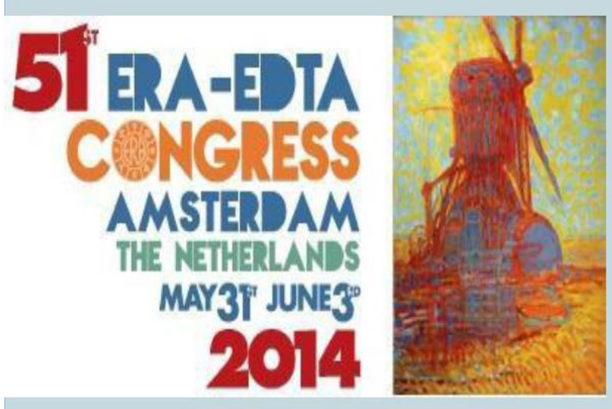


SEVERE HYPOPHOSPHATEMIA IN A PATIENT WITH TYPE 1 NEUROFIBROMATOSIS : CASE REPORT

H. Azar (1), R. Ossman (1), M. Flamant (2), D. Chelala (1)

(1) Hotel Dieu de France University Hospital, Beirut, Lebanon
(2) Bichat Claude Bernard University Hospital, Paris, France

A 46 years old patient presented with severe left upper arm pain of a few months duration along with generalized weakness:

- **No significant past medical history, particularly no history of fractures or rheumatologic disease, no long term treatment, no tobacco or illicit drug use.**
- **8 café-au-lait spots of > 15mm diameter, in the inguinal and axillary regions.**
- **No limb deformities.**
- **2 Lish nodules.**

confirming the diagnosis of Type I Neurofibromatosis.

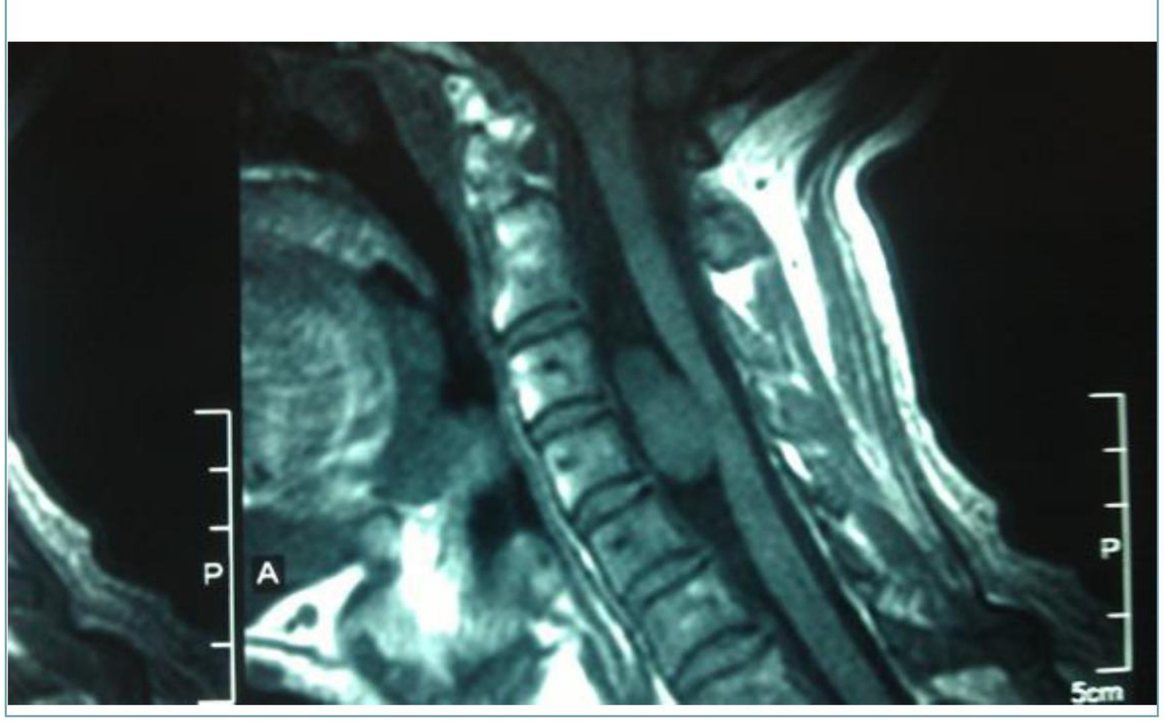
Laboratory exams revealed:
Normal creatinine (49 µmol/l), uric acid (504 µmol/l), calcium (2.35 mmol/l), potassium (4.1 mEq/l), bicarbonate (25 mEq/l) and alcaline phosphatase (78 U/l, N< 122) levels. BUT SEVERE HYPOPHOSPHATEMIA.

Generalized proximal tubule dysfunction was ruled out: uric acid EF 2.57%, no hypokalemia, acidosis, aminoaciduria, nor glucosuria.
The patient was supplemented with Vit D, and operated in November. Vit D supplementation was stopped one month later. Phosphorus level was obtained again in January.

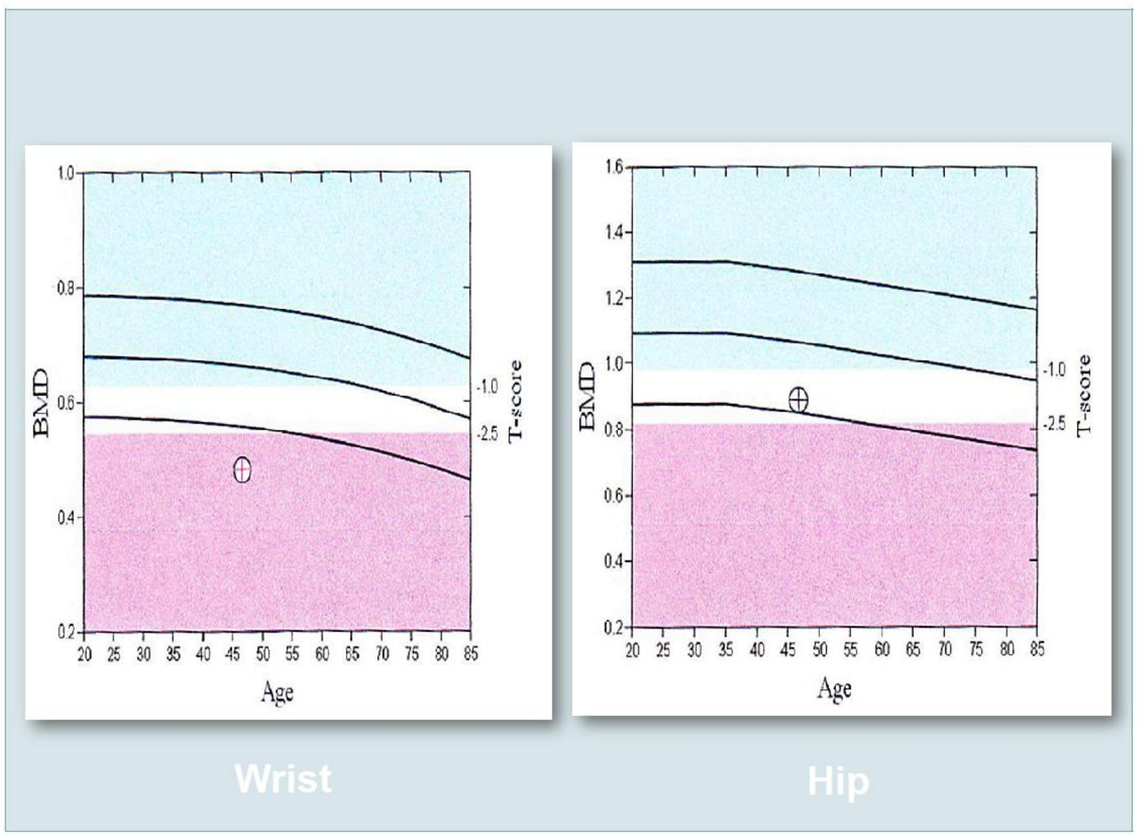
	Before Vit D Supplementation	After Vitamin D supplementation	After Surgery	Normal Values
Phosphorus mmol/l	0.23	0.82	0.77	0.9-1.5
TRP %	89	77	83	85-90
TmPi/DFG mmol/l	0.22	0.65	0.64	0.89-1.34
25 OH Vit D ng/ml	5.7	30	29	>30
1.25 OH2D3 pg/ml	34			20-45
PTH pg/ml	68	65	59	10-65
FGF 23 RU/ml	119			34-97

Supplementation with alphacalcidol 0.25 µg/ day and cholecalciferol 100000 U/l twice a week for 3 months.

Cervical spine MRI



Neurofibroma along C3 et C4 roots extending to the medulla.



Osteodensitometry showing severe osteoporosis with a T score of -4 at the level of the wrist with osteopenia at the level of the hip and vertebral column.

DISCUSSION

FGF23 is a phosphaturic hormone of 251 aa secreted by osteocytes, that inhibits phosphorus reabsorption in the proximal tubule in the presence of KLOTHO while acting on NPT2a, NPT2c, and inhibits one alpha hydroxylase.
FGF23 has been implicated in phosphorus loss and oncogenic osteomalacia in some mesenchymal tumors.
Hypophosphatemia is rare in type I neurofibromatosis. In this case it was associated with abnormal isolated phosphaturia, and was partially alleviated with native vitamin D and calcitriol supplementation. FGF23 level was high and inappropriate in the setting of severe hypophosphatemia.
FGF23 may be secreted by the neurofibroma, like in other mesenchymal tumors. After surgery and stopping vitamin D supplementation, phosphorus level went down again but to a much lesser extent, implicating the neurofibroma tissue in the pathophysiology of hypophosphatemia.
Other phosphatonins (FGF7, sFRP4, MEPE) have not been measured but may have a role in this case.

CONCLUSION

This is the first case in the literature of type I neurofibromatosis associated with hypophosphatemia probably related to abnormally high FGF23.
FGF23 dosing after the surgery or immunohistochemistry study of the excised tissue may further corroborate our hypothesis

1. Saidenberg-Kermanac'h N, Souabni L, Prendki V, Prie D, Boissier MC: Normal plasma FGF23 levels kinetic in tenofovir-related hypophosphatemic osteomalacia in an HIV-infected patient with von Recklinghausen disease. Joint Bone Spine 78 (3): 306-8, 2011
2. Woznowski M, Quack I, Stegbauer J, Büchner N, Rump LC, Schieren G: Oncogenic osteomalacia, a rare paraneoplastic syndrome due to phosphate wasting--a case report and review of the literature. Clin Nephrol 70 (5): 431-8, 2008
3. Carpenter TO: The expanding family of hypophosphatemic syndromes. J Bone Miner Metab 30 (1): 1-9, 2012
4. Jagtap VS, Sarathi V, Lila AR, Malhotra G, Sankhe SS, Bandgar T, Menon P, Shah NS: Tumor-induced osteomalacia: a single center experience. Endocr Pract. 17 (2): 177-84, 2011

DOI: 10.3252/pso.eu.51era.2014