MO802 **DOES ETELCALCETIDE REVERSE MYELOFIBROTIC BONE CHANGES DUE TO HYPERPARATHYROIDISM? A CASE REPORT**

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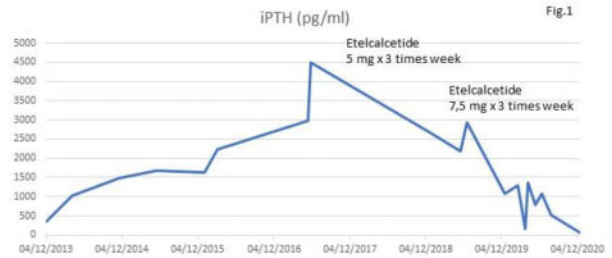
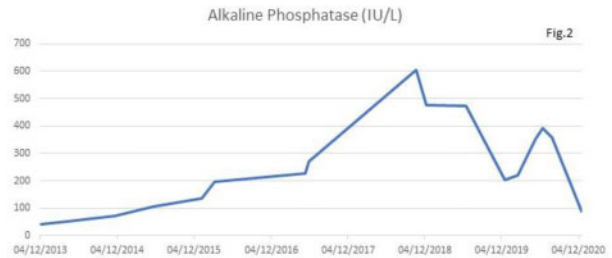
BACKGROUND AND AIMS: A 21 year old boy with a diagnosis of Autosomal Recessive Polycystic Kidney Disease and Caroli disease reached a final stage of chronic kidney disease (CKD) and started haemodialysis.
METHOD: After 3 years in haemodialysis he underwent a kidney transplant from a

cadaveric donor. His transplanted kidney worked fairly well until the patients was 31 year old when he developed graft dysfunction (serum creatinine from 2.7 to 5 mg/dL in a very short period). There was a concomitant increase in serum phosphate levels (8.3 mg/dl) and iPTH that progressively increased to 1032 pg/ml despite a traditional therapy.

RESULTS: At age 32, the patient returned to haemodialysis treatment thrice weekly with a concomitant a progressive worsening of hyperparathyroidism with bone pain . Cinacalcet at a dosage of 30 mg daily treatment was initiated, then it was increased to 120 mg daily without any benefit. Two years later, being the clinical situation without any improvement and being the patient scarcely compliant to the therapy and because a further enlargement of parathyroid glands was observed, a Parathyroidectomy (PTX) was advised.

Nevertheless, PTX was not performed because of patient's refusal. Furthermore, despite Erythropoietic Stimulating Agent (ESA) therapy, he developed severe anemia that required regular and frequent blood transfusions. iPTH increased to 4500 pg/ml [Fig.1] with a parallel rise in alkaline phosphatase >600 UI/L [Fig.2]. A Computed Tomography scan showed multiple bone-thickening lesions. He thus initiated Etelcalcetide 5 mg e.v. 3 times a week, after the HD session but without any benefit. The dosage was then increased to 7.5 mg but the patient gradually became frail and developed pancytopenia and low-grade fever. Hematological evaluation with bone marrow biopsy was performed in December 2019. Bone marrow histology showed severe fibrosis [Myelofibrosis (MF) grade 3] with normal bone marrow cytogenetics. Blood samples for mutations in JAK-2, CALR, and MPL and BCR-ABL rearrangement were negative. There was no evidence for a myeloproliferative neoplasm (MPN) or metastatic lesions.





During the following months, while on a 7,5 mg dose of etalcalcetide, there was a gradual reduction in iPTH [Fig.1] and serum alkaline phosphatase [Fig.2], up to 500 pg/dl and 200 IU/L respectively. The patient developed asymptomatic, often severe, hypocalcemia which was managed with therapy.

The patient's clinical conditions gradually improved, anemia responded to lower doses of ESAs. A bone marrow biopsy was repeated after one year (December 2020) and it showed a reduction in fibrosis (MF grade varying from 1-2). Then etelcalcetide dosage was reduced while serum calcium and phosphate levels were in the normal limit.

CONCLUSION: Myelofibrosis secondary to renal osteodystrophy is an uncommon complication. It has been rarely reported and usually is associated with primary hyperparathyroidism. Marrow fibrosis and pancytopenia is related to the excessive iPTH that upregulates production of cytokines and paracrine factors in the bone marrow (IL-1a, IL-6, FNF-a, TGF–b, and platelet-derived growth factor) and it has an important stimulatory effect on fibroblast proliferation. It is known that surgical parathyroidectomy is associated with a reduction of bone marrow fibrosis in primary hyperparathyroidism. To our knowledge, this is probably the first case of tertiary hyperparathyroidism in which the effect of etelcalcetide is comparable to parathyroidectomy as far as on calcium-phosphate balance, and a significant improvement in bone marrow fibrosis and hemoglobin. In conclusion, etelcalcetide at least in this patient seems as effective as PTX on bone balance, bone marrow and anemia.