Review Article

Buerger's disease (Thromboangitis obliterans): An Update

ABM Moniruddin[1], Hamida Begum[2], Khairun Nahar[3]

Abstract

From the time immemorial, tobacco abuse has been known as an ancient malpractice. The detrimental effects of tobacco are well documented today. Buerger's disease (Thromboangitis obliterans) is one of its curse. Now, it has been postulated that Buerger's disease (Thromboangitis obliterans) is an idiopathic autoimmune response to some constituent of tobacco. The suspected autoantigen of tobacco enters the body during smoking, inhalation or ingestion of tobacco. Limb vessels (arteries & veins) are chronically inflammed as evidenced by round cell infiltration in all three coats of the affected vessels. This is associated with fibroplastic proliferation, occlusion & thrombosis of the vessels, leading to necrosis, ulceration & gangrene with the attendant morbidities. Diagnosis is mostly clinical, based on history of tobacco abuse & claudication, physical examination showing wasting of affected cold limb parts with absent or diminished pulse, aided by relevant serologic & imaging studies. The main treatment is total abstinence from smoking, along with use of low dose aspirin & a prostaglandin analogue (e.g., iloprost) as antiplatelet drugs. Local treatment of ulcer & gangrene should also be instituted. Lumbar sympathectomy is often worthwhile. Stem cell therapy for Buerger's disease (Thromboangitis obliterans) is still in research stage. Due attention needs also to be paid for rehabilitation & follow-up. By far, the anti-tobacco drive remains as the main tool to prevent this awesome disease.

Keywords:

Thromboangitis obliterans (Buerger's disease), tobacco abuse, Lumbar sympathectomy.

Introduction

Buerger's disease (Thromboangitis obliterans) is an idiopathic chronic disease characterized by occlusive disease of the small & medium size peripheral limb arteries (plantars, tibials, radial, etc.), usually distal to the popliteal & the brachial arteries, thrombophlebitis of superficial or deep or both veins, & Raynaud's phenpmenon (episodic symmetric contraction of small arteries of the extremities, resulting in cyanosis or pallor of the part, followed by hyperemia, producing a red color) occurring in young tobacco using patients, (the tobacco use may be in the form of smoking, inhaling, chewing or ingestion, etc). Usually one or two of three manifestations are present & occasionally all three[1,2]. Though signs & symptoms are more or less localized, it is a systemic disease having considerable health burden upon the community. Though previously it was thought that the condition doesn't occur in woman, now it is found that women once representing about 5% of cases, now account for about a third of cases, that reflects changes in smoking habits[3]. It has never been reported in non-tobacco users. Gangrene of toes & fingers is common & progressive[4]. Unhygienic & untreated cases get secondarily infected by pathogenic & oppurtunistic microbes & parasites that may be an aerobe, or an anaerobe or a mocroaerphilic or mixed. One may have to lose toes, sometimes all the limbs & may get permanently crippled. That is to say that it is potentially a life endangering disease with significant complications & morbidities thereof.

1. ABM Moniruddin MBBS, FCPS(S)
Assoc Prof of Surgery
International, Medical CollegeGazipur.
2. Hamida Begum MBBS, DGO, FCPS
Assoc Prof of Obs & Gynae, International Medical College, Gazipur.
3. Khairun Nahar MBBS, FCPS
Assistant Professor, Deptt. of Gynae & Obs, BSMMU, Dhaka

History

The first reported case was by von Winiwarter from Germany in1879 in an article entitled 'A strange form of endarteritis and endophlebitis with gangrene of the feet'. But his description, argument & conclusion were inconclusive. In 1908, Leo Buerger, a professor of urologic surgery of New York Polyclinic Medical School (Mount Sinai Hospital) of the USA published a detailed description of the disease in which he referred to 'presenile spontaneous gangrene', for which the term 'thromboangitis obliterans' was coined later on.. In his original paper, Leo Buerger discussed the pathological findings in 11 limbs amputated from Jewish patients in New York. The disease is thence also called the 'Buerger's disease' after his name[1]. The other synonyms for the disease are 'endangitis obliterans von Winiwarter-Buerger', 'Winiwarter-Buerger syndrome', 'Winiwarter-Manteuffel-Buerger syndrome' and 'Billroth-von Winiwarter disease'.

Epidemiology

The disease is quite prevalent in Bangladesh. But like many other diseases, its exact incidence is unknown here. However, the incidence is falling as the association with tobacco is recognised & tobacco abuse is discouraged nationally for its all harmful effects & no established beneficial effect. In the USA it has fallen from around 100 per 100,000 people to less than 20 per 100,000. It mostly

affects men but women, who used to represent about 5% of cases, now account for about a third of cases. This reflects changes in smoking habits. It usually occurs between the ages of 20 and 45, but recently it has been seen more in people over the age of 50[3]. Rarely it affects children with auto-immune phenomena and a significant degree of underlying inflammation. Although it is a worldwide problem, there are considerable geographical and racial differences. It is more common in those of oriental race, including those from South-east Asia, India and the Middle East, but it is less common in those of African origin. It is also less common in people of northern European descent. Natives of India, Korea, Japan and especially Israeli Jews of Ashkenazi descent, have the highest incidence of the disease. Part of this difference in disease incidence may be due to variability in diagnostic criteria2,5,6,7. The association of Buerger's disease with tobacco abuse, particularly cigarette smoking, cannot be overemphasised. Most patients with Buerger's disease are heavy smokers but some cases occur in patients who smoke "moderately". It has been postulated that Buerger's disease is an "autoimmune" reaction triggered by some constituent of tobacco[3].

Pathology

There are multiple characteristic segmental occlusions of small arteries in the extremities. Healing of the arterial wall lesion is associated with fibrous obliteration of the lumen in segmental fashion. Migratory thrombophlebitis of superficial or deep or both veins is frequently present. Many patients with Buerger's disease have specific cellular immunity against arterial antigens, specific humoral antiarterial autoantibodies, & elevated circulatory immune complexes. HLA typing can differentiate such patients from patients with atherosclerosis & from normal individuals. The role of cigarette smoking & tobacco use is unclear; it is probably facilitative rather than causative. Vascular occlusion causes ischemia of the affected part, especially ischemia of the affected nerves & muscles are responsible for pain. That is to say that pain is the result of dying nerves & muscles. In untreated cases, eventual necrosis, ulceration & gangrene of toes & fingers are common & progressive[1,2,3].

Histology

There are localized inflammatory changes occur in all the three layers of the walls of arteries & veins leading to thrombosis, i.e. infiltration of round cells in all three layers of the arterial wall, in contrast to atherosclerosis, which involves the intima & inner media only[3]

Complications:

Tissue necrosis, ulceration, infection and gangrene[1,2,3] etc.

Diagnosis

History of tobacco use, age, sex & absence of diabetes, hypertension, vascular & coagulation disorders, etc.

Clinical features:

The early symptoms of Buerger's disease include claudication in the feet and/or hands or pain in these areas at rest (about 20% of cases). The pain typically begins in the extremities but may radiate to more central parts of the body. It may be very intense. As the disease progresses, the resting pain can be severe enough to cause insomnia. Other signs and symptoms may include: (a) Two or more limbs being affected, (b) Discoloration of the affected limb, (c) Pain often increases with activity such as walking and decrease with rest, (d) Symptoms may worsen with exposure to cold or with emotional stress, (e) Numbness and tingling in the limbs, (f) Raynaud's phenomenon, (g) Skin ulcerations and gangrene of the digits, (h) Pulses may be decreased or absent in the affected extremity, (i) Later symptoms include enlarged, red, tender cord-like veins[5,6,7].

Examination shows an irregular pattern of digital ischemia. The Allen test demonstrates the delayed filling of affected digital arteries & rapid filling in adjacent arteries. The Allen test is done by having the patient make a tight fist while the examiner occludes the radial & the ulnar arteries at the wrist & asks the patient to open & close the hand rapidly. With the hand in a relaxed position, patency of the radial artery can be determined by releasing the radial artery & noting the return of color. This maneuvre is then repeated for the ulnar artery. The extremity is made ischemic by compressing the proximal artery while the foot or hand is exercised. When the extremity has become pale, the artery is released & the pattern of return of color is observed. In a person with normal arteries & a normal arterial sympathetic tone, a vivid flush appears almost simultaneously in all areas of the hand or foot. Patient with excess sympathetic tone will have a diffusely delayed return of color. When small artery occlusion is present there will be a prolonged delay in reperfusion of the cutaneous area supplied by the occluded arteries of the hand or foot. Patient with excess sympathetic tone will have a diffusely delayed return of color. When small artery occlusion is present there will be a prolonged delay in reperfusion of the cutaneous area supplied by the occluded arteries.

Laboratory studies: There is no specific diagnostic test5. A formal vascular assessment should be undertaken, e.g., ESR & autoantibodies. There are no specific serologic markers to diagnose Buerger's disease. Recommended tests to rule out other causes of vasculitis include FBC (Full Blood Count), LFTs (Liver Function Tesrs), creatinine, fasting glucose, ESR or PV, antinuclear antibody, rheumatoid factor, serologic markers for CREST (Calcinosis, Raynaud

phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasia) syndrome & scleroderma & screening for hypercoagulability[3,4].

Imaging studies: Certain angiographic features are typical & distinctive but not pathognomonic of Buerger's diease[5]. These include a 'corkscrew' appearance of arteries that indicates vascular damage, particularly the arteries in the region of the wrists & ankles. Arteriography sometimes shows a characteristic corrugation of femoral arteries as well as the distal arterial occlusions & helps to distinguish the condition from presenile arteriosclerosis. Other forms of arteritis, e.g., polyarteritis nodosa must be excluded. The artery proximal to the occlusions charactistically is tapered, & arterial wall is smooth & devoid of irregular aherosclerotic plaques. The configuration resembles a dunce's cap. Angiograms may also show occlusions or stenoses in multiple areas of both the arms & legs. It is sometimes necessary to perform angiograms of other parts of the body regions, like a mesenteric angiogram to exclude other forms of vasculitis that involve vascular regions atypical for Buerger's. Doppler ultrasound may be helpful – lately color doppler has been used to distinguish Buerger's disease & other causes of secondary Raynaud's phenomenon from primary cause[6]. Echocarcardiography may be required to exclude a source of recurrent emboli..

Biopsy: A precise diagnosis can only be made by microscopic examination showing the typical segmental vasculities. But skin biopsies of affected extremities are rarely performed because of fear that a biopsy site in an ischemic area will not heal[6].

Recently, an easy diagnostic criterion has been suggested1,5. 1. Age under 45 years, 2. Current or recent history of tobacco use, 3. presence of infrapopliteal arterial occlusive disease indicated by claudication, rest pain, ischemic ulcers or gangrene & documented by non-invasive vascular testing, 4. Either upper limb involvement or phlebitis migrans, 5. Absence of atherosclerotic risk factors other than smoking i.e. exclusion of autoimmune diseases, hypercoagulable states, diabetes mellitus & a proximal source of emboli by echocardiography or arteriography. There must also have consistent arteriographic findings in the clinically involved & non-involved limbs. Confident clinical diagnosis of Buerger's diease requires all above five features.

Differential diagnoses

Raynaud's syndrome, systemic lupus erythematosus, scleroderma, polyarteritis nodosa, autoimmune diseases, hypercoagulable states, diabetes mellitus, atrial fibrillation, valvular heart diseases, proximal arterial aneurysms, hypertension, hyperlipemia, presenile arteriosclerosis, senile arteriosclerosis/ atherosclerosis, traumatic gangrene, etc[5,6].

Treatment

Medical: The main treatment is total abstinence from smoking & total avoidance of all tobacco products, i.e., 'you can have your cigarettes or your legs, but you can't have both!' This will arrest the disease but not, of course, reverse the established arterial occlusions. A mere reduction in smoking isn't sufficient to prevent the relentless progression of this disease. This is the only treatment of choice universally acceptable & known to be effective. Otherwise, there is not yet an agreed consensus on the treatment of choice7. Supportive measures include: a. gentle massage and warmth to increase circulation, b. To avoid conditions that reduce peripheral circulation, like cold temperatures, c. To avoid sitting or standing in one position for long periods, d. Not to walk barefoot to avoid injury, e. To avoid tight or restrictive clothing, f. Aggressive treatment of any injuries (such as ulcers)[8,9,10].

Patients who have claudication but not critical ischaemia should be encouraged to walk whereas those with critical ischaemia should be admitted for bed rest[5].

Although low-dose aspirin has been used, the drug iloprost (a prostacyclin analogue) has been shown to be superior[8,9]. Other proposed treatments have included carperitide (atrial natriuretic peptide), limaprost and a number of other prostaglandin analogues. Calcium channel blockers, steroids, anticoagulants and other antiplatelet drugs are ineffective. Some have suggested that if the disease is due to sensitivity to a component of tobacco other than nicotine then NRT (Nicotine Replacement Therapy) may be used. However, recent findings suggest that there is an association of smokeless tobacco with progressive limb ischemia and therefore all tobacco products must be stopped[10]. Vasoconstricting drugs should be avoided.

There is work being done in the field of stem cell therapy to treat intractable symptoms related to ischemia where conventional therapy has failed but this is still at the research stage[11].

Surgical : Lumbar sympathectomy may provide temporary relief but outcome is variable[12]. Lumbar sympathectomy is sometimes the most useful procedure. Sympathectomy decreases arterial spasm & opens up the collateral circulation. It often results in healing the ischemic ulcers & improvement in skin nutrition, with relief of pain[12]. Bypass surgery for established arterial occlusions has not yielded good results in these patients5. Areas with gangrene must be removed surgically; patients who continue to smoke are likely to require amputation of fingers and toes[13]. Amputation is indicated for persistent pain or gangrene & can be performed adjacent to the line of demarcation with satisfactory primary healing[1,2,11].

Rehabilitation: For loss of a limb or a part thereof, a patient may have to change his or her occupation. It needs proper attention to be paid for that. The patient should be made understand his disease, sequelae of tobacco abuse & how to protect himself or herself from trauma & complications of the disease[11,12].

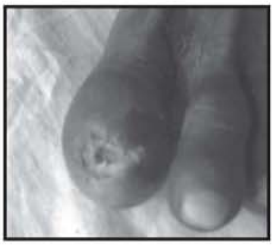

Figure.1 : The healing ulcer of Buerger's disease following stoppage of smoking & bilateral Lumbar Sympathectomy

Follow up: It is an essential part of total care of the patient. It should be streamline & routine to guarantee disease halt & to identify minor signs of disease progress, so that timely treatment & necessary intervention can be forced in case of resurgence of signs & symptoms of the active progressive disease[13].

Prognosis

The disease is progressive in patients who do not stop smoking. The only way to prevent the progression of the disease is to abstain from all tobacco products. The disease may become dormant if the patient can stop smoking & avoid all forms of tobacco, but this is unfortunately difficult to achieve in many who ultimately develop gangrene of additional digits[10,11].

Conclusion

Though the etiology of Buerger's disease is unknown, its intimate link with tobacco & its products is well known. So, simple abstinence from tobacco can prevent the disease. This abstinence is also essential to arrest the progress of the already established disease & to prevent all its complications & morbidities thereof. Mass awareness through mass media can do a lot of job here.

References

1. Arkkila PE. Thromboangiitis obliterans (Buerger's disease). Orphanet J Rare Dis. 2006;1:14.
2. Olin JW. Thromboangiitis obliterans (Buerger's disease); N Engl J Med 2000;343:864-9.
3. Papa M, Bass A, Adar R, Autoimmune mechanisms in thromboangiitis obliterans (Buerger's disease): the role of tobacco antigen and the major histocompatibility complex.; Surgery. 1992;111:527-31.
4. Papa MZ, Rabi I, Adar R. A point scoring system for the clinical diagnosis of Buerger's disease.; Eur J Vasc Endovasc Surg. 1996;11:335-9.
5. Lazarides MK, Georgiadis GS, Papas TT, Diagnostic criteria and treatment of Buerger's disease: a review. Int J Low Extrem Wounds. 2006;5:89-95.
6. Schmidt WA, Krause A, Schicke B, Color Doppler ultrasonography of hand and finger arteries to differentiate primary from secondary forms of Raynaud's phenomenon. J Rheumatol. 2008;35:1591-8. Epub 2008;15.
7. Paraskevas KI. Treatment-of-choice for Buerger's disease (thromboangiitis obliterans): still an unresolved issue. Clin Rheumatol. 2008;27:547. Epub 2008;2.
8. Fiessinger JN, Schafer M. Trial of iloprost versus aspirin treatment for critical limb ischaemia of thromboangiitis obliterans. The TAO Study.; Lancet. 1990 Mar 10;335(8689):555-7.
9. No authors listed. Oral iloprost in the treatment of thromboangiitis obliterans (Buerger's disease): a double-blind, randomised, placebo-controlled trial. The European TAO Study Group.; Eur J Vasc Endovasc Surg. 1998;15:300-7.
10. Lawrence PF, Lund OI, Jimenez JC, Substitution of smokeless tobacco for cigarettes in Buerger's disease does not prevent limb loss. J Vasc Surg. 2008;48:210-2.
11. Al Mheid I, Quyyumi AA. Cell Therapy in Peripheral Arterial Disease. Angiology. 2008;25.
12. Bozkurt AK, Besirli K, Koksal C, Surgical treatment of Buerger's disease. Vascular. 2004;12:192-7.
13. Buerger L. Thrombo-angiitis obliterans: a study of the vascular lesions leading to presenile spontaneous gangrene.Am J Med Sci 1908; 136: 567-80.