Revista Electrónica de Biomedicina
Electronic Journal of Biomedicine

ISSN: 1697-090X

Inicio
Home

Indice del volumen
Volume index

Comité Editorial
Editorial Board

Comité Científico
Scientific Committee

Normas para los autores
Instruction to Authors

Derechos de autor
Copyright

Contacto/Contact:

ERYTHEMA NODOSUM AND PROLONGED FEVER ASSOCIATED TO SECONDARY HYPERPARATHYROIDISM

Enz P*, Musso C, Luque K**, Kowalczuk A*, Galimberti R*, Algranati L**.**

Dermatology* and Nephrology Departments.
Hospital Italiano de Buenos Aires. Argentina**

carlos.musso @ hospitalitaliano.org.ar

Rev Electron Biomed / Electron J Biomed 2005;2:67-72

Comment of the reviewer Omar Abboud, MD, FRCP, FRCPE. Consultant Nephrologist. Hamad Medical Corporation. Doha, Qatar.

Comment of the reviewer Antonio Félix Conde Martín. MD. Pathologist. Hospital Universitario Perpetuo Socorro. Badajoz, Spain.

SUMMARY
Secondary hyperparathyroidism is one of the main deragements caused by chronic renal failure, and parathyroid hormone is considered one of the toxins of the uremic syndrome. Prolonged fever due to primary hyperparathyroidism have already been described in the literature but not yet as induced by secondary hyperparathyroidism. In this case report a patient suffering from an erythema nodosum and prolonged fever associated to secondary hyperparathyroidism that disappeared through subtotal parathyroidectomy is presented.

RESUMEN
El hiperparatiroidismo secundario es uno de los principales disturbios causados por la insuficiencia renal crónica, y la paratohormona es considerada una de las toxinas del sindrome urémico. El sindrome febril prolongado secundario a hiperparatiroidismo primario ya ha sido descripto en la literatura, aunque no lo ha sido aun el inducido por hiperparatiroidismo secundario. En el presente reporte se presenta un caso de eritema nodoso y sindrome febril prolongado asociado a hiperparatiroidismo secundario y que resolvió luego de efectuada una paratiroidectomía subtotal.

Keywords: Secondary hyperparathyroidism, Erythema nodosum, Prolonged fever

Palabras Clave: Hiperparatiroidismo secundario, eritema nodoso, sindrome febril

---

INTRODUCTION

Secondary hyperparathyroidism is one of the main deragements caused by chronic renal failure, and elevated plasma parathyroid hormone is considered one of the toxins of the uremic syndrome. Many chronic renal failure

problems have been attributed to parathyroid hormone effect such as ureamic cardiopathy, erythropoiesis reduction and inhibition of platelet and T-cell functions[1]. Even though prolonged fever due to primary hyperparathyroidism have been already described in the literature, it is infrequent [2], and this entity has not yet been described as induced by secondary hyperparathyroidism. For that reason in the following case report a patient suffering from an erythema nodosum and prolonged fever associated to secondary hyperparathyroidism is presented.

Case Report

Female patient thirty-one years old suffering from chronic renal failure secondary to a vesicoureteral reflux in her childhood. She developed a severe secondary hyperparathyroidism: plasma intact parathohormone 1500 pg/ml (normal value in CRF: 150-300 pg/ml) (Tables 1 and 2).

Table 1: General Laboratories

Test	Result	Normal Range
Hematocrite	34 %	37-47 %
Hemoglobine	11 g/dl	11.5-16 g/dl
Plasma Ferritin	200 ng/ml	500-800 ng/ml (in dialysis)
White blood cells	6.200/mm^3	5.000 - 10.000/mm^3
Neutrophiles	44 %	50-60 %
Lynphocytes	42 %	30-40 %
Monocytes	10 %	4-12 %
Eosinophiles	3.3 %	2-4 %
Plasma urea	104 mg/dl	20-50 mg/dl
Plasma creatinine	6.2 mg/dl	0.5 – 1.2 mg/dl
Plasma glucose	74 mg/dl	70-110 mg/dl
Erythrocyte sedimentation rate (ESR):	102 mm^3	2-20 mm^3
Serum Cholesterol	218 mg/dl	130-200 mg/dl
Serum glutamic-oxaloacetic transaminase (SGOT)	22 UI/L	5-30 UI/L
Serum glutamic-pyruvic transaminase (SGPT)	24 UI/L	5-35 UI/L
Plasma albumin	3.6 mg/dl	3.7 – 5.6 mg/dl

Table 2: Phosphorus-Calcium Metabolism

Test	Results	Normal Range
Parathyroid hormone	1525 pg/ml	150-300 pg/ml (in dialysis)
Plasma calcium	9 mg/dl	8.5-10.5 mg/dl
Plasma phosphorus	4 mg/d	2.5- 4.5 mg/dl
Alkaline phosphatase	695 UI/L	50-130 UI/L
Parathyroid gland Tc 99 scan	increased captation in left inferior parathyroid area.	
Parathyroid gland ultrasound	solid nodule (22 mm) in the left-inferior area.	
Skull and hands x-ray	bone changes compatible with hyperparathyroidism.	

Two months before starting hemodialysis she had begun with fever and an erythema nodosum in the distal and anterior part of her legs (diagnose confirmed through skin biopsy). The fever was vespertine and without chills. The beginning of the dialytic treatment did not modify these symptoms. Many studies were performed in order to roule out infectious, neoplastic or autoimmune diseases. All results were negative or did not justify neither the prolonged fever nor the erythema nodosum (Tables 3, 4 and 5).

Table 3 : Infectological Tests

Test	Result
Urine culture (2 samples):	Negative (even for Koch bacillus)
Blood culture (6 samples)	Negative (even for Koch bacillus)
HbsAg	Negative
HCV antibody	Negative
HbsAg antibody	183 mUI/ml
HIV antibody	Negative
HTLV-1 antibody	Negative
VDRL	Negative
Mantoux reaction	Negative
Stool parasit test	Negative
Epstein Barr indirect immunofluorescence (IgG)	1: 64
Varicella-Zoster indirect immunofluorescence (IgG)	1: 640
Toxoplasmosis antibody (enzime immunoessay) (IgG)	<1:64

Table 4: Immunological Tests

Test	Result
Anticardiolipine antibodies	Ig M: 2 (normal < 15) Ig G: 1 (normal < 15)
Latex agglutination	Negative
Anti DNA	Negative
Lupic anticoagulant	Negative
Antinuclear antibodies	Negative

Table 5: Other tests

Test	Result
Plasma cortisol	24 micrograms % (normal range: 5-25 micrograms %)
Plasma TSH	1.8 microU/ml (normal range: 0.4-5.4 microU/ml)
Ginecological ultrasound	Normal
Abdominal ultrasound	Normal (except for small kidney size).
Thoracic and abdominal TC scan	Normal (except for small kidney size).
Bone densitometry	In normal range
Gallium-67 body scan	Diffuse increased captation in the whole skeleton.
Transesophageal cardiac ultrasound	Normal

Initially her hyperparathyroidism was treated with phosphorus binders (calcium carbonate) and intravenous calcitriol but it had to be discontinued many times due to the high plasma phosphorus levels that she developed. Because of that she had to be operated on her parathyroid gland. She was on no medication except for phosphorus binders, acid folic and B vitamin complex.

After that her plasma parathyroid hormone levels normalized and concomitantly the erythema nodosum and febril syndrome did too.

Discussion

Secondary hyperparathyroidism is promoted by several chronic renal failure deragements that generate an increase in plasma parathyroid hormone level, being the most important ones the hypocalcemia, diminished circulating calcitriol levels and phosphate retention [3].

Under normal conditions this hormone stimulates the bone turn-over, but in chronic renal failure is one of the main toxins resposible of the uremic toxicity. Secondary hyperparathyroidism leads to damage in many parenchymas: bones, ligaments, heart, etc. Even more parathyroid hormone interferes the activity of the immunological system for instance inhibiting the T cell function [1].

In this report we described a case in which the patient suffered from prolonged fever in the evenings for a period of five months and only disappeared after her hyperparathyroidism was solved through subtotal parathyroidectomy.

During her febrile syndrome she developed erythematous, tender nodules and plaques, on her pretibial areas. An skin biopsy confirmed the diagnose of erythema nodosum.

Erythema nodosum has been described in four kind of diseases: infectious, pharmacological, neoplastic and autoimmunological ones. Several immunological diseases have been described as generating erythema nodosum such as: bowel immflamatory diseases, sarcoidosis, Behçet and Sweet´s syndrome. It has not yet been described erythema nodosum induced by hyperparathyroidism [4,5].

Epidemiologically this entity is most frequent between 20 and 30 years of age, being 3 to 6 times more frequent in women than in men[6].

Immunological pathogenesis for this cutaneous reaction pattern is widely accepted[4,5]. Regarding the physiopathology of this disease, the hypothesis of an immunological mechanism is accepted[4,5]. Erythema nodosum is a type III hypersensitivity reaction (Gell and Coombs classification), mediated by antiboby-antigen deposits. After the exposition of the organism for a determined period to a particular antigen (infectious, autoimmune, neoplastic, farmacological or environmental one) it takes place an antibody-antigen union forming immune complexes which are deposited in some organs such as skin, kidney, lungs, etc. Then, an acute immunological reaction begins through complement cascade and immflamatory citokines activation that leads to the characteristic erythema nodosum skin lesion[7].

Our patient was studied in order to roule out the presence of infectious, neoplastic, farmacological or autoimmunological causes of prolonged fever and erythema nodosum, but none of them were found.

In our case parathyroid hormone or some part of its molecule could be the antigen that functioned as the stimulus of the skin immunological reaction. This could also explain the fact that the febrile syndrome and the erythema nodosum appeared in the context of a secondary hyperparathyroidism, and also that the skin lesion lasted beyond the habitual lapse for an idiopatic erythema nodosum (4-6 weeks), and that both manifestations (fever and skin lesion) disappeared after the normalization of plasma parathyroid hormone level due to sub-total parathyroidectomy.

Then we hypothezise that our patient prolonged fever and erythema nodosum could have been associated to secondary hyperparathyroidism.

Conclusion:
Prolonged fever and erythema nodosum seem to be one of the uncommon clinical expressions of the secondary hyperparathyroidism.

REFERENCES

1.- Vanholder R, Ringoir S. The uraemic syndrome. In Cameron S, Davison A, Grünfeld JP, Kerr D, Ritz E. Oxford. Oxford University Press. 1992: 1236-1250

2.- Ricci J, Vlasschaert J, Salit I. Prolonged fever asociated with primary hyperparathyroidism. Can Med Assoc J. 1984: 131(5): 459-460

3.- Delmez J, Kaye M. Bone disease. In Daugirdas J, Blake P, Ing T (Eds). Handbook of dialysis. Philadelphia. Lippincott Williams & Wilkins. 2001: 530-547

4.- Mert A, Ozaras R, Tabak F, Pekmezci, Demirkesen C, Ozturk R.Erythema nodosum: an experience of 10 years. Scand J Infect Dis. 2004; 36(6-7): 424-427

5.- Bondi E, Margolis D, Lazarus G. Disorders of subcutaneous tissue. In Feedberg I, Eisen A, Wolff K, Austen F, Goldsmith L, Katz S, Fitzpatrick T. (Eds). Dermatology in general medicine. New York. 1999: 1284-1287.

6.- Requena L, Sánchez Yust E. Mostly septal panniculitis. J Am Acad Dermatol. 2001; 45: 163-183

7.- Roitt I. Essential immunology. Oxford. Blackwell Scientific Publications. 1994: 326

Comment of the reviewer Omar Abboud, MD, FRCP, FRCPE. Consultant Nephrologist. Hamad Medical Corporation. Doha, Qatar.

The Authors made reference to a report of prolonged fever (without Erythema Nodosum) with primary hyperparathyroidism. This seems to be an isolated report, and fever is not a recognized feature of hyperparathyroidism.

In this article the prolonged fever was associated with Erythema Nodosum (ND). In my opinion the EN is the primary condition and the fever is one of its manifestations. Extensive review of the literature with reports of hundreds of cases of EN, does not list hyperparathyroidism among the causes of EN. In this case report the prolonged duration of the EN and fever and its disappearance after parathyroidectomy do suggest an association between EN and hyperparathyroidism. The immunological explanation given by the authors to explain the association is logical.

This case report is an alert for a lookout for such an association in the future.

Comment of the reviewer Pedro Abáigar Luquín MD. PhD. Nefrología. Hospital General Yagüe. Burgos. España

This case report reflects a new finding in the behavior of the primary hyperparathyroidism like cause of a inflammatory process and with an accompanying reaction that pronounces like erythema nodosum companion of fever, that in most of the occasions would make think us about a tuberculose, but that in this case discards by the absence of data that confirm this diagnosis and by the fact that the regression of the same one has been observed after the parathyroidectomy.

A data more in addition the motley clinical behavior of the parathyroidism and the accompanying inflammatory phenomenon to the same one, that it would justify in many cases the atheroesclerosis that develops these patients.

Received: March 7, 2005. Received revised May 29, 2005
Published June 3, 2005