Cardiovascular Complications in a Child with Chronic Renal Failure

Cesmar Volga Haddad Herdy, Vânia Gloria Silami Lopes, Maria Cecília Olivaes, Isabele Coelho Mota, Marcio Moacyr Vasconcelos
Universidade Federal Fluminense - Niterói, RJ - Brazil

This is the report of an 11-year-old boy with chronic renal disease and secondary hyperparathyroidism. The child had been on dialysis, calcitriol, calcium carbonate, and presented dyslipidemia and calcified thrombi in various vessels and organs in the course of his condition. Pathological examination showed ischemic cerebral necrosis, calcification in coronary arteries, and myocardial infarction.

Introduction
Cardiac complications are the major cause of death in 25% of children with advanced chronic renal failure. Visceral calcifications – which include heart and vessels – may occur in adults with primary or secondary hyperparathyroidism, but are rarely seen in children. The purpose of the present report is to call attention for the occurrence of early severe cardiovascular disease in pediatric patients with chronic renal failure (CRF) and secondary hyperparathyroidism.

Case Report
A male, mulatto, 11-year-old patient was admitted to the Pediatric Unit at the University Hospital due to generalized tonic-clonic convulsive crises. The patient had no recent febrile or infectious condition. Previous pathologic history showed he had been diagnosed with CRF at the age of 4, and had his follow-up at a different hospital. Prescriptions included: calcitriol, calcium carbonate, and erythropoietin, with daily peritoneal dialysis having been started at home. At 8, the patient had a fracture of collum femoris. A year before hospital admission at this point in time the patient had an ischemic stroke, which developed into paralysis of his right limbs. Two months before current admission the patient had peritonitis with purulent secretion from dialysis catheter, and was medicated with cephalothin. The latest clinical occurrences were reported by the mother and treated at a different hospital.

Physical examination at admission showed severe nutritional deficiency – body weight, 14 kg (< 5th percentile), height, 98 cm (< 5th percentile) – and bone malformations.

Key words
Renal insufficiency, chronic / complications; cerebrovascular accident; hyperparathyroidism.

Mailing Address: Gesmar Volga Haddad Herdy • Travessa Antonio Pedro, 10301 24230-030 – Niterói, RJ - Brazil
E-mail: gesmarhaddad@uol.com.br
Manuscript received February 03, 2006; revised manuscript received April 03, 2006; accepted May 9, 2006.
ischemic infarction. Lungs: Calcification area at upper lobe apex and pulmonary atelectasia. Heart: Weight and volume increase; calcifications at right and left atriums, left ventricle endocardium, papillary muscle and tendon chords; abscess at right ventricle myocardium; infarction in left ventricle anterior wall (Fig. 1). Kidneys with diffuse microfolds, right kidney rather hypotrophic. Volume increase in parathyroids, with diffuse distribution of nodules. Metastatic calcifications in vessels, brain, and kidneys. Renal rickets.

Microscopy: Brain: Recent infarction of right parietal lobe; ischemic necrosis of right parietal lobe (left carotid artery territory); previous infarction in left parietal lobe (anterior cerebral artery territory). Lung: Bronchitis, septal thickening with mixed inflammatory afflux in parenchyma, calcification at alveolar sacs and capillary walls, with thrombi formation. Heart: Endocarditis, pericarditis, infarction at the anterior wall, right ventricle myocardium abscess. The anterior descending coronary artery showed intimal thickening, an area with atheroma plaque with collagen, inflammatory infiltrate with mononuclear and polymorphonuclear leukocytes, macrophages, fibrin, necrotic center and calcium deposition. Right internal carotid artery showed calcified thrombus with intimal thickening and inflammatory infiltrate similar to that found in the coronary. Parathyroids: Hyperplasia of major cells (Fig. 2). Kidneys: Glomerular atrophy, hyalinized glomeruli and segmental glomerular fibrosis (Fig. 3); urate crystals in tubules and interstitial calcifications; chronic glomerulonephritis (end-stage kidney).

Causes of death were cerebral edema and right cerebral ischemic infarction.

Pathological conclusion: Chronic glomerulonephritis, secondary hyperparathyroidism, renal osteodystrophy, metastatic calcifications in different organs and vessels. Myocardial infarction. Cerebral ischemic necrosis.

Discussion

In the present case, the long lasting (seven years) CRF triggered the whole pathologic process. An infarction area and thrombosis with calcifications in different vessels were described in the heart. The cardiovascular complications described in patients with CRF are: Arrhythmias from metabolic disorder, uremic pericarditis, hypertension, atherosclerosis (secondary to dyslipidemia), and calcifications in vessels and in the heart. As for our case, dyslipidemia was present, which could explain the previous stroke. Children prepared for transplant with triglycerides level above 150 mg/dL report lesions in the endothelium and in arteries, which include middle layer calcification. Pediatric patients with chronic renal disease in advanced stage are under the risk of accelerated atherosclerosis, associated with coronary lesions, as well as insulin resistance – which explains why statins are recommended. Endothelium integrity rupture triggers a cascade of inflammatory factors that lead to the formation of atheroma plaques; parathyroid hormone elevation contributes to artery calcification. No drug was administered to our patient for dyslipidemia control. Therefore, that pathophysiologic sequence could explain the many calcified lesions that have been found.

Renal disease is known to retain phosphates. In doing so, it decreases serum concentration of total and ionized calcium, in addition to decreasing renal production of 1α,25-dihydroxyvitamin D. It is known that 80% of Vitamin D is produced in the skin by the transformation of dihydrocholecalciferol under the influence of ultraviolet rays. Vitamin D is then hydroxylated to 25-hydroxyvitamin D in the liver and then in the kidney, resulting in 1α,25-dihydroxyvitamin D or 1α,25-(OH) 2-D. Low concentration of ionized calcium is the stimulus for parathyroid cells hypertrophy, as described in the necropsy for our case. When ionized calcium serum...
level is decreased to 4 mg/dL (1 mmol/L) there is stimulus for secretion of parathyroid hormone\(^1\). Increased production of that hormone is body’s attempt to normalize calcium and phosphate serum levels through the activation of osteoblasts and osteoclasts. Therefore, bone calcium mobilization and an increased tubular resorption occur.

The patient described showed significant bone changes that had been developed years earlier through femoral fracture and severe scoliosis. Therefore, he had renal osteodystrophy\(^1\), which includes all bone abnormalities and deranged mineral metabolism that result from renal failure. Secondary hyperparathyroidism is still a challenge for the treatment of pediatric CRF through peritoneal dialysis or hemodialysis, due to the adverse effects in growing patients\(^1\).

In our case growth had been interrupted, since body weight and height were compatible with a 3 or 4-year-old child, which is frequently seen in CRF\(^1\). The treatment carried out (calcium carbonate and calcitriol) is recommended by the authors\(^1\). Those drugs have the purpose to increase calcium concentration, which in turn improves hypophosphatemia. However, calcitriol was shown to inhibit the proliferation of condrocytes and to change the trophic actions of growth hormone in pre-pubertal patients’ bones\(^1\).

Oral or IV administration of calcitriol combined with calcium supplements has been implicated in the causation of episodes of hypercalcemia and/or hyperphosphatemia associated with osteodystrophy (adynamic bone disease), growth interruption,
and vascular calcifications\textsuperscript{13-16}. New vitamin D analogues have been developed recently (19-nor-paricalcitol and doxercalciferol) to control hyperparathyroidism without the biochemical changes secondary to calcitriol\textsuperscript{16}. The case here described was at high risk for cardiovascular disease, and calcitriol may have played an adjuvant role in the calcifications that were found. Myopericarditis and myocardial abscess may have been the result of previous bacterial infection (peritonitis), not treated with adequate doses of antibiotics.

## References


## Conclusion

The changes observed at necropsy were proof of clinical diagnosis. Therefore, treating CRF did not prevent complications such as hyperparathyroidism, osteodystrophy, dyslipidemia, and the serious cardiovascular changes.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.