

Monckeberg's Sclerosis: An Unusual Presentation

MÖNKEBERG'İN SKLEROZU : NADİR BİR PREZANTASYON

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Summary

Calcification of the media of peripheral arteries is referred to as Monckeberg's sclerosis and occurs commonly in aged individuals. However, it also occurs in younger patients with diabetes and chronic renal failure. In diabetic patients, medial calcification appears to be a strong independent predictor of cardiovascular mortality. In this report, we have presented a 20 year-old-patient with extensive peripheral artery calcification. The etiology of calcification was not identified. It has been suggested that this was an unusual form of Monckeberg's sclerosis.

Key Words: Peripheral arteries, Medial calcification

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Özet

Periferik arterlerin mediyal kalsifikasyonu, Mönckeberg'in sklerozu olarak tanımlanır ve sıklıkla yaşlı bireylerde oluşur. Bununla birlikte, diyabetik ve renal yetmezlikli genç hastalarda da oluşabilir. Diyabetik hastalarda mediyal kalsifikasyon, kardiyovasküler mortalitenin bağımsız bir göstergesi olarak görülmektedir. Bu yazıda, yoğun periferik arter kalsifikasyonu olan 20 yaşındaki hasta sunulmaktadır. Kalsifikasyonun etiyojisi bulunmamıştır. Bu durumun, Mönckeberg'in nadir bir formu olduğu düşünülmektedir.

Anahtar Kelimeler: Periferik arterler, Mediyal kalsifikasyon

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Vascular calcification occurs in both the intima and the media of arteries, and there is evidence that these two sites of calcification are distinct entities (1). Intimal calcification only occurs within atherosclerotic plaques and is seen as early as the second decade of life. In contrast, medial calcification occurs independently of intimal calcification and atherosclerosis. It commonly occurs in the peripheral arteries of the lower limbs in otherwise healthy elderly patients (Monckeberg's sclerosis), where it is seen as "rail tracking" on plain radiographs. However, it also occurs in younger patients with diabetes and chronic renal failure (1,2).

Human medial calcification, Monckeberg's sclerosis (MS) is common and occurs independently of atherosclerosis, implying different mechanisms. MS was originally described in aged males (>50 years); however, it is most commonly seen in diabetic individuals. The clinical significance of MS remains controversial ; however, it is as an independent predictor of cardiovascular events in diabetic patients and is associated with trophic foot ulceration and peripheral artery disease (3).

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Case Report

A 20-year-old male with generalized arterial calcification is presented. The patient had no contributory factors in his family history. He had experienced a mild headache and artralgia for ten years. However, he had never consulted a physician. When he experienced artralgia that gradually increased, he was admitted to our hospital.

The patient's physical examination showed normal physical findings dealing with cardiovascular, respiratory, gastrointestinal and the other systems. Routine laboratory data was normal. The serum concentration levels of calcium, phosphorus, alkaline phosphatase and calcium regulatory hormones were between normal limits. The patient did not have diabetes mellitus, renal disease or connective tissue disease, thus the etiology of the calcification was not identified. Also the etiology of the secondary osteoporosis was not identified. Other specific laboratory data related to vascular calcification was summarized in Table 1. Bone scintigram showed increased uptake of 99 mTc-methylene diphosphate in the calcified arteries. There was no supportive findings of metabolic bone disease (Figure 1). Soft-tissue plain radiographs showed extensive calcification bilaterally in the peripheral arteries (Figure 2,3,4). There was no any soft-tissue calcification other than peripheral artery calcification.

Table 1. Specific laboratory data related to vascular calcification

Parathyroid scintigram	Normal findings
Bone scintigram	Increased uptake of 99 mTc-methylene diphosphate in the calcified arteries
Lomber spine bone densitometry	Supportive findings of osteoporosis L1-L4= T score(-3.32), Z score(-3.32)
Right hip bone densitometry	Supportive findings of osteoporosis Neck= T score(-3.01), Z score(-2.98)
Lower and upper extremity radiograms	Dense calcifications, possibly dealt with vascular structures
Temporal artery biopsy	Medial artery calcification

known, but its presence predicts risk of cardiovascular events and leg amputation in diabetic patients (1,3).

Human vascular smooth muscle cells (VSMCs), both in vivo and in vitro express many of the calcification regulating proteins commonly found in bone. Several of these proteins have calcium and apatite binding properties and

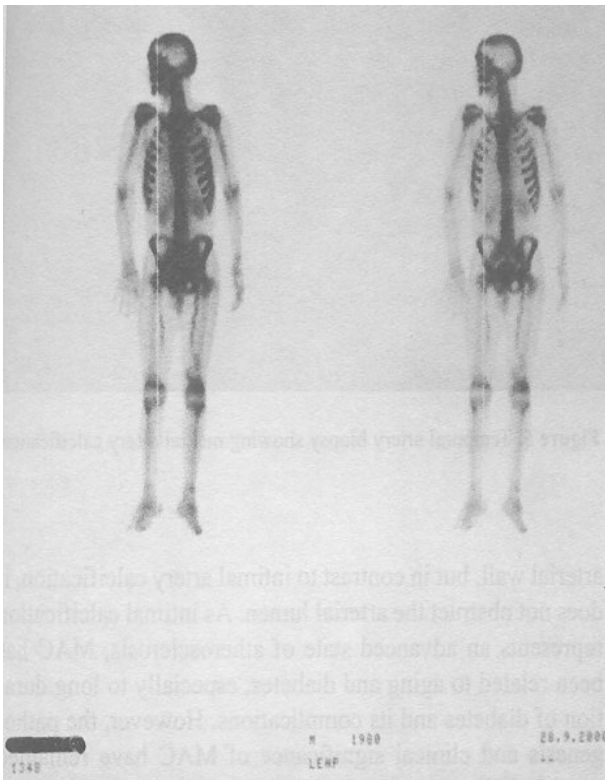


Figure 1. Bone scintigram showing increased uptake of 99 mTc-methylene diphosphate in the calcified arteries

Clinically, the patient was diagnosed with Monckeberg's sclerosis. And the temporal artery biopsy was performed to get definite diagnosis. The temporal artery biopsy showed medial artery calcification (Figure 5).

Discussion

Calcification of the media of peripheral arteries is referred to as Monckeberg's sclerosis and occurs commonly in aged and diabetic individuals. Its pathogenesis is un-



Figure 2. Lower extremity radiogram showing dense femoral artery calcification



Figure 3. Pelvic radiogram showing extensive vascular calcification

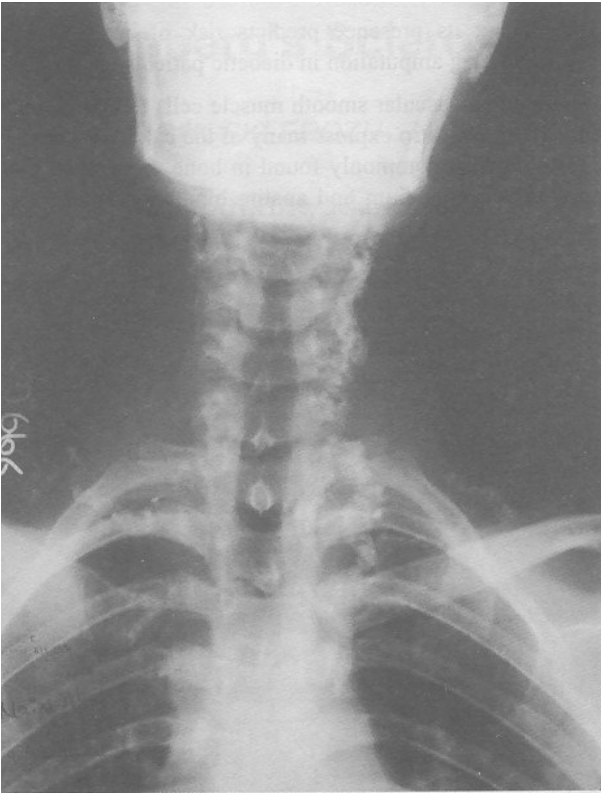


Figure 4. Cervical radiogram showing extensive vascular calcification

are concentrated in areas of vascular calcification. Evidence that some of the proteins are potent natural inhibitors of calcification comes from the development of extensive vascular calcification in mice lacking specific genes. The most impressive of these is the matrix Gla protein (MGP) knockout mouse which develops such extensive medial vascular calcification that it dies of arterial rupture within two months of birth. This suggests that MGP is a potent inhibitor of vascular calcification. The other proteins that have inhibitor effect on vascular calcification are osteoprotegerin, Klotho, carbonic anhydrase and fibrillin I (1,3-8). Recent experimental studies have shown that vascular calcification occurs when there is either physiological or pathological cell death and a failure of clearance of the resulting apoptotic bodies, which go on to nucleate apatite. A relative lack of function of constitutive inhibitory proteins, such as MGP, would lead to crystal growth and a concomitant transition of VSMCs to an osteogenic phenotype (1,5,9).

Medial artery calcification (MAC) is a nonobstructive condition leading to reduced arterial compliance that is commonly considered as a nonsignificant finding. Recent studies have shown that MAC is a strong marker of future cardiovascular events in diabetic patients, unrelated to cardiovascular risk factors (1,2).

MAC, also known as Monckeberg's sclerosis, is a condition that leads to the stiffening of the elastic layer of the

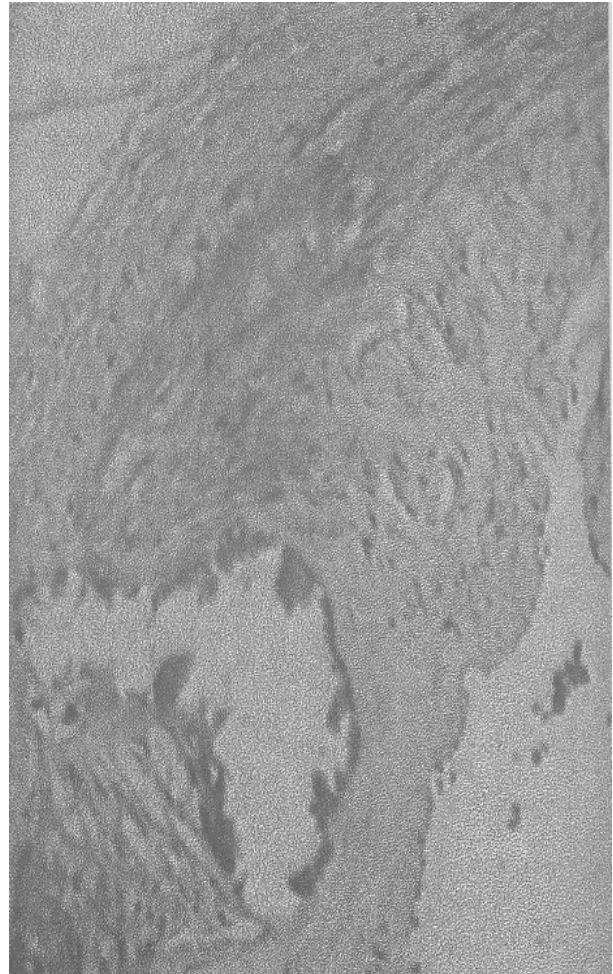


Figure 5. Temporal artery biopsy showing medial artery calcification

arterial wall, but in contrast to intimal artery calcification, it does not obstruct the arterial lumen. As intimal calcification represents an advanced state of atherosclerosis, MAC has been related to aging and diabetes, especially to long duration of diabetes and its complications. However, the pathogenesis and clinical significance of MAC have remained unsettled (2).

Our understanding of the genetic basis of vascular calcification has significantly increased after mouse genetics became available. The generation of two mutant mouse strains, i.e. mice lacking matrix Gla protein or osteoprotegerin, has had the biggest impact on vascular calcification as both strains display isolated medial calcification of arteries. These phenotypes demonstrate that vascular calcification is mostly a passive process and that its inhibition is genetically controlled (4).

Osteoprotegerin (Opg) is a molecule preventing arterial calcification. It is secreted by VSMCs. Opg acts as an inhibitor of terminal differentiation of bone-resorbing osteoclasts. Thus, Opg-deficient mice develop severe osteoporosis

sis caused by increased bone resorption. In addition to this phenotype, Opg-deficient mice display calcification of aorta and renal arteries (10).

Human VSMCs express many of the calcification regulating proteins such as matrix Gla protein, osteocalcin, osteonectin and osteopontin. These proteins can inhibit hydroxyapatite formation and stimulate bone resorption by osteoclasts (1,5).

Vascular calcification is common among diabetic patients with advanced age. Mori et al. were reported a case of 29 year-old male with extensive arterial calcification of unknown etiology (11). However, it is uncommon finding among young and non-diabetic patients. So this case with extensive medial calcific deposits is an unusual presentation of medial artery calcification.

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