THESES

THE STUDY OF CENTRAL NERVOUS SYSTEM INVOLVEMENT IN MITHOCHONDRIAL DISORDERS WITH MITOCHONDRIAL DNA MUTATION. (ABSTRACT)*. **THESIS. SÃO PAULO, 2001.**

*SUELY KAZUE NAGAHASHI MARIE***

Mitochondrial disorders are a heterogeneous group of diseases characterized by the dysfunction of the oxidative phosphorilation. As the protein complexes of the respiratory chain are coded by both nuclear and mitochondrial genomes, there are additional difficulties on the clinical and diagnostic approaches to those disorders.

The RRF detected on muscle biopsy, a hallmark of mitochondrial proliferation, is not always present on those conditions, neither is the increase of lactic acid level.

Since the first description of pathogenic mutation of mitochondrial DNA (mtDNA), in 1988, a molecular criteria has been used for the classification of mitochondriopathies.

Among 377 patients with clinical diagnosis of mitochondrial disease and patients with maternal inheritance of diabetes mellitus, and patients with maternal risk factors of dementia, followed-up between the period of 1991 to 2001, by our group, 145 met the clinical criteria for MELAS (40cases), MERRF (27 cases), Leigh Syndrome (LS) (32 cases), Kearns-Sayre Syndrome (KSS) (14 cases), and Chronic Progressive External Ophthalmoplegia (CPEO) (32 cases).

Measurements of lactic acid level, muscle biopsy, and neuroimaging were performed on the majority of the cases. Molecular analysis were done on all patients looking for 8 point mutations of mtDNA in MELAS, 3 in MERRF, 6 in LS, 1 in KSS/CPEO, and mtDNA rearrangements on KSS/CPEO.

A3243G point mutation of mtDNA was detected in 18 cases with MELAS, including 10 asymptomatic proband's family members.

A8344G mutation was observed in 5 cases with MERRF; T8993G and T8993C in two cases with LS; 14 different mtDNA deletions in KSS and 11 deletions in CPEO, including 3 multiple deletions.

Phenotypic variability was observed in all 5 groups, with overlap of MELAS, MERRF and LS in one patients, and MELAS and LS in another.

An autopsy study of MELAS case showed an universal distribution of A3243G mutation on all tissues studied. The neuropathological findings showed a diffuse degeneration of cerebral cortex with neovascularization, a similar picture observed on LS. Surprisingly the neurons were apparently well preserved even when surrounded by degeneration.

Atrophy and deep grey matter lesion were the most frequent neuroimaging findings, particularly in KSS and LS, when compared to MELAS and MERRF.

The characteristic distribution of lesion on the tegmen of brain stem was observed in KSS and LS, which is similar to the presentation of Wilson's disease. Interestingly, those 3 diseases share a common alteration: mutation in gene coing for the complex V of the respiratory chain.

Although the central nervous system is diffusely lesioned on mitochondriopathies, as show the most sensitive diagnostic methods as functional imaging, and immunohistochemical methods, the order, the degree, and the velocity of those alterations seen to present some differences between the groups, as observed in our cases.

A careful analysis concerning those parameters could reveal new details for better understanding of the pathogenesis of the mitochondriopathies.

KEY WORDS: mitochondrial disorders, mitochondrial DNA, encephalopaty, molecular biology, neuroimaging.

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PITUITARY ADENOMAS: CLINICAL, SURGICAL, IMMUNOHISTOCHEMICAL ASPECTS, INVASIVE AND PROLIFERATIVE CELLULAR NUCLEAR ANTIGEN (PCNA) RELATIONSHIP (ABSTRACT).*. **THESIS. SÃO PAULO, 2000.**

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The author evaluated clinically, radiologically and surgically a series of 76 pituitary adenomas. All cases were assessed immunohistochemically and in 49 patients the PCNA monoclonal antibody was measured.

The most frequent types found were the bihormonal adenomas, followed by prolactinomas and non secreting adenomas. The bihormonal adenomas, non secreting adenonas and the sub unit alpha producing adenomas

were proportionally more invase as determined by radiological criteria (CT scan or MRI).

In 59 patients a transphenoidal approach was used, six cases were operated on transcranially and in 11 patients a combination of both approaches was used. Total resection was achieved in 32 cases, most of which were microadenomas; in 15 cases the resection was subtotal and partial in 29 cases.

Diabetes insipidus was the most frequent endocrine complication.

It was observed that secreting adenomas tend to be associated with an increased PCNA and invasive adenomas correlated with PCNA 3 and 4.

An improvement in vision was observed in 85% of macroadenomas seen after a total, subtotal or partial resection.

KEY WORDS: pituritary gland, transphenoidal surgery, adenoma, immunohistochemistry, PCNA.

*Adenomas hipofisários: relação entre os aspectos clínicos, cirúrgicos, imuno-histoquímicos,invasividade e índice proliferativo tumoral (PCNA) (Resumo). Tese de Livre Docência. Universidade Federal de São Paulo – Escola Paulista de Medicina (Área: Neurocirurgia).

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BIOMOLECULAR STUDY OF SEROINDETERMINATE INDIVIDUALS FOR THE RETROVIRUS HTLV-I/II (ABSTRACT)*. **THESIS. FORTALEZA, 2001.**

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The HTLV-I/II belongs to the Retroviridae family and Oncovirinae subfamily. Its genetic structure is similar to that of other mammalian retroviruses, with gag, pol, env and tax/rex regions. The gag region codes for p19, p24 and p15 proteins; the pol region codes for the reverse transcriptase, RNAse and integrase; the env region codes for the glycoproteins gp21 and gp46; and the pX region codes for the regulatory proteins tax (p40) and rex (p27).

The HTLV-I/II is endemic in Central and West Africa, Caribbean, South America, Japan and Melanesia. In Brazil, its prevalence is of 0.46%. The molecular epidemiology shows that the HTLV-I is divided into the Ia (cosmopolitan), Ib (Central Africa) and Ic (Melanesia) subtypes, and HTLV-II into the IIa, IIb, IIc and IId subtypes. This retrovirus is transmitted vertically (mother-to-child) and horizontally (sexual contact, blood transfusion and parenteral drugs use). The Tropical Spastic Paraparesis / HTLV-I-associated Myelopathy (TSP/HAM) and Adult T-cell Leukemia/Lymphoma (ATL) are their main associated pathologies.

The laboratorial diagnosis of HTLV is done with screening (ELISA and particle agglutination), confirmatory (Western blot, IFA, RIPA, and more recently INNO-LIA) and molecular (PCR, NASBA and bDNA) tests.

Serological tests for HTLV infection are mandatory in some countries since 1986, and in Brazil since 1993. The results from blood banks have shown negative, positive and indeterminate results.

Since the definition of the seroindeterminate condition is important for blood banks and for the patient's families, we intended to delineate a diagnostic, demographic and co-infection and risk factors association pictures of this condition as well as to analyze Western blot protein patterns and isolated proteins with possible predictive meaning.

For this, a preliminary analysis of prevalence of the seroindeterminate and ELISA reactive individuals in the general population of blood donors from the Hematology and Hemotherapy Center (HEMOCE) of Fortaleza City between 1997 and 2000 was done. Subsequently, a sample of 191 ELISA reactive individuals (118 WB seroindeterminates and 73 WB seropositives) from HEMOCE's HTLV Unit was analyzed, with their previous ethical consent. This sample was diagnostically analyzed with ELISA, particle agglutination, Western blot, INNO-LIA and PCR. For PCR, the tax/rex region was amplified.

The results showed that the prevalence of seroindeterminate individuals in the general population of blood donors was of 1.64‰ (0.16%), and the prevalence of the seropositives for HTLV-I/II was of 1.36‰ (0.13%). On the other hand, the prevalence of seroindeterminate individuals was of 21.91% in relation to the ELISA reactive population.

The results of our sample showed that, diagnostically, the PCR evidenced infection in 41 seroindeterminate individuals studied, where 22.2% were positive and 77.8% were negative for HTLV-I/II. Moreover, the comparative analysis of PCR and INNO-LIA showed high concordance of results in both tests. The demographic analysis showed a trend of predominance of males among the WB seroindeterminate and PCR negative individuals as well as a trend of predominance of females among the HTLV-I/II seropositive individuals. In addition, mulattos predominate in both groups. As to age, seroindeterminate individuals are younger than the seropositive ones.

The analysis of distribution of the seroindeterminate and HTLV-I/II seropositives individuals as to the association with Co-Infections showed a higher prevalence of hepatitis B and C for seropositive individuals, and a non-association with HIV, syphilis and Chagas disease. The analysis of association with Risk Factors showed a high percentage of breast feeding similar for both groups, and a high percentage of blood transfusion and sexually-transmitted dis-

eases (syphilis) for HTLV-I/II seropositive individuals.

The analysis of the WB protein patterns and isolated proteins showed that among the WB seroindeterminates the most frequent patterns were p24, GD21 (7.6%) and p19 + gp21 (or gp46) + one or more of the p26, p28, p32, p36, p53 proteins (25.5%), and the isolated p24 protein (55.0%). As to the seroindeterminate PCR negative individuals, the most frequent patterns were p28, p53, GD21 (9.4%) and p19 + gp21 (or gp46) + one or more of the p26, p28, p32, p36, p53 proteins (31.2%), and the isolated gp21 protein (50.0%), p19 (46.9%) and p28 (43.8%) proteins. As to the seroindeterminate PCR positive individuals, the most frequent patterns were p24, GD21 (50.0%) and p19 + p24 + gp21 (or gp46) + one or more of the p26, p28, p32, p36, p53 proteins (77.8%), and the isolated p24 protein (100%).

In conclusion, the study of our sample allowed us to show (1) a high prevalence of seroindeterminates in the population of ELISA HTLV-I/II reactive individuals from HEMOCE, (2) the efficacy of PCR as a diagnostic method for seroindeterminate definition, and INNO-LIA as an optional test, (3) a demographic profile of the seroindeterminate individuals, and (4) the identification of the WB protein patterns and isolated proteins which could be eventual candidates for predictive markers for HTLV-I/II infection positivity or negativity.

KEY WORDS: polymerase chain reaction, Western blotting, Retroviridae, HTLV-I/II, seroindeterminate.

*Estudo biomolecular de indivíduos soroindeterminados para o retrovírus HTLV-I/II (Resumo). Tese de Doutorado, Universidade Federal do Ceará (Área: Neurovirologia). Orientador: Carlos Maurício de Castro Costa.

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CONTRIBUTION OF SKIN IMMUNOHISTOCHEMISTRY IN THE EVALUATION OF NERVE FIBERS IN DIABETES MELLITUS TYPE 2 (ABSTRACT)*.**THESIS. CAMPINAS, 2001.**

*SOLANGE GARCIA GARIBALDI***

Neuropathy is a common complication of diabetes mellitus type 2 (DM-2). Variability in clinical expression of diabetic neuropathy is due to the selective or concomitant involvement of unmyelinated, thin myelinated or thick myelinated nerve fibers. Myelinated fibers may be well assessed by electroneuromyography, whereas evaluation of unmyelinated nerve fibers is still a challenge.

The aims of this study were to evaluate: 1. the usefulness of skin immunohistochemistry to protein gene product 9.5 (PGP 9.5) in DM-2 neuropathy; 2. whether the number of immunoreactive epidermal nerve fibers (IRENFs) to PGP 9.5 differ significantly between subgroups of patients with DM-2, initially examined by clinic and electrophysiological methods; 3. the pattern and frequency of nerve fiber involvement in diabetic neuropathy.

Patients and controls agreed to participate in the research by written informed consent, after UNICAMP Bioethical Council approval.

Forty-nine patients (20 male and 29 female) with DM-2, according to American Diabetes Association, 1997, and 18 healthy subjects as controls (4 male and 14 female) were included. The mean age was 56.69 ± 6.44 for patients and 54.33 ± 7.48 years for controls. Patients were classified into four groups according to clinical scores for neuropathy, routine nerve conduction velocities (NCV) and sympathetic skin response (present, normal; absent after four stimuli, abnormal). Punch skin biopsies of 3 mm in diameter were obtained from the distal part of the right leg, 10 cm proximal to the external malleolus, under local anesthesia, in patients and controls. They were processed using rabbit policlonal antibody to PGP 9.5 and anti-rabbit IgG conjugated with Rhodamine. Immunofluorescence pattern and morphology of nerve fibers were analyzed in a confocal microscope. The linear density of fibers, defined as the number of IRENFs per millimeter of epidermal length, was used for measurements. Statistical analyses were performed using data of age, sex, height, weight, duration of DM-2, duration of neuropathic symptoms, score of symptoms and signs, NCV, sympathetic skin response, level of glycohemoglobin in tables of frequency, measurement of position and dispersion. Fischer, Mann-Whitney and Kruskal-Wallis tests were used with significance level of 5 %.

DM-2 patients were classified as Group 1 (n = 15), absence of neuropathy. Group 2 (n = 8), neuropathy without symptoms. Group 3 (n = 8), symptomatic neuropathy with normal NCV. Group 4 (n=18), symptomatic neuropathy with abnormal NCV.

Clinical symptoms were present in 27 (55.1%) patients, clinical signs were abnormal in 38 (77,6%), NCV were altered in 26 (53.1%), foot sympathetic skin response was negative in 14 (28.5%) DM-2 patients.

The IRENFs densities were 1.40 ± 0.97 in DM-2 patients and 7.04 ± 2.46 in controls. The densities of IRENFs in each group of DM-2 patients were: Group 1 = 2.39 ± 0.53; Group 2 = 1.51 ± 0.49; Group 3 = 1.36 ± 0.41; Group 4 = 0.54 ± 0.79. The densities of IRENFs fibers were significantly (p = 0.001) reduced in patients from Groups 3 and 4, when compared to those of Group 1.

These results suggest that measurement of IRENFs to PGP 9.5 by linear densities allows early detection of the involvement of unmyelinated (C nociceptive) and small myelinated (Ad) nerve fibers in patients with DM-2, in-

cluding those patients without clinical symptoms. A significant distinction between degrees of involvement of small fibers into Groups 3 and 4 in relation to Groups 1 and 2 was possible.

Skin biopsy detected abnormalities of unmyelinated and small myelinated fibers in all DM-2 patients in Groups 1 through 4. Twenty-six (53.06%) patients had large myelinated fiber dysfunction by clinical and neurophysiologycal assessment.

This study indicates that two patterns of involvement of peripheral nerve fibers are found in patients with DM-2: dysfunction of both small and large nerve fibers or selective abnormalities of unmyelinated nerve fibers leading to small fiber neuropathy.

KEY WORDS: skin biopsy, PGP 9.5 immunohistochemistry, diabetic neuropathy, small fiber neuropathy.

* Contribuição da imuno-histoquímica cutânea na avaliação das fibras nervosas no diabete melito tipo 2 (Resumo). Tese de Doutorado, Universidade Estadual de Campinas – UNICAMP (Área: Neurociências - Neurologia) Orientadora: Anamarli Nucci. Co-orientadora: Maria Júlia Marques.

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REPORT ON THE RELATIONSHIP AMONG INSOMNIA, ADAPTIVE BALANCE AND ALPHA FUNCTION (ABSTRACT)*. **THESIS. SÃO PAULO, 2001.**

*SUELI REGINA GOTTOCHILICH ROSSINI***

Patients suffering from chronic insomnia had their adaptive efficiency evaluated by R. Simon's Operationalised Adaptive Diagnostic Scale (EDAO). Major sleep disorders and their effects on patients' quality of life were surveyed by Giglio's Sleep Questionnaire. The dynamics of mind functioning of chronic insomniacs – unrelated to any other organic condition – was assessed by the Thematic Apperception Test (TAT), obeying W.R. Bion's theoretical presupposition on Alpha Function Theory.

Results made know that:1) chronic insomnia is associated to serious damage to adaptive efficiency, with Severe Inefficient Adaptation prevailing in most patients; 2) chronic insomnia associated to organic conditions is related to diagnoses of more serious adaptive imperilment.

Patients present difficulties in all three stages of sleeping, the highest intensity resting on conducing initial sleep; besides day-sleepiness other consequences of insomnia ensue and resorting to medicines is common practice. With regard to mind functioning, chronic insomniacs reveal low tolerance to frustration and psychic pain, intolerance to doubt and novelty, which takes them to a mental condition of imperilment of Alpha Function and, consequently, to the impossibility of falling asleep and waking up. In cases of better adaptive configuration, patients in the control-group displayed adequate functioning of Alpha Function, meanwhile in cases of higher imperilment Alpha Function suffers and parasitic relationships prevail, with deepening of projective identification, the same applying to groups of insomniacs in general. The damage of Alpha Function is not restricted to the condition of insomnia, occurring with patients of the control-group as well.

What determines the possibility of sleeping or keeping awake are the instinctive forces. With insomniacs life instinct drives them to go on seeking a solution a new configuration through insomnia; while patients who managed to sleep seem to have given up trying, resigning to the inevitable and seemingly intensifying the death instinct.

KEY WORDS: sleep disorders, insomnia, Operational Adaptive Diagnostic Scale (EDAO), psychological evaluation, Thematic Apperception Test (TAT), questionnaire.

* Estudo da relação entre insônia, equilíbrio adaptativo e Função Alfa. Tese de Doutorado, Instituto de Psicologia da Universidade de São Paulo (Área: Psicologia Clínica). Orientador: Ryad Simon.

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CLINICAL AND LABORATORIAL ASPECTS OF ASEPTIC MENINGITIS ASSOCIATED WITH MMR (MEASLES-MUMPS-RUBELLA) VACCINE AT A REFERRAL HOSPITAL IN THE STATE OF BAHIA (ABSTRACT)*. **THESIS. SALVADOR, 2001.**

*RITA LUCENA***

Meningitis associated to vaccination has not been a matter of discussion in Brazil. In 1997, after mass vaccination campaign against measles, mumps and rubella (MMR), an increased number of hospital admission due to aseptic meningitis was verified in some Brazilian States. In the Couto Maia Hospital, reference to parasitic and infectious diseases in the State of Bahia, this fact was also observed and permitted the analysis of an outbreak of aseptic meningitis associated to MMR.

The aim of this issue was to establish a risk analysis of

post-vaccinal aseptic meningitis in the city of Salvador and to determine laboratorial, clinic and demographic characteristics of aseptic meningitis associated to MMR and to compare them with cases of aseptic meningitis in children.

Between March and December 1997, we followed all the children admitted in the Couto Maia Hospital, aged between 1 and 12 years, with the diagnosis of aseptic meningitis. At the moment of admission, after cerebral spinal fluid tap and diagnostic of meningitis, a questionnaire was applied in order to obtain clinic, demographic, and laboratorial information. At this moment and every day on neurological examination was performed until discharge. The cases were divided in two groups. In group I, children with history of MMR vaccination between 10 and 35 days before symptoms; in group II, cases of aseptic meningitis not related to MMR vaccination. We performed a coorte and a case series analysis to estimate the incidence and relative risk. Data were analysed with the aid of the SPSS package. Associations with $p<0.05$ were considered significant.

Our results showed that: (1)The estimated risk of post-vaccinal meningitis was 1 to 14000 doses. (2)There was increased frequency of nuchal rigidity and CSF cellularity in children with meningitis associated to vaccine. (3) Greater number of enkephalic problems was verified in the group of meningitis not-associated to vaccination.

In conclusion, we verified an increased risk of aseptic meningitis in children who received MMR vaccine in some Brazilian cities. Post-vaccinal aseptic meningitis needs a special attention because they can compromise the credibility of vaccine campaigns in Brazil.

KEY WORDS: aseptic meningitis, MMR vaccine, mumps, measles, rubella.

* Aspectos clínico-laboratoriais de meningite asséptica associada à vacina tríplice viral em um hospital de referência no Estado da Bahia (Resumo). Tese de Doutorado, Universidade Federal da Bahia (Área: Neurologia). Orientador: Ailton Melo

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IMMUNOLOGICAL CELLS MARKERS IN THE HUMAN NEUROCYSTICERCOSIS (ABSTRACT)*. **THESIS. SÃO PAULO, 2001.**

*EDNÉIA CASAGRANDA BUENO***

The biological interaction of parasite-host involving in the neurocysticercosis (NC) is complex for the parasite antigens in different stages of evolution and the individual genetic variations interfering on the host response, will help to understand the dynamic of the parasite survival and the host defense mechanisms.

To contribute for the elucidation of the mechanism related to the parasite-host interaction in NC, immune response markers of 23 NC patients were studied in different stages of the disease: immunophenotyping (T cell, helper T cell, cytotoxic T cell, B cell, natural killer cells, HCAM and ICAM adhesion molecules and early activation marker CD69) of the cerebrospinal fluid (CSF) and peripheral blood; mononuclear cell proliferation *in vitro* after antigen-specific stimulation; and quantification of citokines (IL-1b, IL-4, IL-6, IL-10, IL-12, TNF-α) and adhesion molecules (ICAM and VCAM) produced in the lymphoproliferation assay.

The mean expression of the early activation marker CD69, in all kinds of cells identified in the samples of peripheral blood and in the CSF of NC patients was higher than the control group. The difference was always higher than 50% in CSF samples, indicating cell activity in the host as a response to the parasite.

Although there is no statistical difference ($p = 0.068$ the lower value), the CSF samples have shown higher percentages of T cells (70.9%), helper T cells (54.4%), B cells (15.8%) and natural killer cells (10.2%) when compared to the samples of peripheral blood (respectively 68.9%; 49.5%; 4.4% and 5.1%), suggesting local action of the defense system involved in the NC.

Patients with active NC have shown, in general, increasing of the cytotoxic T cells in peripheral blood samples (44.5%) and CSF (33.2%) when compared to the control group (respectively 36.0% and 26.9%), indicating the involvement of cytotoxic and suppressor mechanism in immunopathogenic process of the NC.

The mononuclear cells of NC patients have shown antigen-specific suppression *in vitro* (stimulation index, $SI < 2.5$) when compared to those of the control group. This suppression was more intense in samples of patients having no alterations in the image examination ($SI \leq 2.2$) and having cysts in degeneration process ($SI \leq 2.3$), and less intense in samples of patients with different evolution forms ($SI \leq 2.7$) and of patients having calcified cysts ($SI \leq 6.5$).

The suppression observed in NC seems to be induced by the parasite antigen components as it was observed in excretion and secretion antigens part of the vesicular fluid of *T. crassiceps* (VF-Tcra), that inhibited the cellular immune response induced by the mitogens phytohemagglutinin (98%), concanavalin A (99%) and pokeweed (98%). This suppression seems also to be related to the predominance of Th2 response (IL-4, IL-6, IL-10), as it can be observed in the citokines quantification in the supernadant of the lymphoproliferation assay stimulated by VF-Tcra antigen.

The presence of antibodies was observed independently of the response obtained in the lymphoproliferation assay (65% of the positive SI patients and 35% of those with negative SI), suggesting that the activity of the humoral immune response has occurred since the beginning of the infection.

The adhesion molecules were detected in NC patients, in values higher than those found in the control group, for both soluble form of ICAM and VCAM in culture of peripheral blood mononuclear cells after antigen-specific stimulation *in vitro* (respectively 46% and 60% of the patients) and in transmembrane form of HCAM and ICAM in cells of peripheral blood samples (71.4% and 85.7% of the patients) and CSF samples (55.5% and 88.8% of the patients), indicating that these molecules act in the cell migration related with the immune response in NC.

Patients with cysts in degeneration have shown mainly Th1 citokines, while the other evolution phases have shown a mixed profile Th1/Th2 (IL-1β, IL-4, IL-6, IL-10, IL-12 and TNF-a) with predominance of Th2 (IL-4, IL-6, IL-10) in the majority of them (65%), demonstrating the heterogeneity of the immune response in NC.

The production of the TNF-α in 75% of the samples of NC patients also indicates that the cytotoxic mechanism is involved in the NC immunopathogenic process.

KEY WORDS: neurocysticercosis, immune response, flow cytometry, lymphocyte proliferation, cytokine.

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RESULTS OF THE SURGICAL TREATMENT OF SYRINGOMYELIA ASSOCIATED WITH CHIARI MALFORMATION: ANALYSIS OF 60 CASES (ABSTRACT)*. **THESIS. SÃO PAULO, 2001.**

*JOSÉ ARNALDO MOTTA DE ARRUDA***

The author analyzes the results from surgical treatment in 60 patients suffering from syringomyelia associated with Chiari malformation, operated in the period of 1982-2000. Those patients are part of a universe of 129 patients suffering from malformation at the level of occipitocervical transition, that is, basilar impression and/or Chiari malformation, with the simultaneous occurrence of syringomyelia in 46.5% of cases.

Patients' ages ranged between 15 and 58 years, averaging 36.5 years. Patients included 32 females and 28 males. Most frequent initial symptoms included the difficulty to perform simple handworks, occurring in 51.6% of cases, and cervical pain, in 26.6% of cases. The time for the development of the condition averaged 6.2 years. In each case, 15 signs and 16 symptoms were analyzed under a protocol separating signs and symptoms of syringomyelia from signs and symptoms of Chiari malformation. A score system was established in parallel with the protocol, which made the evaluation of treatment results easier.

Surgical treatment was adopted as soon as the clinical aggravation of the patient's conditions was evident. All cases were submitted to craniovertebral decompression and C1 and C2 laminectomy, and cerebellar tonsillectomy with repair of dura mater. Nine patients underwent occipitocervical fixation, while three of them underwent transoral resection of the axis odontoid process. One patient underwent a second surgery of syringopleural derivation. Most frequent surgical complication was pseudomeningocele that occurred in 23.3% of cases. No death occurred among the patients of this study. To evaluate the results, statistical tests of proportion difference and variance analysis were applied with a reliability of 95% ($p = 0.05$).

It was concluded that signs and symptoms of Chiari malformation show very significant statistical improvement. Signs and symptoms of syringomyelia also improved significantly, among which the sign muscular atrophy improved best. An exception was the sign hyporeflexia of upper limbs, which did not improve. Among the signs and symptoms attributed to both syringomyelia and Chiari malformation, only hyperreflexia of upper limbs and sexual impotence did not improve. No statistical difference was found when comparing the improvement of syringomyelia symptoms to that of Chiari malformation. Syringomyelia signs statistically improved more than those of Chiari malformation. In half of patients, the percentage of improvement of signs and symptoms ranged between 40 and 60%.

KEY WORDS: syringomyelia, Chiari malformation, surgical treatment.

*Resultados do tratamento cirúrgico da siringomielia associada à malformação de Chiari: análise de 60 casos (Resumo). Tese de Doutorado, Escola Paulista de Medicina da Universidade de São Paulo (Área: Neurocirurgia). Orientador: Oswaldo Inácio de Tella Jr.

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SURGICAL TREATMENT OF PATIENTS WITH CERVICAL SPINAL CORD INJURY BY ANTERIOR APPROACH USING BONE GRAFT (ABSTRACT)*. **THESIS. CAMPINAS, 2001.**

*MANOEL BALDOINO LEAL FILHO***

The author reports an experience with 39 patients with acute cervical spine fractures and/or dislocations between C3 and C7. The average age was 41 and varied from 11 to 70 years old. Fall down was the most frequent cause of accident, the principal level was C5 and 79,5% of the patients arrived after eight hours of the trauma.

All of the patients were submitted to anterior approach using bone graft fixation without screw and plate systems and only three patients underwent posterior approach associated. Graft dislodgement occurred at a rate of 7.7% in post-operative time and 2.8% at one month because of technical problems with the vertebral endplate that was not drilled enough to receive and fix the graft. No redislodgement occurred.

All fusions became solid after three months, and all spinal columns were stable and painless after six months follow-up. Death occurred in three patients in post-operative time, neither one associated with surgical problems. Their progress based on the Frankel scale before surgery was A.51.3%, B 2.6%, C 15.4%, D 17.9%, E 12.8%, at the moment of the discharge was A 36.1%, B 8.3%, C 16.7%, D 16.7%, E 22.2% and with six months was A 22.2%, B 22.2%, C 11.1%, D 11.1%, E 33.4%.

The present experience shows how patients with acute cervical injury can improve even when the patients were admitted lately after trauma, were operated after the first week, with a bone graft anterior fixation and using a collar for three months till consolidation and had not received metilprednisolone.

KEY WORDS: cervical spine, spinal injury, anterior fusion, spinal fusion.

*Tratamento cirúrgico de pacientes com traumatismo raquimedular cervical pela via anterior utilizando enxerto ósseo (Resumo). Tese de Mestrado, Universidade Estadual de Campinas, UNICAMP (Área: Ciências Médicas). Orientador: Guilherme Borges.

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SURGICAL TREATMENT OF TRAUMATIC LESIONS OF THE MEDIUM–INFERIOR SEGMENT OF THE CERVICAL SPINE (ABSTRACT)*. **DISSERTATION. SÃO PAULO, 1999.**

*MARCO ANTONIO HERCULANO ***

The most frequent injury level of cervical spine is C2, followed by C5 and C6. Injuries are most commonly sustained in the third decade of life, with a decreasing incidence in the advanced age.

As part of these lesions is located in the elements of the anterior column, according to Denis' definition, and taking in consideration the biomechanics studies of the medium-inferior segment of the cervical spine, as well as the mechanisms that cause the lesions, this monograph was elaborated with the intention of presenting the techniques of anterior cervical fusion, with bony graft and plates of Caspar, Morscher (CSLP) and Orion™.

The advantages and disadvantages of each type of anterior fixation are presented accordind to the literature review. The improvements in the material relate to plates and screws fixation techniques are illustrated.

KEY WORDS: cervical spine, injury, surgery.

*Tratamento cirúrgico das lesões traumáticas do segmento médio inferior da coluna cervical (Resumo). Dissertação de Mestrado, Escola Paulista de Medicina – Universidade Federal de São Paulo (Área: Neurocirurgia). Orientador: Oswaldo Inácio de Tella Jr.

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POLYSOMNOGRAPHIC EVALUATION OF CLINICAL PATIENTS SUFFERING FROM MOOD DISTURBANCE (ABSTRACT)*. **DISSERTATION. LONDRINA, 1999.**

*MÔNICA MARCOS DE SOUZA***

Sleep disorders are diagnostic criteria for depression, and highly characteristic in patients suffering from mood disturbances. The sleep patterns of sixty clinical patients suffering from mood disturbance were studied, aged between 16 to 59 years old. These patients were submitted to two nights of nocturnal polysomnographic evaluation and the second night of observation was employed in the statistics.

The following parameters were analyzed: REM sleep parameters (number of REM cycles, and REM density), parameters of sleep continuity, (sleep efficiency, total number of sleep interruptions, sleep latency, time of permanence awake, and number of stage changes) and delta sleep parameters. In general, all parameters evaluated were altered; but only the sleep in stage 4 there was statistical significant diference between the mild depressive and severe.

The statistics evaluations used the Fischer Exact Test and the Kruskall-Wallis Statistics Heterogenecity Test. Descriptive analysis was used to delineate the study. Concerning gender, there was a predominance of females (80%) on males (20%); the age average was between 36.1 ± 11.3 years old; the average and the standard deviation of the variables studied were: REM latency, 75.3 ± 48.2 minutes; duration of the first REM cycle, 22.8 ± 14.0 minutes; percentage of REM sleep, 27.2 ± 8.6; REM density, 22.4 ± 10.3 %; number of REM cycles, most patients presented 3 REM cycles; sleep efficiency, 90.5 ± 10.1 % number of awakenings, 21.2 ± 10.7 episodes; sleep latency, 8.8 ± 10.4 minutes; total awake time, 35.4 ± 36.6 minutes; changes between stages, 72.3 ± 29.4 episodes; percentage of sleep in stage 3, 3.2 ± 2.7 %; percent sleep in stage 4, 3.4 ± 4.4 %; percentage sleep stage 3+4, 6.7 ± 6.0± %. The most common diagnosis established was dysthymia.

The polysomnographic study offers a better understanding of pathophysiology of depression and is be useful for the diagnosis, follow up and therapy for mood disturbances.

KEY WORDS: sleep, sleep disorders, polysomnography, mood disturbance, depression.

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