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# Media sclerosis Mönckeberg affects microcirculation

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SOUHRN

Je známo, že Mönckebergova mediální skleróza je spojena s progredující tvorbou depozit krystalického i amorfního hydroxyapatitu v medii velkých tepen. V tomto článku přinášíme důkazy o kalcifikacích v mikrocirkulaci 66letého pacienta s prokázanou Mönckebergovou mediální sklerózou postihující velké periferní tepny.

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ABSTRACT

Media sclerosis Mönckeberg is known to be associated with progressive deposits of crystalline and amorphous hydroxyapatite within the media of large arteries. Here we provide evidence for calcifications within microcirculation in a 66-year-old patient with known and documented media sclerosis Mönckeberg of large peripheral arteries.

## Introduction

Media sclerosis Möckeberg (MMS) is characterized by progressive deposition of largely crystalline hydroxyapatite within the vascular smooth muscle cells (VSMC) and intercellular matrix of the media of large arteries [1]. MMS occurs predominantly in patients with type 2 diabetes mellitus and chronic kidney disease (secondary media sclerosis). The prevalence of MMS in patients with newly diagnosed type 2 diabetes mellitus was reported 17% [2] and among patients with established disease receiving oral anti-diabetics the prevalence was shown as high as 41.5% [3]. In patients with end-stage renal disease the prevalence was 27% [4]. While crystallization of calcium and phosphate represents the final common pathway, the etiology and pathogenesis of MMS still remains obscure. Based on the current data MS appears to represent an active biological process. It is characterized by transition of the contractile to secretory vascular smooth muscle cells (VSMC) and consequent disequilibrium between the promoters and inhibitors of the calcification process, such as inorganic phosphate, calcium, alkaline phosphatase, osteocalcin, ostenonectin and bone matrix protein – 2, and as matrix Gla protein (MGP), fetuin A, osteoprotegerin, pyrophosphate, osteopontin, bone mineral protein-7, fibroblast growth factor-23, respectively [5]. However, the trigger event responsible for the disturbance of the calcium-phosphate homeostasis still remains elusive [6].

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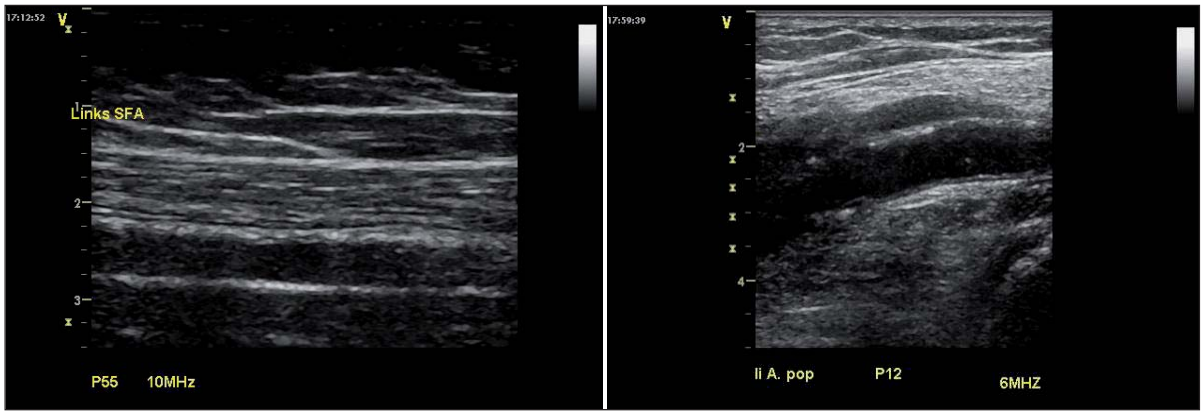


**Fig. 1 – B-mode ultrasound images of the femoral (left) and popliteal (right) arteries. Media with heterogeneously echogenic stripes adjacent to the intima are clearly visualized in both images.**

Although, the clinical relevance of MMS related to the stiffening of the large conducting arteries and resulting progressive loss of arterial pressure wave transmission have been recognized as a major independent cardiovascular risk factor [7], to our knowledge, the presence of and impact on, if any, of MMS on microcirculation, has not yet been reported. Here, we document the presence of calcification in microcirculation in a skin biopsy specimen of a 66-year-old patient with known MMS for past 20 years presenting in a dermatology clinic with a solid basal cell carcinoma.

## Material and methods

### *Patient's history*

66-year-old male has noted a brownish approximately 0.5 cm diameter lesion above his navel and consulted a dermatologist for further recommendations. The history was remarkable for MMS, diagnosed accidentally in 1996 following a cycling accident with femur injury and radiographic examination. In addition, chronic lymphatic leukemia diagnosed in 1997, basal cell carcinoma in 2014 and Raynaud syndrome for the past 30 years were reported. Diabetes mellitus, chronic renal disease, metabolic or any hormone disease were all denied.

*On physical examination* the patient was 177 cm, 73 kg healthy appearing athlete. The exam was unremarkable, except a 2 cm long scar on the left temple following removal of a basal cell carcinoma in the past. Specifically, the pulmonary, cardiac and abdominal findings were normal. The neurologic examination did not reveal any abnormalities.

*Clinical examination of the skin* lesion located approximately 2 cm above the navel revealed a 0.8 cm brownish, sharply demarcated, hyperkeratotic papule.

On *vascular examination* the upper and the lower extremities appeared normal on inspection, no skin lesions were seen, no clubbing was detected. On palpation the skin was warm, no enlarged lymph nodes or resistances were noted. The arterial pulses of the carotid, femoral, popliteal, dorsal pedal and tibial posterior (at the retromalleolar segment) arteries were present.

*Laboratory data* including chemistry panel (alanine aminotransferase [ALT], alkaline phosphatase [AP], aspartate aminotransferase [AST], bilirubin, blood urea nitrogen [BUN], creatinine), electrolytes (sodium, potassium, chloride, phosphorus, calcium), complete blood count, diabetes (fasting glucose, $HbA_1$), bone metabolism (parathormone, PTH, vitamin D) and thyroid (thyroid stimulating hormone, TSH, total and free T3 and T4) screening, lipid panel (triglycerides, total-, LDL- and HDL-cholesterol) were all within the normal range.

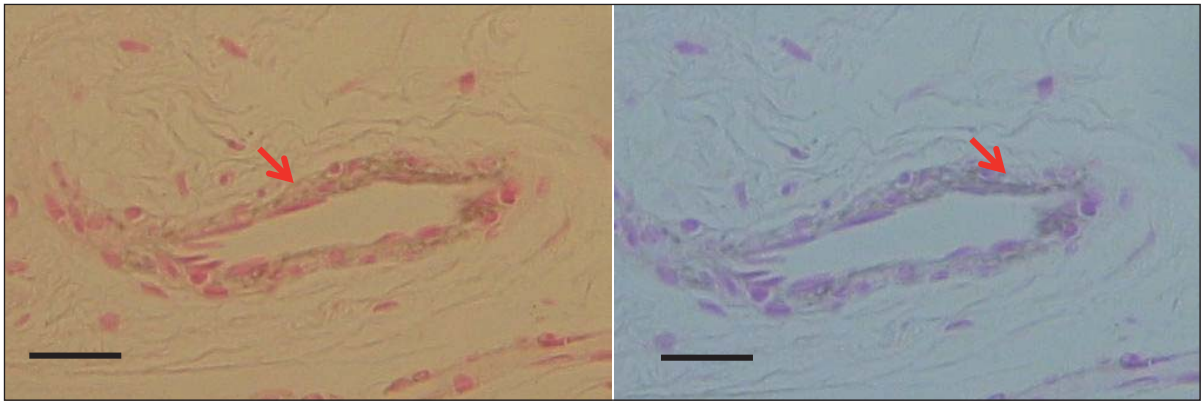

**Fig. 2 – Microvessel calcifications. Shown is a representative example of a microcirculatory vessel with extensive abluminal vessel wall calcifications demonstrated as brownish (left) and black (right), partly confluent dots (light microscopy, bars = 50 µm, Alazarin staining – left image, van Kossa staining – right image).**

On *duplex ultrasonography* of the upper and lower extremities evidence of media sclerosis documented as increased continuous echogenicity of the media of the radial, femoral, popliteal and below the knee arteries was seen on B-mode images (Fig. 1).

Based on clinical examination of the skin the detected lesion was considered suspicious of epithelial tumor and spindle excision with primary closure was performed.

*Histology examination* of the skin lesion confirmed the diagnosis of a superficial multicentric basal cell carcinoma. Because of the known MS the healthy periphery of the skin specimens were also stained for calcifications using van Kossa and Alizarin staining. Light microscopic examination has revealed multiple calcifications in the walls of corium arteriolar walls constituent of the microcirculation of the skin. The calcifications were unevenly distributed; densely and sparsely calcified regions alternated (Fig. 2).

## Results and discussion

MMS is known to involve large peripheral arteries; typical sites are the lower extremity arteries. Because the course of the disease remains clinically silent for decades the diagnosis is established accidentally in most cases. However, with the advancing course of the disease MMS may become clinically apparent due to the development of potentially obstructive bone-like lesions and acceleration of atherosclerosis due to the interference with positive arterial remodeling [8].

To our knowledge the presence of MMS-related calcification in microcirculation has not been previously described. Here, we report and document extensive calcifications of the media in arterioles of the skin in a 66-year-old male patient with known and previously documented MMS. More systematic evaluations are needed to confirm our findings and to determine the extent and impact of small vessels' calcifications on microcirculatory function in patient with MMS and their potential association with other diseases such as primary Raynaud syndrome.

**Authors' contributions**
Both authors contributed equally to the manuscript.

**Conflict of interest**
None declared.

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None.

**Ethical statement**
Authors state that the research was conducted according to ethical standards.

**Informed consent**
Prior to the examination an informed consent was obtained.

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