Original Article

The pathogenesis of unilateral venous varicosity observed in patients with mycetoma

Ahmed H Fahal, MBBS, FRCS, MD*, MS, Hassan S EL Sheikh, MBBS, MD**, Ahmed M El Hassan, MBBS, FRCPath, DCP, PhD, MD***

Professor of Surgery*, Assistant Professor of Radiology**, Professor of Pathology***
Mycetoma Research Centre - University of Khartoum, Khartoum - Sudan

Abstract

Background
The presence of unilateral varicose veins is a noticeable clinical occurrence in mycetoma patients; however its pathogenesis was not studied previously.

Methodology
Thirty patients with confirmed mycetoma were studied prospectively. The venous system of the affected limb was studied using imaging and histologic techniques.

Results
Unilateral varicose veins were more evident in patients with long standing mycetoma, with massive lesions and with radiological bone changes. In histological sections, certain venous abnormalities were demonstrated. The veins and venules showed marked muscular hypertrophy, intimal and adventitial thickening, oedema and lumen narrowing but no venous occlusion or arterio-venous shunts were observed. Venography showed a brisk venous circulation in the vicinity of mycetoma lesion, which was more evident in eumycetoma. However at the site of mycetoma lesion there was displacement and distortion of the venous circulation and in some patients there was evidence of early venous varicosity above the lesions. The vascular doppler study showed brisk both arterial and venous blood flow in the affected limb when compared to the sound limb.

Conclusion
These venous changes could be compensatory mechanism to the increased venous return secondary to increase in the arterial blood flow at the mycetoma lesion due to the
chronic inflammatory changes and condition should be treated conservative.

Keywords: Mycetoma, Varicose veins, Pathogenesis

Introduction
Mycetoma is a chronic granulomatous, progressive inflammatory disease; it usually involves the subcutaneous tissue after a traumatic inoculation of the causative organism. It may spread to involve the skin and the deep structures resulting in destruction, deformity and loss of function\(^{(1,2)}\). Mycetoma may be caused by true fungi or by higher bacteria and hence it is usually classified into eumycetoma and actinomycetoma respectively\(^{(2,3,4)}\).

Mycetoma is characterised by tumefaction and formation of sinus tracts which usually discharge purulent and seropurulent exudate containing grains\(^{(1,2)}\). The commonest site for mycetoma is the foot, the hand is the next commonest site and in endemic areas, other parts of the body may be involved but less frequently\(^{(5,6,7)}\).

The presence of unilateral varicose veins is a unique occurrence in some of the mycetoma patients however, its pathogenesis is unknown. In an attempt to investigate its pathogenesis we examined the venous system at the mycetoma lesion using histological and imaging techniques. As far as we are aware, this is first report on the pathogenesis of this condition.

Patients & Methods
The study was carried at the Mycetoma clinic, Mycetoma Research Centre, Khartoum. Thirty patients with confirmed mycetoma and with unilateral varicose veins in the affected lower limb were studied prospectively. The diagnosis of mycetoma was based on clinical and imaging examinations of the lesions and the histopathological examination of surgical biopsy. All patients gave informed consent.

Histological Examination:
In most of the patients, the lesions were excised surgically. The biopsy material was fixed in 10% formaldehyde. Paraffin sections were stained with Haematoxylin & Eosin (H&E) and with Elastin Van Giessen for elastic tissue.

Imaging investigations:
All patients had radiological examination of the affected site in two views (anterio-posterior and lateral). Fifteen patients had venography; all of them were examined in supine position. Compression to occlude the superficial venous system only was applied using a tourniquet just above ankle or knee joints 30 minutes prior to the percutaneous insertion of a butterfly (21 gauge British standard wire) into a dorsal vein in the affected foot below the lesion. No venous section was done. With swollen and oedematous feet, bed rest and elevation of the lower limb was done for 30 minutes prior to the procedure. Sixty to one hundred mls of contrast media (Urografin 75%) was injected by hand in 40-80 seconds. The contrast flow was monitored by an image intensifier and radiographic views of venous circulation were taken at intervals.

Five patients with massive mycetoma who was planned for amputation had simultaneous venography and peripheral serial arteriography by percutaneous injection of contrast medium into the femoral artery of the affected limb distal to the inguinal ligament and proximal to profunda femoris artery. Thirty mls of contrast medium (Urografin 76%) were injected manually as a bolus. Radiographic views of femoral, popliteal and tibial arteries were taken first. This was followed by taking serial films of the foot at a rate of 2 films/second for a total of 8 films. Two delayed films to demonstrate the venous phase were taken 7 and 8 seconds later.

Vascular Doppler Studies:
Vascular doppler studies were carried out in all patients. The systolic ankle pressure of the affected limb, the sound limb which was used as a control and the right brachial systolic pressure were measured by Sonicaid BV 105
(R) vascular flow detector (Oxford Medical Ltd - England). The ankle - brachial index was calculated for each limb. The test was repeated after exercising the patient for 10 minutes to assess the Doppler vascular changes after exercise. Venous circulation was assessed at the same time.

Analysis:
Descriptive statistical analysis of the obtained data by appropriate tests, Chi square test and Fisher exact test were used as appropriate using SPSS computer program (SPSS 14, USA).

Results
Twenty patients had eumycetoma due to Madurella mycetomatis and ten patients had actinomycetoma. The causative organisms in the latter were Streptomyces somaliensis (n=8) and Actinomadura pelletieri (n=2). The M:F ratio was 3:1. The patients' ages varied between 8 and 65 years (mean 40± 5 years). The duration of disease ranged from 7 months to 20 years. All patients had foot mycetoma except for one with retroperitoneal actinomycetoma. All patients had unilateral varicose veins in the affected limbs. (Fig 1).

Histological Examination:
The veins and venules in, around and proximal (from the amputed specimen) to the mycetoma lesion showed marked muscular hypertrophy and oedema in between the muscle bundles. These changes were predominately marked in large veins proximal to the mycetoma lesion. The intima was thickened by fibrosis and the lumen was narrowed but not occluded. There was also marked fibrous thickening of the adventiitia. (Fig 2).

Ischaemic changes and necrosis in the mycetoma lesions were not seen in any of the examined specimens. However, granulation tissue and neo-vessel formation was a constant feature in all them even in areas remote from the main lesion.

Imaging Findings:
The plain radiographs showed radiological changes in all patients. Those were in the form of soft tissue mass and bone cavities and in some, there was periosteaal reaction. The angiograms revealed the typical pathological circulation described previously(8). The venography showed a brisk venous circulation in the vicinity of the lesion. This was more evident in eumycetoma. At the site of the
mycetoma lesion there was displacement and distortion of the venous circulation and evidence of early venous varicosity above the lesions. No valvular incompetence or deep vein thrombosis was seen. No arterio-venous shunts were demonstrated in any of the patients (Figs 3,4).

Fig 3: A venography of a patient with eumycetoma, showing a brisk venous circulation in the vicinity of mycetoma lesion. There is displacement and distortion of the venous circulation at the mycetoma site and evidence of early venous varicosity above the lesion.

Fig 4: A venography of a patient with eumycetoma, showing venous dilatation above the mycetoma site with early venous varicosity above the lesion, no evidence of other abnormality.

Vascular Doppler Study:
The ankle systolic pressure of the affected limb ranged between 100 and 150 mm Hg, mean ± SD (110 ± 10 mm Hg) and for the sound limb, the ankle systolic pressure ranged from 105 to 155 mm Hg, mean SD ± (109 ± 21 mm Hg). The brachial systolic pressure ranged between 90 and 130 mm Hg, mean ± SD (100 ± 9 mm Hg). The ankle/brachial index for the affected limb varied from 0.9 to 1.5, mean ± SD (1.2 ± 0.1) and for sound limb it ranged between 1.0 and 1.4, mean ± SD (1.3 ± 0.1). The pressures and indexes in the affected limbs were higher but that was not statistically significant (P > 0.1).

After exercise, the affected limb ankle systolic pressure ranged between 110 and 160 mm Hg, mean ± SD (116 ± 10 mm Hg); for the control limb it ranged between 113 and 170 mm Hg, mean ± SD (124 mm ± 12 Hg). The ankle/brachial index for the affected limb varied from 1.2 to 1.7, mean ± SD (1.5 ± 0.5) and for sound limb it ranged between 1.4 to 1.8, mean ± SD (1.7 ± 0.2). The pressures and indexes in the affected limbs were higher after the exercise and that was statistically significant (P < 0.1).

Discussion
There are several causes for varicose veins formation. They may be familial, hereditary or secondary to deep venous thrombosis, valvular damage, incompetent perforators or proximal venous obstruction. The frequent appearance of varicosity during pregnancy is well recognised, but it is not clear whether that is due to hormonal changes, increased venous blood flow and volume or due to the mechanical effect of the enlarged uterus. Rarely venous varicosity may be of congenital origin. In all the patients reported in this communication no predisposing causes for varicose veins was detected.

An important abnormality in both the major superficial veins and their branches, associated with venous varicosity, is valvular incompetence. This was demonstrated neither clinically nor phlebographically in this study. The muscular and elastic nature of the venous wall readily allow it to adjust to variation in blood flow. This physiological response is
commonly observed in the uterine veins during pregnancy, in malignant tumours and collateral veins following obstruction of a major vein. This physiological response may be the explanation of the unilateral venous dilatation noted in these patients as mycetoma lesion was shown to have an increased vascularity due to the chronic inflammatory reaction\(^8\). This fact is supported by the phlebographic appearance of the veins, which showed venous distention, dilatation and in few patients early varicosity. Disuse atrophy and limb immobility can also contribute to the development of the phenomenon since muscular contractions are needed to push venous blood upwards against gravity.

We noticed this unilateral venous dilatation in other conditions where there is an increase arterial blood supply such as septic foot, haemangioma and malignant diseases and this observation may support our explanation that, this venous dilatation is compensatory in nature. It is well known that venous stasis in gravitation venous varicosity causes venous hypertension and impaired tissue nutrition that leads to local dermatoliposclerosis and venous ulceration\(^10\). As the venous dilatation encountered in this study is compensatory with no venous stasis, neither dermatological changes nor ulceration were encountered in these patients.

Lower limbs varicose veins are not a common problem in the Sudan and commonly seen in females and they are usually bilateral. In this study, most of the affected patients were males with unilateral venous dilatation and this may favor the suggestion that, they are compensatory. As the response to medical treatment in patients with mycetoma is slow, rapid disappearance of the distended veins was not observed in this study but most of the patients had the impressions that, the size of veins decrease with response to medical treatment. With aggressive surgical excision and particularly after limb amputation, the veins decreased in size. This is probably due to the removal of the inflammatory mass with its brisk blood supply. It can be concluded from this study that, varicose veins seen in patients with mycetoma are venous dilatation developed as consequence of the brisk arterial blood flow in the lesion and should be treated conservatively.

References