Atrophie blanche

Sreedharan S & Sinha S

Abstract
Atrophie blanche (AB) is typically described as a variable dimensioned, smooth, ivory-white plaque stippled with telangiectases and is surrounded by hyper-pigmentation. AB commonly occurs in middle-aged women on the lower legs or feet, often associated with ulcerations and chronic venous insufficiency (CVI). The ulcers are slow to heal and painful. Histologically, AB shows superficial and deep dermal vascular occlusion by microthrombi resulting in vascular damage to the skin. However, there is still no consensus on the pathogenesis of AB and a standard protocol of management is lacking.

Key points

What is already known on the topic
- AB is a characteristic skin lesion commonly seen in women on the legs and feet.
- AB is associated with ulcers that are slow to heal and painful.
- Main histological finding is microthrombi occlusion of dermal vessels.
- AB is commonly associated with chronic venous insufficiency and other systemic diseases.

What the manuscript contributes
- A review of the current literature on AB.
- Four illustrative cases of venous leg ulcers associated with AB.
- A management plan for AB, which is lacking due to the controversy of its pathogenesis.
- Recommendation against biopsy of AB due to prolonged healing time and patients losing confidence in treatment.

Introduction
Atrophie blanche (AB) was originally described by Milian in 1929 as a lesion of variable dimensions that consists of a smooth, ivory-white plaque with an irregular hyper-pigmented border and surrounding telangiectasias. Since then, the term AB has been surrounded by ambiguity due to the use of several synonyms such as segmental hyalinising vasculitis, capillaritis alba, livedo reticularis with summer ulcerations, livedo vasculitis and painful purpuric ulcers with reticular pattern of the lower extremities (PURPLE). Also, Livedoid vasculopathy, a more extensive variant of AB, has been used interchangeably with AB in the literature. It needs to be emphasised that the term AB, whilst a defined clinical entity, is purely descriptive and does not indicate a specific diagnosis or aetiology. The pathogenesis of AB is controversial and as such there is confusion about its appropriate management. In this article we report four chronic leg ulcer patients associated with AB in order to formulate a tentative plan of management of such cases.

Clinical features
AB is more commonly seen in women with an estimated prevalence of 1–5% in the general population. While the AB lesion tends to occur in the middle-aged, it can, however, occur in any age group and is often described in association with chronic venous ulcers, ischaemia and vasculitis. Approximately 30% of AB cases have been reported to result in ulcerations that are often exceptionally painful and hard to heal. These lesions tend to occur on the lower leg or foot, but can occur elsewhere.

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important to note that AB can also occur post-ulceration or de novo.

Clinically AB can be divided into two categories: primary where the lesion occurs without an underlying disease and is said to be idiopathic and secondary due to various causes (Table 1). A careful search reveals that the most common identifiable cause is chronic venous insufficiency (CVI). It has been proposed that patients with CVI will go through a clinical course of either lipodermatosclerosis or AB, but some patients may have both of these conditions coexisting. Margolis et al. found that patients with lipodermatosclerosis and AB have different fibrinolytic activities, which indicates that a clinical diagnosis of venous disease might not always have the same physiological abnormality.

Pathogenesis
Histologically, AB lesions are characterised by endothelial proliferation, segmental hyaline degeneration of the vessel wall, deposition of fibrin within the vessel wall and lumina and thrombus formation in superficial and deep dermal vessels leading to infarction and ulceration of the epidermis and dermis. AB lesions can also show extravasated red blood cells, scarce perivascular inflammatory infiltrate and an absence of leukocytoclasia, suggesting that AB may not be a true vasculitis.

The exact pathogenesis of AB is currently unknown but several hypotheses have been suggested, such as microthrombi, defective endothelium, enhanced fibrin production, fibrin-cuff formation, increased platelet aggregation, auto-antibodies, primary vasculitis and infection.

Clinically, it has been observed that the use of antiplatelet, fibrinolytic and anticoagulant therapies have been successful in treating some ulcers with AB. This, in combination with the histopathology of vascular occlusion, suggests formation of microvascular thrombi as a contributing factor of AB. Although an increase in fibrin formation, decrease in fibrinolysis or vasculitis has not been demonstrated in AB it seems that the most likely process is a decrease in capillary flow leading to coagulation and impaired fibrinolysis.

The primary process in vasculopathies is occlusion leading to tissue necrosis and inflammatory changes, whereas in vasculitis the inflammation is the primary event that results in occlusion. Hence, AB probably represents the end-stage of vascular damage to the skin and the term “vasculopathy” is more appropriate than vasculitis.

Management
Due to the uncertainty about its exact pathogenesis, many treatments for AB have been rather empirical. While there has been a range of treatment regimes described in the literature (Table 2), none of the therapies have been studied in a well-designed clinical trial. A combination of phenformin

Table 1. Various diseases associated with secondary AB.

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<th>Disease</th>
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<td>Venous stasis</td>
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<td>Vasculitis necroticans</td>
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<td>Polyarteritis nodosa</td>
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<td>Collagen vascular disease</td>
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<td>Abdominal aortic pathology</td>
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<td>Aortic calcification</td>
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<td>Atherosclerosis</td>
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<td>Aneurysm</td>
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<td>Thalassaemia minor</td>
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<td>Chronic myelogenous leukemia</td>
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<td>Sneddon’s syndrome</td>
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<td>Cryoglobulinemia</td>
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<td>Lymphoma</td>
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<td>Antiphospholipid syndrome</td>
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<td>Autoimmune disease</td>
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<td>Systemic lupus erythematosus</td>
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<td>Scleroderma</td>
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Table 2. Empirical treatments of AB described in the literature.

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<th>Therapy</th>
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<td>Silver nitrate cautery</td>
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<td>Minidose heparin</td>
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<td>Nifedipine</td>
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<td>Nicotinic acid</td>
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<td>Anti-inflammatory drugs</td>
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<td>Sulfasalazine</td>
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<td>Hyperbaric oxygen therapy</td>
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<td>Pentoxyfylline</td>
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<td>Topical, intralesional or systemic steroids</td>
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and ethylestrenol has been shown to be effective in treating AB, in which the pair act synergistically as a fibrinolytic agent. However, phenformin is no longer available due to its adverse effect of lactic acidosis and the combination of metformin and ethylestrenol appears to be ineffective. Intraliesional injections of lignocaine and triamcinolone have been reported to relieve the pain associated with AB lesions dramatically. Consultation with the specialists at the pain clinic, if available, in addressing the issue of pain in AB is recommended.

As mentioned earlier, AB is a clinical descriptor and, therefore, management should be aimed at identifying and treating the underlying disease. CVI being the most common cause in AB patients should be first evaluated for this. The use of compression therapy with leg ulcers should be considered as the initial treatment in the presence of CVI and in the absence of CVI a patient should then be assessed for systemic diseases associated with AB. Management should then include therapy for any associated systemic diseases found. If the cause is unclear, elaborate diagnostic tests like antinuclear antibody, antineutrophilic cytoplasmic antibody, rheumatoid factor, anticardiolipin antibody and cryoglobulin level are indicated.

It has been suggested that if there is a lack of improvement, a biopsy may help to confirm vasculopathy. In such a case, the combination of low-dose aspirin and dipyridamole, which affect platelet aggregation have been recommended. On the contrary, a diagnosis of vasculitis may prompt application of anti-inflammatory drugs like sulfasalazine. However, through clinical experience it has been found that a biopsy of AB lesions tend to have prolonged healing times and causes patients to lose confidence in their treatment. Furthermore, there are instances where the histological changes are less defined. An outline of a management plan for the clinical entity, AB, has been proposed (Figure 1).

Case reports

Patient 1

A 66-year-old woman first presented to the wound clinic in October 2003 with a full-thickness ulcer located on the lateral aspect of the dorsum of her left foot. The ulcer was present for more than 12 months prior to presentation and was associated with intermittent pain. The patient’s comorbidities included CVI, hypertension, peptic ulcer disease, depression and osteoarthritis. Her medications included omeprazole, paracetamol/codeine, irbesartan/hydrochlorothiazide, frusemide, fluoxetine, buprenorphine and amiodipine. The patient’s ankle brachial index (ABI) was 0.89 on both legs, indicating mild peripheral vascular disease. In April 2006, the patient underwent an angioplasty for stenosis of the left superficial femoral and popliteal arteries but the ulcer did not show any resultant improvement. She was seen again in the wound clinic in August 2006, when AB was noted medial to the chronic ulcer (Figure 2).

The patient was commenced on pentoxifylline on the basis of earlier reported success in the treatment of venous ulcers. The dose was subsequently reduced to 400 mg bid as the patient suffered from considerable nausea. Minimal change was noted in the healing of the ulcer and appearance of AB.

![Figure 1. Proposed management plan for AB.](image-url)
As there was no improvement, a repeat duplex scan was arranged and on this occasion it was found that the left saphenofemoral junction was incompetent with a grossly incompetent distal segment and perforators. The patient then underwent a high ligation and stripping of the long saphenous vein (LSV) in August 2009. The ulcer improved by 50% within five weeks of the surgery. While the patient still showed the AB lesion around the healed ulcer it had regressed in size (Figure 3).

The patient was followed up in December 2010 and the AB lesion had regressed further in size. The patient is still using compression stockings and regularly moisturises her legs and feet. Since her discharge from the wound clinic, the patient has not had any ulcerations or pain associated with the AB lesion, although this might have been due to the analgesics she uses for chronic back pain.

**Patient 2**

A 69-year-old woman was first referred to the wound clinic in October 2001. She presented with a six-month history of bilateral ulcers below the lateral malleoli. These ulcers healed in early 2002 but recurred once in 2005. The patient’s comorbidities included CVI, atrial fibrillation, hypercholesterolaemia, osteoarthritis, hypertension and histologically unconfirmed temporal arteritis. The patient’s current medications are low-dose aspirin, atorvastatin, frusemide, indapamide, paracetamol/codeine, sotalol and ramipril.
In November 2007, the patient presented again to the wound clinic with a superficial venous ulcer on the lateral aspect of her right foot, which started four months earlier. The patient stated that she first suffered from right foot pain, then subsequent skin breakdown, which resulted in a discharging ulcer. The ulcer was 8 cm in diameter and the surrounding skin showed prominent AB. The ulcer caused severe pain and had a burning sensation. The pain was controlled with the use of paracetamol/codeine. The patient’s ABI was 0.96 on both legs with evidence of chronic venous disease. The duplex scan revealed no signs of peripheral arterial disease. This ulcer healed by March 2008 with the use of compression stockings and dressings. The AB was still present over the lateral aspect of her right foot at the time of discharge (Figure 4).

In May 2008, the patient developed a new superficial ulcer on her left foot. This ulcer also had surrounding AB and caused the patient constant pain. The patient was commenced on pentoxifylline 400 mg tds but this was stopped two and a half weeks later as it was causing her severe headaches. The ulcer healed in September 2008 and AB was still present.

The patient was followed up in December 2010 and the AB lesions were still present below her right and left lateral malleoli with occasional pain, burning sensation and itchiness. The patient currently uses compression stockings and regularly moistures her legs and feet.

**Patient 3**

A 77-year-old woman presented to the wound clinic in November 2007 with two ulcers on her right leg. The patient’s comorbidities included are CVI, non-insulin dependent diabetes mellitus, ischemic heart disease with two acute myocardial infarctions, hypertension, dyslipidaemia, osteoarthritis, previous right breast cancer treated with lumpectomy and radiotherapy, hearing impairment and urinary incontinence. Her current medications are ramipril, simvastatin, aspirin and prednisone. The first ulcer was partial thickness, 2.5 cm in diameter over her right lateral malleolus and has been present for more than three years. The second is a punched out ulcer, 0.8 cm in diameter over her right medial malleolus and has been present for approximately two months. In the two weeks prior to her presentation, the patient’s pain had become severe. The patient also had marked lipodermatosclerosis with multiple fibrous dermal nodules on the anterior aspect of both legs. A duplex scan of the patient’s right leg showed peroneal artery occlusion and distal tibial arterial disease. The patient was, however, not suitable for any arterial reconstruction.

In January 2008, the patient was referred for hyperbaric oxygen therapy (HBO) in attempt to heal the ulcers. The patient’s ulcers were hypoxic to transcutaneous oximetry on room air but were responsive to 100% oxygen at 2.4 atmospheres. The patient then continued to have 40 HBO treatments. The ulcers showed marked improvement after the HBO but the AB lesion was still evident surrounding the healing ulcers (Figure 5). The ulcers had fully healed by August 2008 and the patient was discharged from the clinic. The patient was recommended to moisturise both legs and elevate them when sitting during the day.

The patient was followed up in December 2010 and the AB lesions were still present over her right malleoli. The patient stated that she had no pain or ulcers since her discharge from the wound clinic.
**Patient 4**

An 80-year-old woman was referred to the wound clinic with persistent venous ulcers on both legs in October 2007. She had a past history of slow healing leg ulcers and her comorbidities included hypertension, osteoporosis and hypothyroidism. Her current medications are aspirin, alendronate, candesartan, amlodipine, paracetamol/codeine, thyroxine and temazepam. The first ulcer was full thickness, approximately 15 cm², located over the right medial malleolus and had surrounding AB. The patient also had a small ulcer about 1 cm² over the left medial malleolus. The patient had pain associated with the ulcers and required paracetamol/codeine to sleep at night. In December 2007, the right leg ulcer was improving and decreased in size but the left leg ulcer had increased in size. In February 2008, two new ulcers were noticed on the left leg above the pre-existing ulcer. There was marked AB on the left lower leg between the three ulcers (Figure 6). The patient was also experiencing pain over the left lower leg as well. During this time the patient’s ulcers were treated with multiple debridement, compression stockings and various dressings. The patient subsequently underwent high ligation and stripping of LSV in 2008.

High doses of pentoxyfylline (800 mg tds) were reported by Falanga et al. to significantly improve both healing time and success rate of venous ulcers. Pentoxyfylline acts by reducing blood viscosity, potential platelet aggregation and thrombus formation. Patients 1 and 2, who were prescribed pentoxyfylline 400 mg tds suffered from adverse reactions and thus its efficacy on treatment of AB ulcers remains uncertain. Patient 3 underwent HBO showed hypoxia around the ulcers with AB and benefited from therapy, both in terms of healing and relief of pain. Furthermore, patients 1 and 4 that underwent high ligation and stripping of LSV for their venous incompetence showed marked improvement to their ulcer with AB. This adds support to the proposition that CVI is an important factor and thus addressing this issue has a definite role in treating AB.

**Conclusion**

The term AB is surrounded by confusion and as such it is important that a consensus is reached for an agreed nomenclature, avoiding multiple synonyms. As vascular occlusion is most commonly found in AB, it is likely that it is caused by the formation of microthrombi, which suggests that AB is a type of vasculopathy. As AB is a clinical finding and not a diagnosis, each patient should be evaluated for an underlying disease such as CVI, which following appropriate venous ablation is likely to heal the associated ulcer and reduce or relief symptomatic AB. It is our experience that biopsies are not very helpful and often prolong healing time. Further, research is needed to identify the exact pathogenesis so that appropriate guidelines can be formulated towards a clear management plan in dealing with patients that present with AB, with or without ulcerations.

**References**
