 %), subclavian arteries (85 %), ophthalmic arteries (visual disturbances 50 %), renal arteries (renovascular hypertension) and arteries of the lower limbs (10 %). Involvement of the arteries in the extremities leads to Raynaud's phenomenon.

The name "pulseless disease" refers to the fact that the pulse can no longer be felt at one or both wrists. Patients complain of severe pain on lifting, dizziness, and loss of consciousness on exertion, and they suffer from high blood pressure, visual disturbances, strokes, and heart attacks.

Laboratory testing shows a rather non-specific constellation of inflammatory markers with a high ESR, raised C-reactive protein (CRP), fibrinogen, gamma-globulins, thrombocytosis, anaemia, and leucocytosis. Antinuclear antibodies (ANA) and antineutrophil cytoplasmic antibodies (ANCA) are negative. Duplex ultrasound shows a hypoechoic circumferential thickening of the arterial wall with a halo (Macaroni sign) in the transverse section of the artery. CT or MRI angiography shows the extent of the vascular involvement. PET may be performed to assess disease activity.

The most pressing aim of treatment is to reduce the inflammation of the vessel wall. Humoral inflammatory symptoms act as indicators. Glucocorticoids in combination with non-steroidal anti-inflammatory drugs (NSAIDs) are prescribed. Treatment usually lasts for one year. Should this treatment prove inadequate, cyclophosphamide has to be added (according to Fauci's regimen). Once the chronic scar stage is reached, the question of recanalisation has to be addressed in the individual case.

Progression of the disease tends to be unfavourable and is marked by complications of a neurological (stroke) or cardiac (valve insufficiency, coronary artery disease, heart attack) nature. The five-year mortality is about 50 %.

Giant cell arteritis

Giant cell arteritis (temporal arteritis) is the most common and most important form of vasculitis. It is characterised by the chronic segmental granulomatous obliterative involvement of the larger arteries. It usually manifests in the carotid artery and its branches. The underlying pathology consists of granulomatous giant cell arteritis in the media and adventitia of the affected arterial segments with subsequent sclerotic changes in the vessel walls.

As a rule, the disease affects people over the age of 60 and characteristically has a sudden onset.

General symptoms are fever, malaise, arthralgia, myalgia, morning stiffness, and weight loss. Depending on the vessels involved and their supply territories, the symptoms include visual disturbances such as amaurosis fugax, unilateral or bilateral throbbing headaches (especially in the temporal area and the forehead), pain on chewing (jaw claudication), and claudication in the arms and legs.

Apart from the clinical examination with pulse status and comparison of the blood pressure on the two sides, diagnostic investigation includes duplex ultrasound of the temporal arteries, the carotids and the subclavian/axillary arteries, addressing the questions of wall thickening, pulsation, and the typical halo phenome-

non. Temporal artery biopsy is possibly even up to seven days after the start of steroid therapy.

Laboratory tests show an acute phase reaction with very high ESR (often > 80 mm/hour. NB: it is normal in 5 % of patients) and increase in the C-reactive protein, associated with eosinophilia and leucocytosis. There is no positive rheumatoid factor or evidence of ANA and ANCA.

Clinical diagnosis according to the American College of Rheumatology (ACR) criteria for the diagnosis of temporal arteritis [13]:

1. Age > 50 years
2. New-onset headaches
3. Abnormal temporal arteries (tenderness, decreased pulsation)
4. ESR > 50 mm in the first hour
5. Histological changes on temporal artery biopsy (NB: segmental vasculitis with "skip lesions"; several biopsies may be necessary. Arterial Doppler beforehand to rule out flow noise)

The presence of three or more of the five criteria yields a diagnostic sensitivity of 75–95 %, with a specificity of 90–93 %, a positive predictive value of only 29 % but a negative predictive value of 99 %.

The therapeutic goal is to reduce the inflammation of the vessel wall. Humoral inflammatory symptoms act as indicators, while CRP is the marker of disease progression.

The dose of glucocorticoids is gradually reduced to a maintenance dose of < 10 mg/day orally for a year. Moderate doses of NSAIDs may be added to the steroids. Should this therapeutic regimen prove inadequate, cyclophosphamide has to be added in doses according to Fauci's gold standard. Methotrexate may be used as an alternative to cyclophosphamide.

Course of disease/prognosis

There is usually a good response to glucocorticoids and, as a rule, complete remission after 6–24 months. Less often, the disease follows a recurrent or chronic course.

Polyarteritis nodosa

Three times more men than women suffer from this rare form of vasculitis (in Germany, less than one per 100 000 residents are affected). Inflammation of the small and medium-sized arteries is characteristic of polyarteritis nodosa (PAN), forming nodules that appear like a string of pearls (*nodosus* is Greek for nodular). They can be found especially in the calf, the forearm, and the internal organs. The nodules progressively narrow the blood vessels until they are completely blocked ("thrombosis"), and the territory supplied by these arteries may die off. Fingers and toes or the entire hand or foot are often affected by these "infarctions".

The skin becomes clearly blue to black in these cases. The disease starts with fever, a feeling of numbness, and tingling in the hands and feet; PAN may become slowly worse but may also advance rapidly and be life-threatening. There is a good chance of healing if the disease is diagnosed and treated promptly before permanent damage ensues.

Secondary vasculitis

The group of diseases collected together as secondary vasculitis can be attributed to an underlying disease (rheumatic diseases, autoimmune diseases such as AIDS or syphilis, viral hepatitis or tumours), a specific medication, or an infection. This form of vasculitis usually affects the small vessels. Secondary vasculitis occurs particularly in association with rheumatoid arthritis, systemic lupus erythematosus, and cryoglobulinemia.

Peripheral aneurysms

Peripheral aneurysms, defined as a widening of the arterial lumen to more than twice the average diameter of the vessel, are also rare [14]. In the lower limbs they most often affect the popliteal artery. It must be remembered that popliteal aneurysms are bilateral in 50–60 % of cases and up to 50 % of those affected may also have an abdominal aortic aneurysm. Locating other aneurysms should always be a part of the diagnostic investigation.

The initial clinical presentation may be an acute onset with persistent intense pain from a peripheral embolus, usually in the digital arteries. Rupture or dissection or the aneurysm and thrombotic occlusion are less common presentations. Chronic disease shows symptoms due to the displacement of neighbouring organs or recurrent microembolism with distal vascular occlusion but may be asymptomatic for a long time.

Besides physical examination finding a classical "hard" pulse over the popliteal artery, duplex ultrasound is the main investigation. It will show the size of the aneurysm, the degree of thrombosis, and allow an assessment of the outflow tract.

With a diameter of > 2 cm, surgical treatment may be considered; with a diameter of 3-4 cm or more, there is an absolute indication for surgery as well as in critical ischemia of the limb.. As a rule, the aneurysm is excluded by a vein or synthetic graft, or bypass grafting. Alternatively, endovascular procedures may be carried out, with the insertion of a plastic-coated stent.

Summary

Arterial pain in the legs is mainly arteriosclerotic in origin. Other causes are embolism, vascular dissection, compression syndrome, and inflammatory diseases. The primary goal is to estimate the severity of the circulatory disorder and the risk of amputation of the limb. Acute perfusion disorders are associated with a high mortality, and require prompt specialist treatment.

The clinical examination of the pulse status, assessment of the skin, sensorimotor function, and the general cardiovascular condition of the patient is extremely important. Diagnostic investigations such as Doppler ultrasound, determination of the ABI, pulse oscillography, duplex ultrasound and more sophisticated radiological imaging such as CT and MRI angiography provide further information.

Depending on the cause of the pain, basic treatment encompasses measures for treatment and secondary prophylaxis of the risk factors, optimal analgesia, and inhibition of inflammatory reactions. Minimally invasive endovascular procedures and invasive surgical techniques are available for recanalisation of the vessel with the aim of improvement and, in the best-case scenario, a return of the perfusion to normal. Interdisciplinary and interdivisional cooperation are the cornerstones of successful treatment for these sometimes life-threatening conditions.

Conflict of interest

The authors declare that they have no conflict of interest.

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