Case 1. Uterine fibroma, autoimmune disease – 35 years old/ 1,56m/ 44 kg

SPE – laboratory values

Serum Protein %	Normal Values %	Result %
ALB	**52-68**	**51,6**
α_1	**2-5**	**2,9**
α_2	**6,6- 13,5**	**12,3**
β	**8,5 – 14,5**	**11,8**
γ	**11 - 21**	**21,4**
A/G	**1,2 – 2,23**	**1,06**

TP = 7,64 g/dL (6,6 – 8,7)
ALB = 51,6% ; GL = 48,4%
TCa = 9,1 mg/dL (8,6 – 10,2); Ca^{2+} = 3,81 mg/d/L (3,82 – 4,82)
Other diagnoses:
- Breasts presenting a dense fibro-glandular structure
- Hashimoto Hypothyroidism
- Nephrolithiasis

Code: R15/28 - B10, Apitherapy Medical Center database

Uterine fibroma is one of the most obvious and frequent feminine dysproteinaemias. This type of dysproteinaemia manifests itself through "depositing" the excess fibroproteins (especially collagen) in the uterus. This excess accumulates in the blood due to the deteriorated albumin/globulins (A/G) ratio, combined with a decrease of ALB synthesis in the liver, or with a pathogen increase of one or several globulins (GL) - α_1, α_2, β or γ. ***Uterine fibroma disease is one of the most avoidable – more prophylactic – feminine diseases. Its prophylaxis however, and especially genuine treatment of uterine fibroma will not have the expected effect as long as this disease is not regarded as a dysproteinaemia with an autoimmune characteristic at the quantitative-structural level of TP and SPE.***

We feel under obligation to clarify the statement above, particularly as uterine fibroids prophylaxis is not a common subject in medical literature. However, using the apitherapeutic method proposed by us, we can prove that uterine fibroma prophylaxis is possible.

Many processes that last reasonably extensive periods of time take place before the appearance of the fibroma in a woman's body. These support undertaking some predictive tests and investigations. The most edifying tests are TP, SPE, TCa, Ca^{2+}, and among other investigations, a colour Doppler ultrasound.

Usually, tests show a quantitative TP dysproteinaemia, which increases, in most cases, over 7,50 g/dL (7,67 g/dL in this case). If SPE were a routine test, the results of a woman who is at risk of having a uterine fibroma would show a decrease of ALB towards or under the lower limit of n.v. level (51,6% in this case), combined with an increase of fibroproteins synthesis, emphasized by the increase of the GL level (to 48,4% in this case), resulting in the deterioration of the A/G normal ratio (1,06; n.v being 1,2-2,23) in favour of GL. Among GL, ***an important recorded increase is one of the γ[1] globulin (it reaches 21,4% in this case), a fact which orients us towards the autoimmune[2] character of uterine fibrosis.*** We can also observe – simultaneously with the decrease of ALB synthesis – a decrease in the value of Ca^{2+}, regardless of the TCa value (see results below).

In the absence of homeostasis (ie. the body's potential to self regulate), the quantitative level of TP increases through excessive synthesis of fibroproteins. If no steps are taken to quantitatively and structurally rebalance TP, the body "finds" its own alternative way to eliminate the fibroprotein excess that circulates in the blood. However, the elimination of the fibroproteins can only be done through the blood. But this modality has to be "constructed". Under the condition of an ALB decrease, synthesis of the globulin proteins that enter the structure of the "builder" cells of the vascular endothelium (wall) increases, and the tubulin plays an important role in this process. The uterus undergoes neoangiogenesis (neovascularisation): starting from pre-existing vessels – present at birth, blood neoformation micro-vessels, which were previously

[1] γ globulin (gammaglobulin) comprises the immunoglobulins (serum antibodies). It is part of the globulins (GL) determined through SPE, together with the other globulins (α_1 ,α_2 şi β). According to some criteria, immunoglobulins (antibodies) that are part of the γ globulin were classified into immunoglobulin IgA, IgD, IgE, IgG şi IgM. These immunoglobulins are found in specific values in the human body and are tasked to protect it by acting like antibodies (to insure its immunity). The decrease in γ globulin below the n.v. lower limit indicates the beginning of an autoimmunity state (the quantitative value of some antibodies increases over particular limits transforming them into autoantibodies).

[2] In uterine fibrosis, γ globulin increases, usually towards and especially above the upper limit of n.v. This has given us confidence to ***propose the "registration" of this dysproteinaemia into the autoimmune class*** of diseases manifested by organ or systemic fibrosis. The common characteristic of autoimmune diseases of exogenous or endogenous aetiology is the decrease in serum ALB, decrease in ionized calcium values and the increase of γ globulin. Once uterine fibroma is approached as a dysproteinaemia, this disease becomes fully explainable.

inexistent, start to appear. The purpose of these new vessels is to transport the excess of circulating fibroproteins and to store them in the uterus. Through ultrasound one can see a transformed fibromatous uterus, or accumulations of fibroproteins of different sizes can appear (called fibromatosis, fibroid nodules, fibroma, leiomyoma, fibromyoma).

The synthesis of excess fibroproteins or neovascularisation (neoangiogenesis) only occurs when, as observed through SPE, hypoalbuminemia and hyperglobulinemina are present (see SPE test above). The values of SPE recorded should "lead" the woman to have an ultrasound, which could indicate the existence of a uterine fibroma. If the fibroma is not yet developed, then the test would highlight the "site preparation": the appearance of some blood micro-vessels on the uterus which, starting from the pre-existing vessels, are heading towards the location where the excess fibroproteins are going to be "deposited". Consequently, the appearance of uterine fibrosis is preceded by a decrease of ALB and Ca^{2+} synthesis, as well as the quantitative increase of blood circulating fibroproteins; on a secondary level takes place a local process of neoangiogenesis (neovascularisation).

There is also a hormonal component, apart from the above: a certain increase of estradiol, manifested in a thickened endometrium, heavier menstrual periods that become longer and either slightly painful or not painful at all. The thickened endometrium and heavy menstrual periods are related to the hypervascularization of the endometrium, which is a consequence of a decrease in ALB synthesis, determined by a local hypervascularisation[3]. The breasts do not become tense before menstruation, which is evidence for a normal prolactinemia[4]. An ultrasound will show the breasts developing an increased fibroglandular structure, which would indicate, simultaneous with the appearance of the fibroma, an increase in fibrosation in the breasts as well.

There are also many cases where the appearance of uterine fibroma is followed by hormonal androgenisation, which can take place due to the most diverse causes, the most frequent being the embolization and the administration of estroprogestatives. In such cases, among other symptoms, there will be changes in the flux and duration of menstruation, which becomes painful and in many cases presents blood clots, a sign of a disorganized trilaminar endometrial pattern; the breasts become tense before menstruation, a sign of ante menstrual increase of prolactin (PRL)[5], that triggers an increase in progesterone (PRG), and the aromatase enzyme is reducing its activity at the ovaries. In addition, nodules and ovarian cysts can occur as well. In some cases exterior signs of hormonal androgenisation will occur; sometimes the disease evolves towards endometrioses and infertility. All these changes can occur after the occurrence of uterine fibroma.

It is very edifying - and certainly not insignificant - to see the hormonal androgenised evolution of the daughters whose mothers suffered from uterine fibroma. Clinical studies on this subject could reorient fundamental medical research towards more useful subjects for the therapeutic logics of this type of ***androgenisation with maternal-foetal transmission.*** Reasons for this might include, amongst others, the fact that maternal hyperestrogenemy may influence the decrease in the aromatase level of the daughter, as well as dysfunctions of the adrenal glands, with an increase of plasma cortisolemia and an excess of dehydroepiandrostenedione (DHEA) and 17-hydroxyprogesterone, this being one of the causes of ***Androgenital Syndrome***.

There are many questions waiting for an answer, but this answer cannot be given by a medical research that follows opposite paths: clinical (where the clinical research is quasi-absent) and fundamental. The fundamental research will never be able to create the complexity of the internal environment of the human body in its integrity.

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[3]Uterine endometrial neovascularization is normal each month during the menstrual period of the woman.

[4]Prolactinemia – the level of prolactin hormone (PRL) circulating in the blood.

[5]PRL increase should begin when a woman becomes pregnant. At the same time, the progesterone (PRG) increases and the estradiol begins to decrease. If the PRL increases before menstruation, it can lead to the cancellation of normal menstruation, preventing the action of the aromatase enzyme at the ovaries level. This enzyme transforms PRG into ESTR at the ovaries level, leading to hormonal androgenisation. We believe that estroprogestatives do the same thing at the ovaries level as the abnormally increased PRL (aside from pregnancy): they prevent the normal functioning of the aromatase.

Prophylaxis of uterine fibroids is possible through rebalancing TP, indicated by the SP values which are determined through SPE. Restabilising the normal values of ALB leads to a synchronized increase in Ca^{2+}, as well as to a reduction in the synthesis of fibroproteins GL. Uterine neovascularization is secondary to the excessive increase of fibroproteins in TP structure and does not begin unless these proteins reach levels which impose the "discharge" of their excess. By rebalancing SP, which leads to rebalanced TP, neovascularization becomes unnecessary and will no longer occur. In the same way – we will present clinical proof for this – by rebalancing SP and restabilising the quantitative level of ALB, the micro vessels of neoangiogenesis are either resorbed, or their lumen[6] become so tight that any blood flow is prevented. We claim – and indeed we achieve it through apitherapy – that the only way of prophylaxis and also an efficient treatment of neoangiogenesis is through restoring the normal quantity and structure of A/G ratio, an indicator of the rebalance of SP and TP. If albuminemia and globulinemia are quantitatively and structurally within the physiological limits, this internal environment state will not permit the action of angiogenic factors. If neoangiogenesis has already occurred, through rebalancing the proteinaemia – at SP and TP levels – we obtain the re-activation of antiangiogenic factors that normally exist in the human body, but whose action was stopped by the quantitative-structural dysproteinaemia which in turn enabled the angiogenic factors to occur.

Our theory's axiom is that by restoring TP balance, through rebalancing SP, by restoring the physiological albuminemia, the excess synthesis of fibroproteins, precursor to uterine fibroma and neoangiogenesis is remitted; in the same way, autoantibodies involved in autoimmune disease are negativized; their positivity is proved by the γ GL increase towards and especially above the upper limit of n.v. It is interesting that researchers and producers of antiangiogenic[7] drugs, as well as producers of mAbs (monoclonal antibodies) do not make any reference to SPE, neither to the evolution of ALB and Ca^{2+} levels, nor to the most normal way of remission of autoimmunity: rebalancing TP.

We are eager to discover if there are any published reports of real cases of prophylaxis or of neovascularization remission obtained with the help of antiangiogenic drugs. Until these reports are published, we should address at least one question to the biologists, biochemists and producers of these "revolutionary" drugs. The neovascularization is secondary to the accumulation of excess fibroproteins in the blood. The task of the newly formed blood vessels is to provide a means to eliminate this fibroprotein excess. Our question is the following: if the said drugs block the neovascularization, what will happen to the excess of fibrosed globulins accumulated in the blood? Especially when we consider the fact that antiangiogenics cannot and should not block the continuation of fibroproteins synthesis. What will be the effects of their accumulation in the blood, if the antiangiogenics really block the neovascularization? We could expand excessively our "dissertation" on this topic, if we decided to go further into it.

In our theory, as well as in clinical apitherapeutic practice, ***we have included uterine fibroma among the autoimmune diseases with fibrosing effects.*** And our theory is substantiated by the following:

- uterine fibroma appears in similar conditions of quantitative and structural dysproteinaemia of TP, similar to other autoimmune diseases marked by the quantitative increase of positive acute-phase proteins
- SPE signals a decrease of ALB under 60% of total SP (usually under 53%), a fact that leads us to suspect a pathological increase of blood circulating fibroproteins, in such cases an ultrasound of the uterus is necessary

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[6]Lumen – the opening, inside space of a tubular structure of an anatomic channel, whatever it may be.

[7] Molecular biology makes reference to a series of angiogenic factors – that stimulate angiogenesis -, as well as to antiangiogenic factors – that oppose angiogenesis. It would be unproductive to list them here. Anyway, they have no place in the practical approach of uterine fibrosis in medical clinics. The clinics do ***not undertake any prophylaxis of uterine fibrosis***. This would be possible through prophylaxis of TP imbalance, and if the imbalance has already occurred, by re-establishing their balance. Instead of prophylaxis, drugs that should have antiangiogenic effects are being produced. Antiangiogenic drugs have almost the same illogical approach as the use of the "revolutionary" mAbs (HDB: monoclonal antibody) in autoimmune diseases. However, autoimmune diseases, as well as uterine fibroma, begin only under the conditions of a quantitative and/or structural hypoabluminemia, and their long-lasting remission can only be achieved through restoring the physiological liver synthesis of ALB and normal calcium metabolism. As we concluded in our doctoral thesis, it is very difficult, if not impossible to report an autoimmune disease's complete remission without rebalancing SP, as a means to rebalance TP. Drugs that have antiangiogenic effects, whether or not they are real, and mAbs do not restore normal values of ALB, and therefore do not eliminate the cause.

- as in any autoimmune disease, γ globulin level is increasing towards or above the upper limit of n.v (see SPE above), and this growth is significant in the appearance of autoantibodies, as in the case of autoimmune diseases;
- as in autoimmune diseases, whatever the TCa level might be, Ca^{2+} level decreases towards and even below the lower limit of n.v.;
- a certain number of other autoimmune diseases – especially Hashimoto thyroiditis – occur frequently in women who have had uterine fibroma;
- an ultrasound scan will enable us to observe: absence of the neovascularization debut, its debut through the appearance of vascular sprouts (these usually appear when ALB decreases below the value of 53-55% of SP), the progressive increase of neoformation micro-vessels or the end of this process with the debut of fibrosis, or fibroid nodules already formed.

As a method of prophylaxis, an increase of liver synthesis of ALB – as a negative acute-phase protein, is the most efficient method for preventing both increased synthesis of fibroproteins and neoangiogenesis. ALB in normal values, of over 60% of total SP is the most valuable factor of antiangiogenesis: it is the best inhibitor, without having to use any antiangiogenic drug!

The current clinical approach in the field of uterine fibroma can be:

- *embolization (blockage) of the blood vessels* to stop the flow of the fibroproteins towards the fibroma; this method, although sometimes successful, does not re-establish the TP balance, and therefore the cause remains active;
- *surgical resection of the fibromas,* which is also done with the intention of protecting the reproductive potential of the woman; this method does not re-establish the physiological proteinaemia either, and recurrences are frequent, accompanied or not by other unwanted side effects;
- *total or partial hysterectomy,* surgically eliminates the "deposit" of excess fibroproteins, but does not re-establish the physiological proteinaemia: the cause remains.

Other methods of medical intervention for treatment of uterine fibroma are under research at present, one of them being to "bombard" it with focused ultrasound. However, although uterine fibroma is one of the most obvious feminine dysproteinaemia, none of these methods takes into consideration the "disorder" that occurs quantitatively and structurally at TP level, or at PS and ionized calcium level.

We will discuss uterine fibroma in more detail later in this paper and we will also present a large number of clinical cases which ***will comprehensively corroborate our proposal to add this feminine disease into the category of autoimmune diseases manifested by organ and systemic fibrosis.*** Also, we will discuss again the prospect of uterine fibrosis and neoangiogenesis prophylaxis.

There is one other reason that we started our medical study on dysproteinaemia with this disease. The balance or imbalance of maternal proteinaemia has a determining influence on the health of children. The real cause of many of these diseases that are considered to be idiopathic (cryptogenic, unknown) in medical literature will be known if they are studied in the light of maternal dysproteinaemias. A significant number of children's diseases, with a maternal-foetal debut or occurring at birth, usually only occur in old aged people. Considered to have unknown causes, they occur because of the biochemical resemblance of maternal blood – "the source" of all the substances that enable the foetus to grow – to that of old people's blood. The difference is that the "age" dysproteinaemia is physiological, ALB synthesis being in a permanent and normal regress, while the maternal dysproteinaemia is an imbalance precursor to many diseases, including many diseases that are transmitted from mother to foetus.

Rather atypically compared to other clinical studies, approaching uterine fibroma as a dysproteinaemia, as well as the apitherapeutic intervention in this disease are concepts that we have put forward. The prevention and the treatment of uterine fibroma are very important not only for the female patient and mother, but also for the health of their descendants. Prophylaxis of an astonishingly large number of diseases of the descendants – congenital or with a congenitally acquired predisposition – depends on the prophylaxis of the maternal imbalanced proteinaemia. However, in order to be able to start the prophylaxis it is necessary to turn TP, SPE and Ca^{2+} into routine medical tests. Until this is accepted, ensure that you request these tests when you have any other tests done by a laboratory.