CASE REPORT

SUCCESSFUL TREATMENT OF SOFT TISSUE CALCIFICATIONS IN UREMIA
THERAPY OF STC IN UREMIA

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Abstract: The appearance of soft tissue calcifications in patients with chronic renal failure has been recognised as one of the serious complications of uremia. An elevated serum calcium-phosphate product has almost invariably been detected, although the exact mechanisms of precipitation are still not fully understood. Among the factors responsible for triggering the precipitation process are: hyperphosphatemia, secondary hyperparathyroidism, hypercalcemia, treatment with vitamin D₃, etc. Phosphate binders have been used to prevent, among other things, soft tissue calcifications, and parathyroidectomy has most frequently been applied as the therapy of choice, once precipitation of calcium salts has occurred. We present a case of soft tissue calcifications in the gluteal regions of a chronic haemodialysis female patient. The therapy we chose was a combination of bisphosphonate and deferoxamine. The patient was treated for two months. The regression of the soft tissue calcifications was very significant, as registered both clinically and radiologically. The exact mechanism by which this reversal was achieved needs further investigation.

Key words: Kidney failure chronic, haemodialysis, soft tissue calcifications, therapy.

Introduction

The association of soft tissue calcification (STC) and uremia has been recognised for more than 140 years [1], but it has become an important problem...
since the widespread use of regular dialysis and transplantation [2]. Factors which contribute to the elevation of the calcium-phosphate product are accused of precipitating STC, although the mechanism of this process in uremia still remains obscure [2, 4]. These factors include: hyperphosphatemia, hyperparathyroidism, treatment with vitamin D3, hypercalcemia, etc. Recently, a case of calcium carbonate induced calciphylaxis has been reported [5]. Varieties of STC in uremia have been described: arterial, ocular, periarticular, cutaneous and subcutaneous, and visceral. However, calcifications of the small and medium-sized arteries of various tissues have been described most frequently [3]. Aluminium and calcium containing phosphate binders, as long term treatment, are almost invariably prescribed to chronic haemodialysis patients, to control hyperphosphatemia, and to prevent secondary hyperparathyroidism and STC. Parathyroidectomy has been described as the most effective treatment for STC [3, 4]. We would like to present a case of successful conservative treatment of STC.

Case report

A 52-year-old woman with chronic glomerulopathy had had a 20-year history of proteinuria and erythrocyturia. The patient refused renal biopsy. At the age of 43, chronic renal failure and arterial hypertension were diagnosed. Chronic haemodialysis treatment was started at the age of 46, with a dialysis regime of 4 hours twice weekly, and after a few months she was transferred to a weekly dialysis regime of three times four hours. An acetate bath and a cuprophane membrane of 1.1 m² were used. The blood flow was 250 ml/min. She was dialysed on a Gambro AK 10 machine. The dialysate calcium concentration was always 1.75 mmol/l. The patient was polytransfused because of renal anemia. One year after the onset of haemodialysis therapy she was found to be hepatitis B antigen positive. Over the last five years she has remained well on dialysis, receiving a combination of Aluminium hydroxide and Calcium carbonate as phosphate binders and antihypertensive therapy. During this period her serum calcium has ranged between 2.2 and 2.6 mmol/l and serum phosphate between 1.8 and 3.3 mmol/l. Alkaline phosphatase remained around the upper limit of normal value for the first three years of dialysis, and thereafter it has slowly risen to twice the upper normal limit over the period of two and a half years. Then she reported the appearance of hard lumps in her gluteal regions bilaterally. Radiography of the pelvis revealed symmetrical extensive soft tissue calcifications in the gluteal muscles (figure 1A). Her serum PTH level at the time was 287 pg/ml. She was placed on a combined treatment of bisphosphonate...
Successful treatment of Soft...

(clodronate)-(Bonefos®-OyStarAb-Finland) 400 mg orally twice daily, and
deferoxamine methanesulfonate (Desferal®-Ciba-Geigy, Basel, Switzerland)
500 mg in 250 ml of 5% glucose solution once weekly, infused slowly in the
venous line during the last hour of a dialysis session. During the treatment we
did not register any significant changes in her serum calcium, phosphorus and
alkaline phosphatase. No adverse effects of the drug treatment were noted. After
two months of this treatment a control radiography was performed (figure 1B).
There was a striking reduction of the STC bilaterally. Clinically, the hardness of
the gluteal regions was gone, and the patient felt completely recovered and
comfortable.

Figure 1A – Radiography of the pelvis of our patient before treatment. The black
arrows point the areas of soft tissue calcification

Слика 1А - Рентгенска графија на карлица на пациентка пред лекување.
Црните стрелки ги покажуваат мекоткивните калцификации
Figure 1B – Control radiography of the pelvis of our patient following two months combined treatment with biphosphonate and deferoxamine. On the right side only about 10–15% of the soft tissue calcification remained, while on the left side there was practically complete resorption of the calcium deposits.

Discussion

We have presented the history of a dialysis patient with prolonged hyperphosphatemia, which eventually led to secondary hyperparathyroidism, and precipitation of STC. Because the level of PTH was not too high, and because parathyroidectomy did not appeal to the patient as an immediate treatment, we tried a combination of drugs which has so far not been described in...
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the literature. Diphosphonate therapy alone, has been used previously in a 30-year-old patient with calciphylaxis, but the treatment was unsuccessful [4]. This drug is known, once absorbed from the gastrointestinal tract, to bind to the hydroxyapatite crystals in the bone and prevent the osteoclasts splitting the crystals and inducing a breakdown of the bone.

Deferoxamine methanesulphonate is a chelating agent used successfully for treatment of overload with trivalent ions, such as iron and aluminium overload, because the complex formation constants with these ions are $10^{31}$ and $10^{25}$ respectively. The affinity of deferoxamine for the divalent ions such as calcium exists but is substantially lower. These complexes are easily dialysable.

We are not certain which of the two drugs was more useful during this treatment, nor whether there was an additive effect with this combination. Further investigations are necessary to elucidate these questions.

REFERENCES


Ре з и м е

УСПЕШНО ЛЕКУВАЊЕ НА МЕКОТКИВНИТЕ КАЛЦИФИКАЦИИ КАЈ УРЕМИЈАТА

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Појавата на мекоткивни калцификации кај болните со хронична бубренска слабост на лекување со хронична хемодиализа, претставува сериозна компликација. При тоа скоро секогаш биле присутни заголемени вредности на продуктот калциум-фосфор во крвта на болните. Точниот механизам на предципитација не е сè уште потполно познат. Се смета дека неколку фактори се одговорни за таложењето калцификати во меките ткива: хиперфосфатемија, секундарен хиперпаратиреоидизам, хиперкалциемија, терапија со витамин Д₃ (калцитриол), и др. Врзувачите на фосфатите се употребуваат за превенција од мекоткивните калцификации, а паратиреоидектомијата била најчесто применета како терапија на избор при појавата на предципитации на калциумовите соли.

Прикажуваме случај на мекоткивни калцификации во глуталните ложи кај жена лекувана со хронична хемодиализа. Терапијата што ја одредивме беше комбинација на бифосфонат и десфероксамин. Пациентката ја третираше два месеци. Постигнавме значајна регресија на мекоткивните калциумски депозити. Тоа го регистрираше со клинички и радиографски методи. Точниот механизам на терапевтичкиот успех треба да се утврди со дополнителни исследувања.

Клуинни зборови: хронична бубренска инсуфициенција, хемодиализа, мекоткивни калцификации, лекување

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