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Case report

Benign Transient Hyperphosphatasemia in a Renal Transplant Recipient - A Case Report

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Abstract

Transient hyperphosphatasemia (TH) is characterized by isolated elevation of serum alkaline phosphatase (ALP). This condition was first recognized in children but only few cases reported this problem in adult population. There is no evidence of liver or bone disease and no signs of infection and usually levels of ALP return to normal levels within few months.
Here we report a case of benign TH in a 60-year-old male renal transplant recipient.

Key words: renal transplantation, alkaline phosphatase, elevated, hyperphosphatasemia, tacrolimus

Introduction

Most common conditions in which elevated serum alkaline phosphatase may be found are liver disease, some infections and bone disease as the most frequent condition in patients with renal dysfunction. Idiopathic elevation of serum alkaline phosphatase was first described in 1954. It was considered as benign condition which occurred mainly in children under 5 years old [1]. Few years later, the term of transient hyperphosphatasemia (TH) in infancy was established [2].
This condition is characterized by elevation of serum alkaline phosphatase several fold the reference upper limits, with no evidence of liver or bone disease and spontaneous return to normal levels after approximately 4 months [3,4]. Later on, there have been some publications of transient hyperphosphatasemia in pediatric renal transplant recipients [5-7]. Only few cases reported this condition in adult population and it was associated with liver disease, antiviral therapy, acute infection and lymphoma [8]. Just few years ago the first three cases of TH were described in renal transplant recipients without any other condition responsible for these elevated levels of serum ALP [9,10]. After the first cases that have been reported of these conditions in adult population it has been suggested that the term should be changed from transient hyperphosphatasemia in infancy to benign transient hyperphophatasemia [11].

Case report

A 60-year-old male was diagnosed with polycystic renal disease 12 years ago. He started with hemodialysis in January 2012. After no contraindications have been found he received renal transplant from deceased donor in June 2012. Immunosuppressive protocol included basiliximab induction, tacrolimus, corticosteroids and mycophenolate mofetil. The patient was discharged from the hospital 10 days after the transplantation with serum creatinine within the reference range. Shortly afterward serum creatinine started to rise and obstructive uropathy caused by lymph collection was found. After a surgical intervention the problem was solved and the patient was regularly followed up at the transplant outpatient clinic with a stable graft function. In January 2013 routine laboratory analyses demonstrated isolated elevation of ALP to 333 IU/I. As all the other results were in the reference range and the patient was asymptomatic, control on outpatient basis was planned. One month later ALP was 1040 IU/I, so we started diagnostic evaluation to exclude all the possible conditions which might explain ALP elevation. There was no evidence of acute infection, no acute gastrointestinal disease,

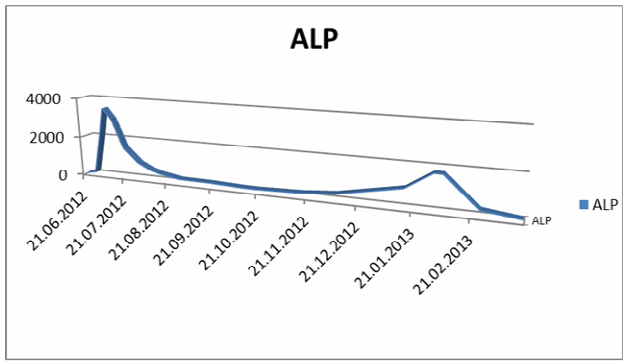

Fig. 1. Timeline of ALP (alkaline phosphatase) levels

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no ultrasonographic and CT evidence of lymph node enlargement or malignancy, and the bone scan showed no pathology. The tumour markers (CEA, AFP, CA 19-9, PSA) and other serum parameters were normal. One month later ALP was 1444 IU/I (Figure 1), but then for the first time serum calcium was slightly elevated to 2,74

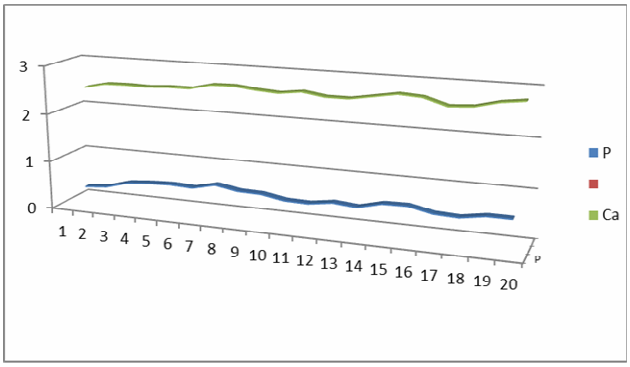

Fig. 2. Timeline of phosphorus and calcium levels

mmol/l and calciuria was detected (Figure 2). Intact parathyroid hormone was 18 pmol/L (range 1.0-6.0 pmol/L). Parathyroid glands scan revealed hyperfunctional parathyroid tissue near the lower pole of the left thyroid lobe. ALP isoenzymes showed most of ALP was bone related. So far mystery was solved. In the presence of hypercalcemia and high rise in serum ALP we considered to introduce calcimimetics in the therapy, but in March 2013 the regular control revealed serum ALP within the normal range.

There was no correlation of tacrolimus trough level on elevation of the serum ALP (Figure 3).

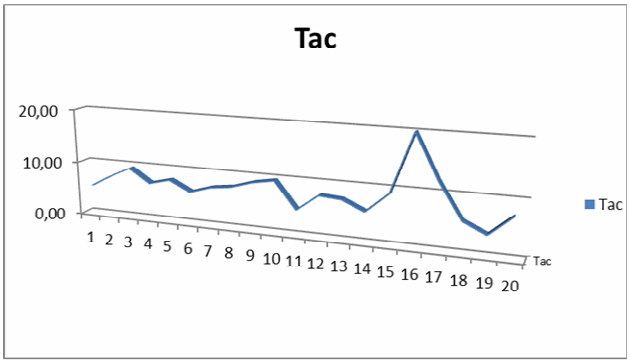

Fig. 3. Tacrolimus trough concentrations were not connected to alkaline phosphatase elevation

As the ALP levels returned spontaneously to 103 IU/l 3 months after diagnosis we suspected that benign transient hyperphosphatasemia was responsible for this condition.

Discussion

Little is known about transient elevations of alkaline phosphatase in adults. All our knowledge is based on several case reports, which differ significantly. Our patient is a good example. Many tests, which were done, might explain ALP elevation in the context of bone disease but still there is an open question why ALP return to normal level spontaneously. And considering this, the possibility of occurrence of benign TH in adults in association with renal transplantation must be observed [9,10]. However, while isolated hyperphosphatasemia in renal recipients may be a benign, self-limited condition, such cases must be differentially diagnosed from other conditions that can trigger hyperphosphatasemia, which include malignancy, infections, bone and liver disease [12,13].

Interestingly, recent studies have suggested that tacrolimus can induce in vitro bone formation. In such study investigators cultured rat bone marrow cells with tacrolimus hydrate (FK506) and observed that numerous cell clusters became positive for alkaline phosphatase activity. Later on by electron microscopy they revealed mineralized bone matrix in the cell clusters [14]. Having in mind these new research results, when we approach our patients and analyze laboratory test results we should think also about the effect of therapy that our patients receive,which is still unknown or is still the object of investigation. All the immunosuppressive drugs beside their main activity probably influence all the other organs which we still do not know, and therefore new studies and research are necessary.

Conflict of interest statement. None declared.

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