

# RESTLESS LEGS SYNDROME ASSOCIATED WITH CARDIAC FAILURE AND AGGRAVATED AFTER VALVULAR REPLACEMENT

## Vesper's curse?

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The restless legs syndrome (RLS) is a neurological disorder characterized by symptoms of discomfort (usually paresthesias) in the limbs, predominating in the afternoon, present mainly at rest and alleviated by movement. The symptoms usually appear in the late afternoon or at night, which may bring on a significant increase in sleep latency and contribute to poor sleep quality<sup>1</sup>. Since the prevalence of RLS increases with age<sup>2</sup>, heterogeneous conditions are likely to be identified in association with other illnesses typical of advanced age, making diagnoses more complex, and indicating the importance of studying these secondary forms, and their possible physiopathological mechanisms.

We report a case of RLS associated to important abnormalities of the cardiac function in an elderly patient, who underwent several cardiac surgical interventions, and discuss the possible implications of this cardiac dysfunction in the etiology and maintenance of the motor symptoms. This case is reported after approval of our Institution and informed patient's consent.

### CASE

A 73-year-old female, with congestive cardiac failure and severe mitral valvulopathy presented a history of chronic insomnia. She had been submitted to three valve replacement surgeries over a period of 30 years. After the last surgery (January 2007) she developed a temporary renal failure. She also reported diabetes mellitus, hypothyroidism, osteoporosis and, in childhood, rheumatic fever. She had been prescribed opioids during the immediate post-operative period. The patient came to the visit on 15 February 2007 taking several medications including pramipexole (used for less than thirty days), clonaze-

pam, codein+paracetamol, diazepam and iron quelate-glicinate (prescribed less than 2 months prior). She had also taken dolantin one week before the visit for "pains in the legs".

One year before the patient began to report a feeling of "impatience", "agony" and "restlessness" in her legs, being forced to move around to provide some relief. These symptoms were predominantly nocturnal, and hampered the onset of sleep. She reported similar symptoms in her upper limbs, though less intense. Nearly one month before her neurological check-up, and immediately after her last cardiac surgery, the patient noticed a significant worsening of lower limb discomfort.

The physical examination revealed a depressed mood with no important neurological alterations.

A polysomnogram taken some days after the first visit observed: increase in sleep latency (100 minutes), superficial sleep (stages 1+2=84%) with low efficiency (37%) rates, a percentual decrease in REM sleep (0.5%), and a micro arousal rate of six per hour. Eleven respiratory events per hour of sleep (ranging from apnea to hypopnea) were noticed. Oxyhemoglobin saturation varied between 90% and 78% during the night. Thirteen periodic limb movements were detected per hour of sleep.

An analysis of iron metabolism revealed serum ferritin levels of 182 ng/mL (normal 10-280 ng/mL).

In the weeks following the first visit the patient's condition deteriorated, in spite of the re-adjustment of pramipexole and introduction of trazodone 100 mg at night. She reported discomfort throughout her body needing to move around during most of the night, thus not being able to sleep. At that occasion, oxycodone 10 mg and subsequently 20 mg was prescribed for the evening. After that, improvements were noticed in both the sensitive-motor symptoms and sleep quality.

Her most recent echocardiogram (Jan 3, 2008) revealed an

### SÍNDROME DAS PERNAS INQUIETAS ASSOCIADA A INSUFICIÊNCIA CARDÍACA E AGRAVADA APÓS TROCA VALVULAR: MALDIÇÃO DE VÉSPER?

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ejection fraction of 47%, a slight increase in the left atrium, a moderate increase in the right-side cavities, a small systolic deficit of the left and right ventricles, an important tricuspid insufficiency and pulmonary arterial hypertension. A normofunctioning prosthetic biologic mitral valve was observed.

At present the patient remains neurologically stable, although she abandoned the treatment with dopaminergic agonist keeping a daily use of oxycodone 20 mg at night.

## DISCUSSION

The pathophysiology of RLS has yet to be fully elucidated. Besides the loss of inhibition of subcortical movement pattern generators<sup>3</sup>, there probably exists a vesperal increase in the excitability of the spinal motoneurons, reinforcing the final portion of the spinal reflex<sup>4</sup>. The literature has been interested in the prevalence of RLS under special circumstances, such as during renal insufficiency and pregnancy<sup>1,3,5</sup>. More recently, however, special consideration has been given to post-operative patients, especially those who have undergone major thoracic surgery<sup>6,7</sup>.

Cortese et al.<sup>7</sup> described a case of pediatric RLS whose symptoms began after heart surgery to correct a slight atrial malformation. The patient did not report any prior complaint suggesting RLS, although many cases existed in the family. The symptoms of RLS persisted after surgery. This is a curious observation, especially considering that Högl et al.<sup>8</sup> have described only temporary RLS symptoms in 8.7% of a series of 161 patients submitted to raquianesthesia.

The presence of RLS after major thoracic surgery (cardiac or pulmonary) was also studied by other researchers. The available data suggest a prevalence rate between 20%<sup>9</sup> and 47.6%<sup>6</sup>, with possible higher risk among females and in the presence of thyroid disorders<sup>6</sup>.

However, it seems that most of the few existing studies were cross-sectional and did not conduct causal analyses nor tried to determine the prior existence of RLS in a specific population. Such data would be most interesting to obtain as some studies have indicated that, in certain situations, heart or kidney transplants may have an important and positive influence on the clinical course of RLS symptoms<sup>10,11</sup>.

In the patient described in this study, several risk factors associated with the development of RLS were present, namely diabetes mellitus, hypothyroidism, as well as an episode of post-operative renal failure. The patient was also a female and elderly.

The reasons for the appearance or aggravation of RLS symptoms in patients who have undergone heart surgery are not clear. Cerebral iron deficiency secondary to the inevitable blood loss during this type of surgical proce-

sure, or immediate post-operative metabolic alterations (hypocalcemia, hypomagnesemia) may also contribute<sup>6,7</sup>. Prolonged immobilization and sleep deprivation may be pointed out as additional aggravating factors<sup>6-8</sup>. The patient in question presented normal serum ferritin levels. Nevertheless, as is known, this condition may coexist with deficient brain levels, which are ultimately responsible for the sensitive-motor disorder<sup>12</sup>. On the other hand, we cannot formally dismiss the influence of an unfavorable hemodynamic condition that implicitly accompanies patients requiring this type of surgery.

It is known that the reduction of cardiopulmonary complacency in certain situations may be responsible for pain and paresthesias in the lower limbs during the afternoon, sometimes associated with cramps and fasciculations, which is known as "Vesper's curse"<sup>13</sup>. From a practical perspective, an increase in the right atrium filling pressure secondary to a state of chronic heart failure causes a delay in venous circulation that may lead to an increase in the pressure and enlargement of the lumbar veins with a relative narrowing of the spinal canal and reduced oxygenation<sup>13</sup>. It is possible to imagine that, in this condition, there may exist an increase in afferent sensorial stimuli which, associated to the spinal hyperexcitability present in patients with RLS, may act as an important generating factor for the motor symptoms.

"Vesper's curse" has been considered an uncommon occurrence<sup>1</sup>. However, a more detailed analysis of the literature demonstrates that this condition has already been described in several situations, including those associated with spondylothetic alterations or lumbar spondylolisthesis<sup>13</sup>.

Hanly et al. reported a case of a patient with congestive heart failure, chronic insomnia and an important periodic limb movements (PLM) syndrome, whose condition improved dramatically three months after heart transplantation<sup>10</sup>. The authors, even if they did not explicitly refer to "Vesper's curse", considered that a low cardiac output could be in part responsible for the presence of PLM and stated that the correction of the ventricular dysfunction contributed to the overall improvement of the sleep disruption.

The patient described in this paper presented a highly unfavorable cardiac and hemodynamic condition, probably secondary to a chronic rheumatic valvular cardiopathy. In spite of the three prior valvular replacements, a recent echocardiographic evaluation demonstrated significant alterations represented by a low ejection fraction (47%), signs of hypertrophy in the right chambers and pulmonary hypertension. It seems possible that the pathophysiological process, which goes by the inauspicious

name of "Vesper's curse", has fully developed, and contributed significantly towards the progressive aggravation of the symptoms of RLS, in spite of the many attempts to surgically correct the valvulopathy.

Furthermore, a recent study of patients with myocardial pathology using imaging, electromyographic and evoked potential techniques demonstrated the existence of a significant link between pulmonary hypertension and the presence of symptomatic lumbar spine stenosis during the afternoon<sup>14</sup>.

On the other hand, the appearance of RLS symptoms after major thoracic surgery may be relatively delayed, which certainly hampers the precise determining of its prevalence. This is generally attributed to the early use of opiate analgesics to control post-operative pain<sup>7,8</sup>, as was the case for this patient.

In conclusion, the case reported here and the review of the pertinent literature suggest that the so-called "Vesper's curse" may not be so uncommon and may represent a significant cause of secondary RLS or even contribute towards its aggravation in susceptible patients with associated cardiovascular disease. Cardiac surgery *per se* appears to be a causative factor of only minor importance to RLS. Contrariwise, it may contribute positively to the resolution of motor symptoms through the improvement of cardiac function and hemodynamic recovery.

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