# Endocrine function in abetalipoproteinemia: a study of a female patient of greek origin

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**Abstract**

*FUNZIONE ENDOCRINA NELLA A-BETALIPOPROTEINEMIA: STUDIO SU UNA DONNA DI ORIGINE GRECA*

*In questo lavoro abbiamo indagato sulla funzionalità ipofisaria, genitalia, surrenale, tiroidea, paratiroidea e pancreatica (endocrina) di una paziente affetta da abetalipoproteinemia, prima e dopo, un nostro tentativo di miglioramento della sua alimentazione con degli aggiustamenti dietetici. La paziente fu unica. Sono stati determinati nel siero della paziente in considerazione con delle tecniche radioimmunologiche le concentrazioni di cortisolo libero, A4, ACTH, aldosterone, renina, DHEA-5, progesterone 17 - OH progesterone testosterone SHBG, estradiolo LH, FSH, T3, T4, TSH, FT3, FT4, paratormone osteocalcina, prolattina preinsulina insulina, glucagone somatomedina - C (IGF - 1), IGF 1 - BP3, 25 OH) vitamina D3 e della 1 - 25 (OH) 2 vitamina D3. Sono stati effettuati anche il Test Synachten ed il calcolo della concentrazione del cortisolo delle urine delle 24 ore. L'ormone leptina è stato determinato con una tecnica enzimatica ad alta sensibilità. La frazione ionizzata del calcio sierico, è stata determinata tramite una apposita apparecchiatura (CORNING) e la fosfatasi alcalina ossea tramite una tecnica radioimmunologica. Dai calcoli effettuati risultava che il progesterone ed il 17-OH progesterone, erano diminuiti in entrambi i periodi della nostra osservazione (sia prima cioè, che dopo gli aggiustamenti dietetici alla paziente). Diminuiti i livelli del progesterone nel siero anche nel 21nesimo giorno del ciclo mestruale della paziente. La prolattina nel siero si è trovata aumentata. I livelli di IGF - 1 e di leptina nel siero, si sono trovati minori dei limiti inferiori del normale range di valori preso in considerazione dal nostro laboratorio. Nonostante il livello del paratormone nel siero fosse normale, i livelli della frazione ionizzata del calcio - ione nel siero e della 25 - OH vitamina D erano diminuiti, mentre la fosfatasi alcalina ossea era aumentata. La preinsulina sierica era aumentata, mentre l'insulina sierica era diminuita. I livelli invece di TH, glugagone, paratormone, FSH, LH, ACTH, testosterone, estradiolo e del SH13G nel siero, erano fisiologici. Il profilo ormonale della paziente, nonostante i tentativi di miglioramento del suo stato nutrizionale, non sono migliorati nel corso dei 5 anni di studio. In conclusione le pazienti di sesso femminile affette da abetalipoproteinemia, presentano diminuita produzione di*

## Introduction

Abetalipoproteinemia is a rare genetic disorder of lipoprotein metabolism (1-9). The main biochemical characteristic of the disorder is the complete absence of lipoprotein β both from serum and intestinal mucosa. The lipidemic profile of the peripheral blood is characteristic and includes very low levels of cholesterol and almost absence of high density (HDL), low density (LDL) and very low density (VLDL) lipoproteins (1-3). It is well known that synthesis of progesterone in the human corpus luteum and steroidal hormones in the adrenal cortex requires a source of cholesterol, which can be derived both from local synthesis and uptake of LDL. Because of the low levels or even absence of LDL from plasma in patients with abetaliproteinemia it could be argued that these patients would have an abnormal genitalia and adrenal serum hormonal profile. The newly described hormone leptin which is secreted by adipocytes, is thought to participate in the regulation of body weight by suppressing food intake and increasing energy expenditure (10-12).
So far, there are three descriptions concerning progesterone synthesis of patients with homozygous and heterozygous hypobetalipoproteinemia but not in patients with abetalipoproteinemia (13-15). To determine whether an almost complete absence of plasma LDL and the

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*progesterone ed un metabolismo osseo patologico. La diminuita produzione di progesterone va attribuita ai diminuiti livelli di LDL e di colesterolo nel siero, mentre i diminuiti livelli di IGI - 1 e di leptina sierica, sono dovuti alle carenze nutrizionali. I tentativi di miglioramento dello stato nutrizionale delle pazienti, non migliorano il loro profilo ormonale.*
Parole chiave: *Abetalipoproteinemia, funzione endocrina*.

impaired nutritional status affects serum hormone concentrations including leptin through the time in patients with abetalipoproteinemia, we estimated the pituitary, genitalia, adrenal, parathyroid and thyroid function in a woman with abetalipoproteinemia, at the time of diagnosis and five years later.

## Patient and methods

### *Patient*

The subject consisted of a previously reported 36-year-old female patient with abetalipoproteinemia (16). At the time of presentation her body weight and height were 33 Kg and 157 cm respectively and the body mass index (BMI) 13.38. (The 5$^{th}$ and 95$^{th}$ position of BMI in the normal Greek population being 17.8 and 33.2 respectively). The diagnosis of the disease was based on the findings of small bowel histology, the characteristic serum lipidemic profile, and the typical findings of fundoscopy. There were no clinical signs suggesting the presence of endocrine abnormality of any kind. She mentioned menarche at the age of 14. Thereafter she had almost regular menstrual cycles, except of the periods of severe clinical deterioration.

### *Hormonal measurements*

Serum samples were collected in the morning, after overnight fasting and were kept frozen (-70 degrees Celcius) up to the day of examination. Plasma lipids and lipoproteins were determined chromatometrically and nephelometrically, respectively. Concentrations of serum cortisol, A4, urinary free cortisol, dehydroepiandrosterone sulfate (DHEA-S), aldosteron, renin, progesterone, 17-OH-progesterone, sex hormone binding globulin (SHBG), estradiol, luteinizing hormone (LH), falicle stimulating hormone (FSH), adrenocorticotropic hormone (ACTH), 3, 5, Y, Y-tetraiodothyronin (T3), free T3 (FT3), free T4 (FT4), thyroid stimulating hormone (TSH), insulin, proinsulin, insulin-like growth factor (Somatomedine, IG17-1), IGF-I BP3, testosterone, free testosterone, prolactin, parathormone, osteocalcine, 25 (OH) vitamin D3 and 1-25 (OH) 2 vitamin D3 were estimated by radioimmunoassay (EZMA or RIA). Ionized part of serum calcium was measured by a special machine (CORNING), while serum and bone alkaline phosphatase were measured by RIA. The estimation of serum leptin was carried-out by a sensitive enzymatic technique.
The estimation of serum hormones was carried-out on two different time periods: at the time of diagnosis and five years later. However, Synachten test was performed only on the second period of examination. The hormonal profile of the patient was repeated in order to see if the application of the modified diet and the subsequent improvement in the nutritional status could influence serum hormone levels.

### *Dietetic manipulations*

After the establishment of diagnosis, the following diet modifications were introduced: a) Strict restriction of dietary fat (total amount of fat per day not greater than 20g including 10.3 g contained in Clinifeed solution), b) administration of medium-chain fatty acids in the form of NICT oil and c) administration of lipid and water-soluble vitamins provided in the form of Clinifeed solution (Roussel). Additional oral Vitamin E (Ephynal, Roche), in a dose of 600 mg per day (initially it was administered parenterally in a dose of 100 mg intramuscularly per day) was supplemented, d) administration of Clinifeed solution by which an additional 500 Kcal/day was supplied. The Clinifeed solution was administered every day in a total amount of 500 ml. It contains 18.8 g protein, 19.5 g lipids (9.2 g in the form of MCT), 62.5 g carbohydrates and 5 mg of iron. The protein needs of the patients (1.5-2.0 g ideal body weight/24 h) were provided as lean meat and fish. Strict compliance with modified diet was strongly encouraged, especially in regard to fat consumption. After five years, a substantial improvement in most of anthropometric and serum parameters tested was achieved. The levels of serum vitamin E increased from 0, to 0.36 mg% (NV: 0.5-1.5 mg%).
The patient became pregnant two years after the application of the modified diet!! However, an abortion was carried out on the third month, because of the unpredictable course of the gestation.

## Results

### *a) Hormonal and biochemical profile*

Table I shows the patient's lipidemic profile which is a typical one of abetalipoproteinemia. The values of serum lipids remained so in repeated examinations.
Table II shows the patient's genitalial hormonal profile at the time of diagnosis and five years later. Serum estradiol and SHBG were normal, while serum progesterone

Tab. I – SERUM LIPID AND LIPOPROTEIN PROFILE

| *Total lipids (mg%)* | *Cholesterol (mg%)* | *Triglycerides (mg%)* | *HM-C (Mgo%)* | *LDL-C (mg%)* | *VLDL-C (mg%)* | *Apo-A (mg%)* | *Apo-B (mg%)* | *L.a.(a) (mg%)* |
|---|---|---|---|---|---|---|---|---|
| 249 | 44.0 | 4.0 | 42.0 | 1.2 | 0.8 | <23.4 | 80 | 2 |

(Normal values: Total lipids: 500-700, Cholesterol: 270, Triglycerides: 40-140, HDL: 48-75, *LDL:* 108-188 VLDL: 60, Apo-A: 115-190, Apo-B: 70-160, *L.p.:* 30 mg/dl)

Tab. II – GENITALIA HORMONAL PROFILE AT THE TIME OF DIAGNOSIS AND 5 YEARS LATER

| *Hormone* | *Age* | |
|---|---|---|
| | *31* | *36* |
| Testosterone (10-110 ng/ml) | 28.0 | 30.0 |
| Free testosterone (0.1-1.5 ng/ml) | 2.2 | 2.1 |
| Progesterone (0.1-1.4 ng/ml) | 0.1 | 0.1 |
| (21st day of the menstrual cycle) (1.6-21.0 ng/ml) | 0.2 | 0.2 |
| 17 (OH) progesterone (0.1-2.0 ng/ml) | 0.1 | 0.2 |
| (21st day of the menstrual cycle) (1.0-5.4 ng/ml) | 0.2 | 0.2 |
| Estradiole (E2) (10-200 pg/ml) | 96.0 | 86.0 |
| SHW (20-10Onmol/L) | 63.8 | 70.2 |

*(Numbers in parentheses are normal values for our laboratory)*

Tab. III – THYROID HORMONAL PROFILE AT THE TIME OF DIAGNOSIS AND 5 YEARS LATER

| *Hormone* | *Age* | |
|---|---|---|
| | *31* | *36* |
| Thyroxin (T4) (5-15 µg/dl) | 10.0 | 10.4 |
| Free thyroxin (FT4) (0.6-2.0 ng/dl) | 1.2 | 1.1 |
| Trfiodothyronin (T3) (80-200 ng/dl) | 105 | 126 |
| Free Triiodothyronin (FT3) (1.4-5.0 pg/ml) | 3.4 | 2.9 |
| Thyroid Stimulating Hormone (TSH) (0.1-5.5 µIU/ml) | 2.3 | 1.9 |

*(Numbers in parentheses are normal values for our laboratory)*

and 17-OH-progesterone were constantly low. The estimation of serum progesterone and 17-OH-progesterone on the 21st day of the menstrual cycle showed concentrations below the lowest normal limits. Total serum testosterone was normal, while serum free testosterone was elevated.

Table III shows patient's basal serum thyroid hormonal profile. As it can be seen, the thyroid hormonal profile was completely normal in both periods.

Table IV shows the patient's adrenal hormonal profile. As it is obvious serum adrenal hormone levels were normal in both periods.

Table V shows the patient's basal serum parathyroid gland hormonal profile, as well as calcium metabolism at the time of diagnosis and five years later. As it can be seen, serum parathormone levels were normal in both periods of time. The ionized part of serum calcium as well as serum 25 (OH) vitamin D3, were below the lowest normal limits at the initial period. However, on the second test period the level of both vitamins were inside the normal limits. Serum alkaline phosphatase was normal while its bone isoenzyme (ostase) was increased.

Tab. IV – ADRENAL HORMONAL PROFILE AT THE TIME OF DIAGNOSIS AND 5 YEARS LATER

| *Hormone* | *Age* | |
|---|---|---|
| | *31* | *36* |
| Cortisol (5-25 µg/ml) | 15.1 | 14.2 |
| D4 (0.1-3.0 ng/ml) | 1.8 | 1.6 |
| DHEA-S (Sulfure) (35-430 ug/dl) | 70 | 102 |
| Free cortisol (urine) (10-80 ug/24h) | 37.8 | 41.1 |
| Aldosteron (rest) (1-16 ng/dl) | 3.9 | 4.2 |
| Renin (rest) (0.2-2.8 ng/ml/h) | 0.7 | 0.5 |

*(Numbers in parentheses are normal values for our laboratory)*

Tab. V – PARATHYROID GLAND HORMONAL PROFILE AND CALCIUM METABOLISM AT THE TIME OF DIAGNOSIS AND 5 YEARS LATER

| *Parathyroid function* | *Age* | |
|---|---|---|
| | *31* | *36* |
| Parathyroid hormone (intact) (10-65 pg/ml) | 40.6 | 32.0 |
| BGP (Osteocalcine) (2.4-10.0 ng/ml) | 4.2 | 4.4 |
| 25 (OH) vitamin D3 (9.245.2 ng/ml) | 8.6 | 13.6 |
| 1,25 (OH) vitamin D3 (18-62 pg/ml) | 24.0 | 32.0 |
| Alkaline phosphatase (21-98 U/L) | 45.0 | 34.0 |
| Bone alkaline phosphatase (Ostase) (1.8-10.1 Rg/1) | 10.6 | 10.8 |
| Calcium (ionized) (1.12-1.3 mMol/L) | 1.04 | 1.14 |
| Phosphorus (2.53.0 mg/dl) | 3.6 | 4.2 |

*(Numbers in parentheses are normal values)*

Tab. VI – PITUITARY HORMONAL PROFILE AT THE TIME OF DIAGNOSIS AND 5 YEARS LATER

| *Hormone* | *Age* | |
|---|---|---|
| | *31* | *36* |
| ACTH (9-52 pg/ml) | 50.0 | 65.0 |
| Prolactin (movement) (2-16 ng/ml) | 27.5 | 29.3 |
| Prolactin (rest) (2-16 ng/ml) | 21.6 | 24.7 |
| Folicle Stimulating Hormone (FSH) (2.8-18 mIU/ml) | 11.0 | 6.7 |
| Luteinizing Hormone (M) (2.6-2 mIU/ml) | 20.0 | 9.3 |
| Synacthen test for cortisol: Time 0' (NV: 5-25 µg/dl) | 18.0 | |
| Time 30' | | 22.0 |
| Time 60' | | 26.0 |
| Time 120' | | 25.0 |

*(Numbers in parentheses are normal values)*

Tab. VII – SERUM LEPTIN, INSULIN, PROINSULIN, GLUCAGON, IGF4 AND IGF-I BP3 LEVELS OF THE PATIENT AT THE AGE OF 36

| *Hormone* | *Serum levels* |
|---|---|
| Leptin (ng/ml) | 2.4 |
| Proinsuline (<10 pmol/L) | 36.2 |
| Insulin (3-35 gRJ/ml) | 1.9 |
| Glucagon (40-130 pg/ml) | 86.0 |
| Insulin-like growth factor-I (IGF-1) (120-382 ng/ml) | 83.0 |
| IGF-1 BP3 (1.38-4.7 µg/ml) | 1.9 |

*(Numbers in parentheses are normal values)*

Table VI shows the patient's basal pituitary hormonal profile at the time of diagnosis and five years later. FSH, LH and ACTH level were normal, but serum prolactin was increased both in rest and movement. Synachten test was normal.

Table VII shows the levels of leptin, insulin, proinsulin, glucagon IGF-I and IGF-1 BP3 at the age of 36. The levels of serum leptin, IGF-1 and proinsulin were below the lowest normal limits of our laboratory.

### *b) Long-term follow-up*

Up to June 2004 the patient was alive. Her clinical situation is relatively good, although symptoms related to the CNS are quite prominent. Symptoms regressed or failing to progress were those mainly related to nutritional deficiencies and not those related to retinal or central nervous system. Nutritional support and administration of vitamins is continued under close surveillance. The usual hematological and biochemical parameters are almost inside normal limits.

## Discussion`

Abetalipoproteinemia is an inherited disorder of the genesis and secretion of apolipoproteins, transmitted with a single autosomal recessive gene (17). Another type of this

family of genetic disorders is familial hypobetalipoproteinemia, in which both homozygotes and heterozygotes have symptoms identical to abetalipoproteinemia and hypobetalipoproteinemia with selective depletion of B48 apolipoprotein (chylomicron retention disease). A special type of protein, the Microsomal Transfer Protein (MTP), seems to be the key element for the appearance of Abetalipoproteinemia (18). Mutations in MTP which result in an absence of MTP function and defects in of the MTP gene have been shown to cause abetalipoproteinemia, being the predominant cause of hereditary abetalipoproteinemia (19).

So far, few reports concerning the hormonal profile of these patients have been published and thus little information is available. The relevant descriptions are referred only to patients with heterozygous and homozygous hypo-betalipoproteinemia in which no clinically obvious endocrine abnormality was noticed (13-15). On a theoretical basis patients with abetalipoproteinemia might have disturbed synthesis of a number of serum hormones as a result of the abnormal lipid metabolism. This assumption is based on the fact that serum synthesis of adrenal and pituitary hormones requires a source of cholesterol, which can be derived from both local synthesis and uptake of LDL. Based on *in vitro* assessments of the activity of hydromethylglutaryl-CoA reductase in corpus luteum. tissue, as well as on *in vitro* experiments on progesterone synthesis by the human corpus luteum, tissue maintained in organ culture, it bacame clear that LDL serves as a primary source of cholesterole for progesterone biosynthesis and that the rates of *de novo* biosynthesis were inadequate to satisfy the daily needs for progesterone biosynthesis (20, 21). It has also been found that in patients with abetalipoproteinemia an increased synthesis of cholesterol exists, which could be explained on the basis of a compensatory mechanism to maintain cholesterol homeostasis in the face of enhanced fecal losses (15).

### *Genitalia gland function*

The estimation of serum testosterone, estradiol and SHBG in our patient showed normal values. However, serum levels of progesterone and 17-OH-progesterone were below the lowest normal limits and remained so during the whole menstrual cycle. We suggest that the absence of LDL leads to an impairment of progesterone production by the corpus luteum. and probably by the placenta and that this impairment can be found during the whole menstrual cycle. However, this abnormality in the menstrual cycle seems not to play a major pathophysiological role, as no disturbances in the regular rhythm of menstrual cycle were mentioned by the patient. Moreover, our patient became pregnant during the observation period. Pregnancy was interrupted at the third month of gestation for reasons mainly related to the social environment of the patient as well as to the unpredictable course of gestation and the possible influence on the patient general situation on the fetus. We suppose that despite the reduced biosynthesis of progesterone by the placenta, pregnancy can be successfully terminated, although the exogenous administration of progesterone during pregnancy seems to be logical (13). On the other hand, although serum testosterone level was normal, free testosterone level was somewhat higher compared to the upper normal limit of our laboratory. We have no obvious explanation for this observation although the low level of serum albumin could be responsible for this discrepancy.

### *Thyroid function*

It is well known that thyroid hormones bind specifically to apolipoproteins and that additional binding by solubilization in the lipid components of the lipoproteins may also occur (22). The estimated iodothyronine binding in normal plasma to HDL, LDL and VLDL is 3%, 0.2% and 0.03% for T4 and 6%, 0.05% and 0.02% for T3. In patients with abetalipoproteinemia the distribution of iodothyronines reflects the lipoprotein abnormality (22). In our patient the basal thyroid gland function assessed by the measurement of T4, T3, FT3, FT4, and TSH was normal in both periods of time. Moreover, the size of thyroid gland assessed by ultrasonographic examination was also normal. No clinical signs compatible with thyroid gland abnormality of any kind were noticed during the follow-up. It is possible that even the very low concentrations of LDL found in patients with abetalipoproteinemia, are capable to maintain the thyroid function inside the normal limits.

### *Adrenal function*

In this patient, basal production of adrenal corticosteroids assessed by the concentration of serum cortisol, D4 and urine free cortisol, was normal. Illingworth et al suggested (23) that patients with abetalipoproteinemia disclose impairment in adrenal corticosteroid production after stimulation with ACTH, manifested by low levels of serum cortisol and urine free cortisol and this could be of clinical significance in cases of severe surgical or infectious stress, requiring increased production of corticosteroids. In our patient, serum levels of ACTH and Synachten test were normal, supporting the concept that despite the abnormal serum LDL (which serves as an important source of cholesterol for adrenal corticosteroid synthesis), there is no impairment of adrenal production of steroids in the basal state and so no clinical implications are expected to occur. No differences between the two periods of adrenal assessment were noticed. We suggest that the normal plasma steroid levels are due to the

ability of the adrenal tissue to synthesize steroids using cholesterol synthesized *de novo* from two-carbon fragments (acetate). However, the direct regulatory role of serum leptin on adrenal function via its receptors on adrenocortical cells further emphasizes the complexity of the hormonal secretion and regulation on patients with abetalipoproteinemia (24).

### *Parathyroid gland function and calcium metabolism*

So far, there are no data concerning parathyroid function and calcium metabolism in patients with abetalipoproteinemia. The estimation of serum parathormone in our patient revealed normal values in both periods, as well as normal levels of osteocalcine. However, total serum calcium was at the lowest normal level of our laboratory on the first examination probably due to reduced levels of ionizing part of calcium, and returned to normal on the second examination. Despite the normal levels of serum alkaline phosphatase, its bone fraction was increased. This increase represents probably a secondary phenomenon aiming to increase the amount of serum calcium. On the other hand the initially low levels of serum 25-OH vitamin D3 due to fat malabsorption probably contributed further to the abnormal bone metabolism. The levels of this vitamin returned to normal after application of the special diet.

### *Pituitary function*

Serum FSH, LH, and ACTI-I were normal, while prolactin serum levels were increased both during movement and under resting conditions. The normal levels of ACTH, LH and FSH can be easily explained as the target organs can synthesize the relevant hormones. Increased serum prolactin levels during the luteal phase found in our patient was also noticed by others (13). The increased levels of prolactin (which was not accompanied by relevant symptoms) can not be explained as no obvious reason could be identified (idiopathic?).

### *Other hormonal estimations*

The low levels of serum leptin and IG17-1 found in our patient are consistent with the expected ones at least from a theoretical point of view (25, 26). We were not able to find data concerning the levels of these hormones in patients with abetaliproteinemia. It is well established that hyperleptinemia is an essential feature of human obesity and that a strong correlation exists between body fat and leptin levels. The low BMI observed in our patient correlates well with the low serum leptin concentrations. The high proinsulin/insulin rate in our patient was due to the abnormally low serum insulin levels and the abnormally increased serum levels of proinsulin. It has been suggested that high fasting proinsulin/insulin ratios reflect impaired insulin secretion. Moreover, the low level of leptin found in our patient fits well with recent observations suggesting that serum leptin levels are inversely correlated with proinsulin/insulin rate (27).

The levels of IGF-1 were low. However, the levels of IGF Binding Protein-3 were normal. According to recent observations (28), leptin plays a significant role in the secretion of growth hormone due to its effect on hypothalamic growth hormone releasing hormone and somatostatin-producing neurons. Leptin seems to inhibit the activation of hypothalamo-pituitary-adrenal axis (29).

### *Repeated examination*

The application of modified diet, including the administration of Medium-Chain Triglycerides (MCT) in the form of MCT oil (30) despite the fact that many anthropometric and immune parameters improved, did not produce any significant effect on serum hormonal profile although some improvement on serum ionized calcium and serum 25-OH-vitamin D3 was observed.

From the study of the hormonal profile of this patient with abetalipoproteinemia at two different, time periods we can conclude that an over-the-time impairment in the production of progesterone certainly exists probably due to the low levels of serum cholesterol and LDL. The improvement of the nutritional status does not result in improvement in the production of progesterone and 17-0H-progesterone. The slightly abnormal bone metabolism probably has a multi-factorial etiology and must be managed accordingly. The low levels of serum leptin and insulin-like growth factor as well as the increased ratio of proinsulin/insulin, are compatible with the impairment nutritional status of the patient.

**Abstract**

*Aim:* To investigate the pituary, genitalia, adrenal, thyroid, parathyroid and pancreatic endocrine function of a female patient aged 37 with abetalipoproteinemia at the time of diagnosis and 5 years thereafter (after application of a modified diet).

*Subject-Methods:* Serum concentrations of cortisol, A4, ACTH, aldosteron, renin, dehydroepiandrosterone sulfate (DHEA-5), progesterone, 17-OH progesterone, testosterone, SH13G, estradiol, luteinizing hormone, follicle stimulating hormone, T3, T4, TSH, FT3, FT4, parathormone, osteocalcin, prolactin, proinsuline, insulin, glucagon, somatomedin-C (Insulin-like Growth Factor-1, IGF-I), IG171-13P3, 25 (OH) Vitamin D3 and 1-25 (OH) 2 Vitamin D3, were measured by radioimmunoassay. Synactlien test, and 24-hour urine

cortisol, were also estimated. Serum leptin estimation was carried-out using a sensitive enzymatic technique. Ionized part of serum calcium was measured by the use of a special machine (CORNING), while bone alkaline phosphatase was measured by radioimmunoassay.

*Results:* Serum progesterone and 17-0H-progesterone were reduced in both examinations. Estimation of serum progesterone performed on the 21$^{th}$ day of the menstrual cycle revealed again values below the lowest normal limit. Serum prolactin was increased both in rest and during movement. The levels of both, somatomedin-C (IGF-I) and leptin were below the lowest normal limit. Despite normal serum parathormone, serum-ionized calcium and 25-OH vitamin D were low, while serum bone alkaline phosphatase was increased. Serum proinsulin was increased, and serum insulin was low. Serum thyroid hormone, glucagon, parathormone, FSH, LH, ACTH, testosterone, estradiol and SH13G were normal. The hormonal profile of the patient estimated 5 years later did not differ substantially suggesting that the metabolic improvement due to the adoption of the modified diet had not any significant impact on it.

*Conclusion:* Female patients with abetalipoproteinernia have reduced production of progesterone by the corpus luteum and slightly abnormal bone metabolism. The reduced production of progesterone is probably due to the low levels of serum LDL and cholesterol, while reduced serum levels of Leptin and IG17-1 are probably due to the impairment nutritional status. The adoption of a modified diet does not alter the hormonal profile significantly.

Key words: Abetalipoproteinemia, hormonal profile, leptin, Greece, clinical features.

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