Dystrophic Calcifications and Raynaud's Phenomenon in an Eight-Year Old Girl

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SUMMARY

Introduction Dystrophic calcifications are the most common subtype of skin calcinosis. Tumorous soft tissue calcium deposits usually contain hydroxyapatite and amorphous calcium phosphate. Differential diagnosis of skin calcinosis encompasses Thibierge-Weissenbach syndrome, systemic sclerosis, scleroderma, CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia), dermatomyositis, systemic lupus erythematosus, ad myositis ossificans progressiva.

Case Outline We present the case of an eight-year old girl with tumorous soft tissue calcium deposits and Raynaud's phenomenon. At the age of 3.5 years, our patient was admitted to Pediatric Surgery Clinic because of bilateral acrocyanosis localized at the fingertips area of hands, with the signs of vascular trauma. Therapy with vasodilators and hyperbaric oxygen treatment were completed. This therapy resulted in improvement. At the age of eight, the patient was admitted again due to intermittent, painful cramps localized in both hands. Punctiform deposits were present at the tips of fingers and toes, which looked like calcifications and were spontaneously eliminated, with the remnants of crater-shaped defects. A hard tumorous deformity localized in soft tissue was present in the extensor area of the right elbow. Laboratory indicators of inflammation were within the reference values, and antinuclear antibodies were positive. A nodus localized at the right elbow was extirpated. Pathohistological findings: connective and fat tissue with large deposits of calcium.

Conclusion Further follow-up of our patient is necessary due to possible development of complete picture of CREST syndrome or systemic sclerosis.

Keywords: Raynaud disease; calcinosis; child

INTRODUCTION

Skin calcinosis represents deposits of calcium salts in skin and subcutaneous tissue. It can be divided into 4 subtypes: dystrophic, metastatic, idiopathic and iatrogenic [1, 2]. The most common subtype of calcinosis is dystrophic calcinosis seen in connective tissue diseases such as scleroderma, CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia), systemic sclerosis, dermatomyositis or systemic lupus erythematosus [3, 4, 5]. We present the case of an eight-year old girl with tumorous soft tissue calcium deposits and Raynaud's phenomenon.

CASE REPORT

At the age of 3.5 years (November, 2006) our patient was admitted to Pediatric Surgery Clinic because of marked, bilateral acrocyanosis localized at the fingertips area of hands, with the signs of vascular trauma. An episode of vasospasm typically lasted 10 to 15 minutes a day with spontaneous disappearance. However, over time vasospastic changes led to ischemic lesions of fingertips. Her personal history revealed that she came from rural area. In addition, prior to the appearance of the first symptoms she was in contact with corn, so it was suspected to be the case of ergotism. After an initial laboratory evaluation and exclusion of coagulopathy, diagnosis of Raynaud's phenomenon was established. Nail-bed capillaroscopy was performed showing that the majority of capillaries were in a shape of hairpin, the loop diameter was narrower alongside the smaller number of capillaries of moderately widened granulated lumen, and the flow speed was slower, whereas there were no arrays without capillaries. Doppler ultrasound of arteries and veins of the upper extremity did not reveal pathological changes. Therapy with vasodilators and hyperbaric oxygen treatment in duration of nine days were carried out. This therapy resulted in improvement of capillaroscopic findings and epithelialization of previous necrotic changes. In due course, the girl was controlled by a vascular surgeon. Occasionally, she used to have more expressed ischemia of fingertips on hands and feet, but they were promptly treated with vasodilators and did not lead to serious ischemic lesions. In the meantime, smaller deposits of calcium were surgically removed from the right palm in a local hospital.

In May 2011, at the age of eight, she was re-admitted to Pediatric Surgery Clinic due to

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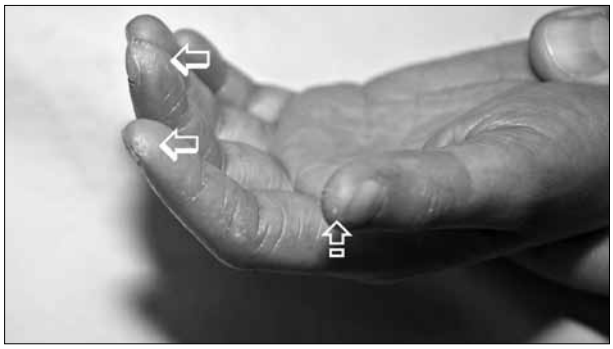

Figure 1. Callosity and thickening of fingertip skin

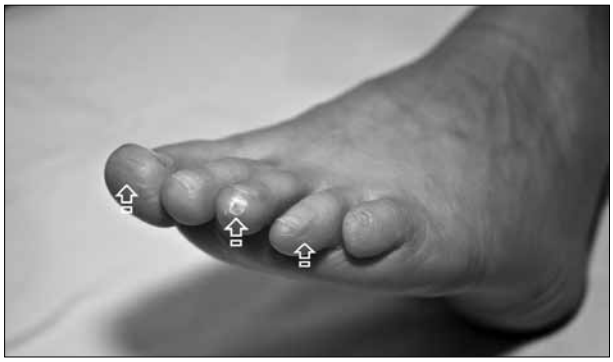

Figure 2. Punctiform deposits were present at the tips of some fingers and toes

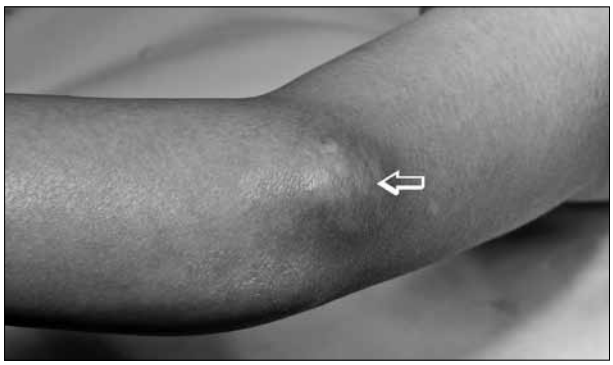

Figure 3. A hard tumorous deformity localized in soft tissue in the right elbow area

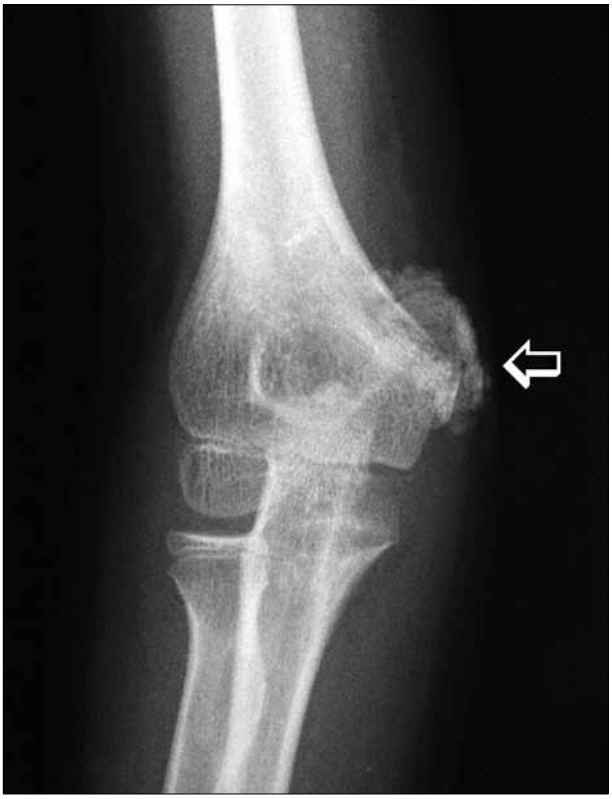

Figure 4. X-ray of the right elbow

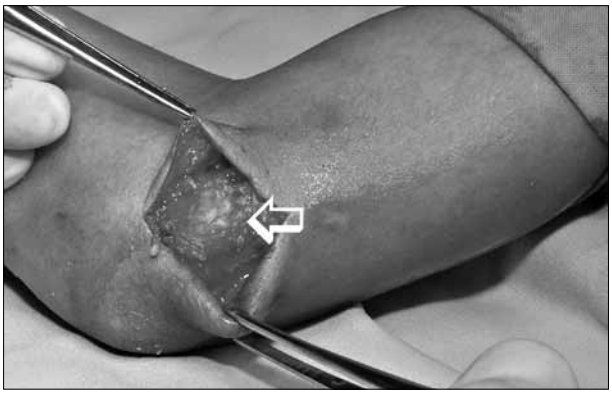

Figure 5. Nodus in the right elbow area

anamnestic data of intermittent, painful cramps localized in both hands. The immunologist was consulted. Physical examination revealed callosity and thickening of fingertip skin together with the loss of normal papillary lines. Punctiform deposits were present at the tips of fingers and toes, which looked like calcifications and were spontaneously eliminated, with the remnants of crater-shaped defects (Figures 1 and 2). A hard tumorous deformity localized in soft tissue was present in the extensor area of the right elbow. (Figure 3). Radiographic examination of the right elbow: irregular calcareous shadow in the area of medial malleolus of the humerus and dorsally placed in the soft tissue (Figure 4). The following laboratory analyses were performed: laboratory indicators of inflammation were within the reference values; calcium, phosphorus, alkaline phosphatase, bone alkaline phosphatase isoenzyme, parathormone, osteocalcin, and vitamin D (25-OH) were within the limits; antinuclear antibodies (ANA) on Hep2 cells were positive, nucleoplasm was positive, homogenous, intense; positive anticentromere antibodies; lupus anticoagulans, anticardiolipin antibodies IgM and IgG, anti β_2 glycoproteins IgM and IgG were negative. Esophagography: the action of swallowing with sustained oropharyngeal and esophageal phase, without any contrast residue in vallecula epiglottica and piriform recessus, esophagus was regularly positioned and had regular caliber, smooth contours and regular creases in mucous membrane. Nail-bed capillaroscopy showed longer capillaries. Loops of rather expanded diameter, mostly mega forms, slower blood flow, and no arrays without capillaries were also found.

Extirpation of nodus localized at the right elbow was performed at our Clinic (Figure 5). Intraoperatively, all relevant anatomic structures were found to be displaced but not damaged. Pathohistological findings were as follows:

doi: 10.2298/SARH1404239G

connective and fat tissue with large deposits of calcium. Calcification zones were surrounded by inflammatory infiltrate built from histiocytes, plasma cells, lymphocytes and giant multi-nuclei cells of foreign body type. Final histopathological diagnosis was dystrophic calcification.

DISCUSSION

Dystrophic calcifications are the most common subtype of skin calcinosis and most frequently occur in association with the systemic connective tissue diseases. Tumorous soft tissue calcium deposits usually contain hydroxyapatite and amorphous calcium phosphate [1]. Pathophysiology of dystrophic calcinosis has not been properly clarified. The appearance of calcinosis could be enhanced by chronic inflammation, structural damage to the tissue, hypovascularity and hypoxia [2, 6]. Calcium is deposited at phosphate-bound denaturated proteins of necrotic cells [7]. Activated macrophages have an important role in development of tissue calcinosis [8]. Mitochondria have high affinity for calcium and phosphate. Abnormally high mitochondrial calcium and phosphate levels may lead to crystal deposition and cell necrosis. In addition, cell necrosis creates more acidic environment. Certain calcification inhibitors lack in acidic environment, contributing to more crystallization [9].

Differential diagnosis of skin calcinosis includes Thibierge-Weissenbach syndrome, systemic sclerosis, scleroderma, CREST syndrome, dermatomyositis, systemic lupus erythematosus, and myositis ossificans progressiva [10]. Anticentromere antibodies are considered the markers of CREST syndrome, although they can be found in patients who suffer from Raynaud's phenomenon as well as in those suffering from diffuse form of systemic sclerosis [11, 12]. These autoantibodies can have direct toxic effect on endothelial cells [13]. Anticentromere antibodies are highly specific for CREST syndrome, but their sensitivity is low [14]. Our patient has positive anticentromere antibodies but she does not meet all diagnostic criteria of CREST syndrome. This syndrome is a subtype of limited scleroderma, which implies calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly and telangiectasia. Raynaud's phenomenon is usually the first symptom and it can appear several years before sclerodactyly [2, 15, 16]. In comparison to systemic sclerosis, the prognosis is significantly better for CREST syndrome but in rare cases, the visceral organs can be also affected. Association of CREST syndrome with pulmonary, cardiac and renal spread correlates with poor prognosis and shorter period of survival [17].

The first manifestation of disease in our patient was Raynaud's phenomenon, followed by sclerodactyly and subsequent calcinosis. Capillaroscopic changes characteristic for systemic sclerosis were not seen. The appearance of calcium deposits on the palm of the right hand, which were surgically removed, preceded sclerodactyly. In further course, the calcium deposits developed on fingertips and toe tips, which spontaneously disappeared, followed by calcinosis in the right elbow area. Neither spreading out to esophagus nor telangiectasia was established.

In conclusion, close follow-up of our patient is necessary because she may develop complete CREST syndrome or systemic sclerosis.

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Дистрофичне калцификације и Рејноов феномен код осмогодишње девојчице

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КРАТАК САДРЖАЈ

Увод Дистрофичне калцификације су најчешћа манифестација кожне калцинозе. Туморски мекоткивни депозити калцијума обично се састоје од хидроксиапатита и аморфног калцијум-фосфата. Диференцијална дијагноза кожне калцинозе обухвата Тибијерж–Висенбахов (*Thibierge–Weissenbach*) синдром, системску склерозу, склеродерму, синдром *CREST* – који чине калциноза, Рејноов (*Raynaud*) феномен, езофагеални дисмотилитет, склеродактилија и телеангиектазије, затим дерматомиозитис, системски еритемски лупус и прогресивни осифицирајући миозитис.

Приказ болесника У раду је приказана осмогодишња девојчица с туморским, мекоткивним депозитима калцијума и Рејоовим феноменом. Болесница узраста од три и по године примљена је на Клинику за дечју хирургију у Новом Саду због обостране акроцијанозе локализоване на врховима прстију шака, са знацима васкуларне исхемије. Лечена је вазодилататорима и терапијом у хипербаричној комори, након чега јој се стање побољшало. У узрасту од осам година поново је примљена због интермитентних, болних грчева у обе шаке. На врховима прстију су уочени пунктиформни депозити који су изгледали као калцификације и спонтано се повлачили остављајући оштећења у виду малих кратера. У меком ткиву екстензорне стране десног лакта установљена је тврда туморска промена. Лабораторијски показатељи запаљења су били у границама референтних вредности, а антинуклеарна антитела позитивна. Нодус локализован у пределу десног лакта је екстирпован. Патохистолошки налаз је гласио: везивно и масно ткиво са депозитима калцијума.

Закључак Даље клиничко праћење болесника је неопходно због могућности развоја комплетне слике синдрома *CREST* или системске склерозе.

Кључне речи: Рејноов феномен; калциноза; дете

Примљен • Received: 19/03/2013 **Прихваћен • Accepted:** 10/06/2013

doi: 10.2298/SARH1404239G