**TYPE I PRIMARY NEUROPATHIC AMYLOIDOSIS
(ANDRADE, PORTUGUESE)**

A CLINICAL AND LABORATORY STUDY OF 21 CASES

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Amyloidosis is the name of a group of diseases characterized by the storage, in several tissues, of a protein (globulins rich in tryptophan) bound to 5% of mucopolysaccharids⁴³, showing a fibrillar ultra-structure endowed with dichroic birefringence when stained with Congo red³⁵.

The amyloidoses are classified²² in: (1) primary, including familial and sporadic forms, and the form accompanying multiple myeloma; (2) secondary to various chronic diseases. The amyloid substance in both groups has the same physico-chemical properties^{27, 35}.

Familial amyloidoses may be localized or systemic. These latter comprise two subdivisions³⁷: one without damage of the nervous system (Oster-tag's amyloid nephropathy⁴⁶, familial Mediterranean fever^{12, 25, 26}, amyloid urticaria-deafness-nephropathy⁴⁴, hypersensitivity to cold^{37, 38}, and cardiac amyloidosis²⁰) and other markedly neuropathic (type I, Andrade or Portuguese; type II, Rukavina or Indian; type III, Van Allen or Iowa).

The purpose of this paper is to analyse the results of the clinical and laboratory study of 21 patients with type I primary neuropathic amyloidosis.

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CASE MATERIAL

Twenty-one patients have been studied. The diagnosis was based on anamnestic data, clinical manifestations with prevalence of peripheral neuritis and gastrointestinal signs, and the demonstration of amyloid substance in biopsy material.

The patients have been examined from 1947 to July 1974. Case 13 was quoted by Julião and Mignone³⁰ in 1950; cases 3 and 4 were reported by Julião²⁸ in 1960; cases 3, 4, 6, 10, 11, 12, 13, 14, 15, 16, 17 and 18 were described by Julião²⁹ in 1963; cases 11 and 12 were fully analysed later (1974) by Julião et al.³¹.

Cases 3 and 6, 7 and 8, 11 and 12, 19 and 20, were affected sibs.

Sex and age — The age at the onset of symptoms and the sex of the patients are summarized in table 1.

Sex	Age (years)			Total
	21-30	31-40	41-50	
Male	11	3	2	16
Female	1	4	0	5
Total	12	7	2	21

Table 1 — Age at the onset of symptoms and sex

Birth place and familial incidence — In all cases Portuguese nationality or ascent was found. Sixteen patients had one or more cases (up to a maximum of 9) with a similar disease in the family; four Portuguese patients were unable to inform about familial incidence, because they had emigrated to Brazil and lost contact with their relatives, in this way rendering doubtful the assumption that the cases were sporadic (table 2). The inheritance from father and mother was equivalent, both paternal and maternal ascent being recorded in cases 7 and 8 (sibs).

Nationality	Familial incidence				Total
	Negative	Paternal	Maternal	Paternal and Maternal	
Brazilian *	1	5	4	2	12
Portuguese	4 **	1	4	0	9
Total	5	6	8	2	21

Table 2 — Nationality and familial incidence: * with Portuguese ascent; ** the patients lost contact with their relatives.

In 17 patients an exact information on the Portuguese place of origin was obtained: 10 were born on Póvoa do Varzim, 4 on Coimbra, 2 (sibs) on Morro do Caudal, and 1 on Barcelos, all the cities located in the Northwestern quadrant of Portugal, on the coast or near to it.

CLINICAL MANIFESTATIONS

The *first manifestations*, analysed in 19 cases, were single in 7 cases and multiple in 12 (6 patients showed association of two symptoms, 5 of three, and 1 of four). The most frequent was the association of motor and sensory symptoms (6 times). By the analysis of the first symptom, the following remarks were made possible: sensory disorders in 11 patients; gastrointestinal complaints in 8; motor disorders in 7; perforating plantar ulcers in 4; impotence in 4 among 14 men; sphincteral incontinence in 2; fainting crises in 1; irritability in 1.

Nineteen patients could be followed up for periods of several years. Their symptomatology in the full developed illness will be described now.

Sensory disorders — a) Superficial hypo or anesthesia with a peripheral distribution (boot and/or glove) in 18 patients; b) paresthesias in 16; c) deep hypo or anesthesia in 14, with a predominant impairment of the vibration sense in the lower limbs; in 2 cases loss of testicular sensation was found; d) fulgurating pains in 5; e) other symptoms, such as bilateral hyposmia (1) and bilateral hypoacusis (1).

Motor disorders — a) Diminution or loss of deep reflexes and hypotonia were found in all cases but one; b) impairment of motor strength in the four (11 cases) or the lower limbs (17); c) steppage in 10; d) 7 patients were unable to walk; e) dysphonia in 6; f) bilateral peripheral facial paralysis in 4; g) other disorders, like laryngeal paralysis (3), dysphagia (1), intercostal paresis leading to death (1) and diplopia (1).

Trophic disorders — a) Muscle atrophies were absent in 1 patient only; b) bed sores and/or perforating plantar ulcers were present in 8 patients; c) other disorders, like diffuse thickening of nerve trunk (1), hypotrophy of the trapezius (1), myoedema of the deltoid (1), ichthyosis (1), cutaneous hyperpigmentation (1), hypochromia of the hands (1), and hypotrophy of the masseters (1).

Gastrointestinal disorders — a) Diarrhea was present in 16 patients; b) loss of body weight greater than 10 kg. in 13; c) obstipation in 8; d) nausea and/or vomiting in 7; e) anorexia in 6; f) gripes in 3.

Cardiocirculatory disorders — a) Edema and/or dyspnea was observed in 6 patients; b) other disorders, like precordialgia (1), varices, acrocyanosis and claret edema of the lower limbs (1), Stokes-Adams crises, congestive heart failure and bradycardia (cause of death) in 1, and gallop rhythm (1).

Autonomic disorders — a) Impotence in all males; b) urine and/or stool incontinence in 13; c) neurogenic (autonomous) bladder, tested through cystometry, in 6 patients.

Other types of disorders — a) Urinary infection in 11 patients among 16 who made laboratory examination; b) amenorrhea in 3 patients among 5 (ages between 32 and 38 years); c) other disorders, as seizures (1), irritability (1), hepatomegalia (1), and psychic depression (1).

Course of the disease — Three patients died while being followed up, 7, 11 and 14 years after the onset of symptoms,

LABORATORY AND OTHER COMPLEMENTARY EXAMINATIONS

Only the most frequently abnormal or the most significant results will be discussed. Other tests were performed with the purpose to find out associated diseases

or in order to make the differential diagnosis: in the blood, determination of amylase, glucose, phosphatases, liver, kidney and thyroid function tests, prothrombin time, hemogram; in urine, determination of 17-ketosteroids, 24-hour protein content, Bence-Jones protein; cholecystogram:: excretory urography; myelogram; search for occult blood in feces; skin tests for tuberculosis and hanseniasis; serologic tests for syphilis; rectosigmoidoscopy; and immunoelectrophoresis of the blood and cerebrospinal fluid.

Electromyogram and electrodiagnosis — The electromyography, performed in 12 patients, showed damage of peripheral nerve in 8 and of the anterior horn in 3, being normal in 1. The electrodiagnosis was made 9 times in 8 patients, always showing a partial or complete reaction of degeneration.

Electrocardiogram — It was made at least once in 16 patients, resulting normal in 4 cases only. The most frequent changes were disorders of repolarization (11), ventricular overload (6), first degree atrioventricular block (5), extrasystolia (4), and complete block (2).

Electroencephalogram — The EEG was made in 7 patients with personal or familial history suggesting epilepsy. It resulted normal in 3 and showed paroxysmic irritative abnormalities in 4 patients.

Ocular biomicroscopy — This examination was designed to find out the presence of amyloid storage and consequent opacification of the lens. It was performed in 11 patients, resulting negative in 10 and doubtful in 1.

Radiological examination of the gastrointestinal tract — X-ray examination of esophagus, stomach and duodenum was made in 9 patients, with normal results in 2. In none an organic lesion was detected, but in 7 functional disorders were found, mainly hypotonia, emptying delay and gastric stasis. Intestinal transit, made in 7 patients, was normal in 1, slow in 4 and accelerated in 2. Opaque enema, made in 4 patients, was normal in 3 and showed inflammation of the sigmoid in 1. The radiological examination is very difficult to perform in these patients owing to the vomiting and diarrhea.

Iodized oil myelography was made in 2 patients only, being normal in 1 and showing diffuse arachnoiditis in the other.

Tests regarding the malabsorption syndrome — In some cases the intestinal absorption was extensively studied. The following tests were performed: glucose tolerance test, Katsch-Kalk test, excretion of radiolabeled proteins (Cromalbin), balance of fat in feces, xylose absorption, tests of gastric stimulation with Histalog and Pentagastrin, Lipiodol absorption, fraccionated gastric test, absorption of labeled oleic acid, coprologic examination, culture of feces, and proctoparasitologic examination. This research was designed to characterize the pattern and severeness of the digestive disorder in each case. Nevertheless, the small number of data and the variability of the results have hindered the settlement of a definite pattern of gastrointestinal absorption in patients with neuroamyloidosis. Consequently, only the results of the study of labeled vitamin B12 and triolein absorption will be analysed.

Absorption of vitamin B12 labeled with ^{57}Co according to the Schilling method ⁴⁰ (normal excretion in 24-hour urine greater than 10% of the oral dosis) — Twelve patients have been studied, and the initial rates were: 5 patients showed a percentage lower than 10%, 5 between 10 and 20%, and 2 showed rates over 20%. In these 2 cases the test was repeated later, when the course of the disease pointed to an aggravation of the gastrointestinal condition, and rates of 5% in one and 12% in other were

obtained. In 3 patients with rates lower than 10%, the repetition of the test with the association of intrinsic factor made possible an increase to figures greater than 10%.

The oral administration of ^{131}I -triolein uses two parameters in the evaluation of its absorption: one is the serial measurement (each 6, 12 or 24 hours) of the percentage of triolein excreted in urine during the first 72 hours, and other is concerned with the percentage excreted in feces in the same period. This test was performed in 6 patients; in 1 the result was normal, in 2 it evidenced slow absorption, and in 3 it showed the presence of steatorrhea.

Blood serum proteins — In 14 patients, 28 determinations of the total proteins were made; normal values were found in 19, while 8 were low and 1 was high. Out of these patients, 6 have shown, once at least (in a later stage), a definite hypoproteinemia.

The proteinogram was made in 17 patients, according to a method of paper electrophoresis standardized for our population⁵¹. Three patients (6 examinations) showed normal results and 14 (22 examinations) evidenced alterations. As concerns the number of patients the most frequent changes were an increase of α_2 -globulin in 8, reduction of albumin in 7, increase of γ -globulin in 6, low α_1 -globulin in 5, and low γ -globulin in 2.

Cerebrospinal fluid proteins — The determination of total proteins, made in 14 patients, showed abnormally high results, with values between 40 and 83 mg/100ml, in 9 cases.

The electrophoretic study of the CSF proteins⁵¹, made in 10 patients, showed an abnormal profile in 5, with an increase of γ -globulin (values between 15.5 and 23.5%) in 4, low albumin in 3, increased α_2 -globulin in 2, low β -globulin in 2, and high albumin in 1.

Determination of urinary gonadotrophins — The test was performed in 6 patients (5 males), and low values (less than 6.7 U in 24-hour urine) were found in 5 (4 males).

*Bennhold's test*⁹ — This test consists of the intravenous injection of Congo red and the determination of the amount of this dye in the blood serum one hour later. The limit of normality is 60%, the lower values being attributed to an increase of the tissue absorption. This test was performed 9 times in 7 patients, the results varying from 58% to 20%.

Histopathologic examination — The presence of amyloid substance was investigated in 18 patients. This study was made through repeated biopsies of several tissues, and resulted valueless in 1 case only. In another case the presence of the amyloid became doubtful, but, owing to the fact that in the patient's sister the histopathology was positive, the biopsy was not repeated.

In one patient the postmortem examination was performed. The causa mortis was ascribed to heart failure. Focal or perivascular areas of amyloidosis were found in the heart, epiploon, thoracolumbar cord (leptomeninges and spinal vessels), sciatic nerve, skin (annexa and nerve fibers), kidney (secondary type) and adrenals.

The results of the histopathological examination of 54 biopsies of various tissues are summarized in table 3.

Tissue	Positive		Negative		Total	
	N.º of Biopsies	N.º of Cases	N.º of Biopsies	N.º of Cases	N.º of Biopsies	N.º of Cases
Nerve	17	15	8	2	25*	17*
Rectum	1	1	6	6	7	7
Skin	1	1	8	4	9	5
Testicle	3	3	3	2	6	5
Muscle	0	0	4	4	4	4
Jejunum	0	0	1	1	1	1
Gingival mucosa	0	0	1	1	1	1
Epiglottis	1	1	0	0	1	1

Table 3 — Results of the histological examination for amyloid substance (54 biopsies):
* one doubtful case.

DISCUSSION

The literature on the amyloidoses is expanding every year with new investigations on the nature of the amyloid and reports of varied clinical pictures associated with the storage of this material. Its chemical composition is known but the cause of the amyloid deposition is still not identified^{7, 27, 37}.

Virchow⁵⁵, who has named the substance, was the first author to describe, in 1857, the presence of amyloid storage in peripheral nerves, in a case of chronic suppuration. Many investigations were carried out trying to explain the pathophysiology of the peripheral nerve damage^{17, 18, 53}. Lampert³⁵, Henson & Ulrich²⁷, and Gimeno et al.²³ ascribe the nerve degeneration to two causal factors: ischemia, secondary to a decrease of the blood flow in arterioles severely involved by the disease (perivascular depositions)³⁴, and mechanical compression of the nerve fibers (perineural depositions)¹⁹.

Regarding the site of involvement, Missmahl⁴¹ and Heller et al.²⁴ have found two patterns of histologic distribution according to the structure — collagen or reticulin fiber — where the amyloid is stored. Perireticulin amyloidosis occurs in the secondary type, which is characterized by a prevailing damage of the little vessels, the alterations starting on the intima and spreading later to the media layer. Pericollagen amyloidosis is found in the primary type, and involves the blood vessels, the perivascular connective tissue, the stroma of several organs, the sarcolemma of all muscle types, and the neurilemma. The deposition begins on the tunica media and the precipitation around the veins is massive.

Reports of sporadic cases of polyneuritis caused by primary amyloidosis are numerous^{16, 34, 45}. Chambers et al.¹⁶ emphasized that the average age of involvement of peripheral nerve in amyloidosis is lower than that one of damage of other structures. Predominance in males (84%) was found by Munsat & Poussaint⁴⁵.

Recent reviews on the hereditary systemic amyloidoses have been made by Becker⁷, Cohen¹⁷, and Mahloudji et al.³⁷. These latter created the division, here adopted, into neuropathic and non-neuropathic forms. The type of inheritance for the familial forms is the autosomic dominant, except in the familial Mediterranean fever (recessive)^{12, 25, 26} and in heart amyloidosis (still unknown)²⁰.

Currently, three types of hereditary neuropathic amyloidosis are known:

a) Type I was described by Wohlwill⁵⁶ and Andrade^{1, 2, 3}. The name "Portuguese type" is inadequate since it does not include families without such naturality but showing the same pathologic condition³⁷.

b) Type II, described by Rukavina et al.⁴⁸ in a group of Swiss ascent living in Indiana (USA), was later studied by Mahloudji et al.³⁷ in 53 patients of German origin living in Maryland (USA), belonging to 11 families descending of a common pair married in 1775. This type is characterized by the onset of symptoms on the 5th decade, initial sensitive (carpal tunnel syndrome) and motor impairment on the hands, rare gastrointestinal, sphincteral, sexual potency or trophic manifestations, slow course (14 to 40 or more years), absence of kidney involvement, and high frequency of vitreal opacification due to amyloid deposition^{23, 33}.

c) Type III, reported by Van Allen et al.⁵⁴ in a family with English, Scotch and Irish ascent living in Iowa (USA), and also studied by Gimeno et al.²³ in a Basque family of Irish origin, is characterized by the onset of symptoms at the 4th decade, initial involvement of feet and hands (there is no carpal tunnel syndrome), frequent gastrointestinal, sphincteral and sexual potency impairment, rare perforating ulcers, average course of 17 years, constant nephropathy (cause of deaths), and high incidence of peptic ulcer with digestive hemorrhages. Gimeno et al.²³ suggest that this type seems to be a bridge between amyloid nephropathy and amyloid neuropathy.

Clinical and pathological studies of type I amyloidosis are numerous^{1, 2, 3, 4, 6, 8, 29, 30, 31, 39, 47, 56} even in families without Portuguese ascent^{4, 5, 15, 32, 42}, but Andrade³ has reported the greater number of cases (74). Becker et al.^{7, 8} studied the genetics of the disease, and drew the conclusion of a dominant autosomic inheritance with 60% penetrance; 40% of the heterozygote females show no amyloidosis and the remaining 60% get ill later than males (average of 44 years for females and 33 for males). The prevalence in males was demonstrated ($63 \pm 4.1\%$ for males and $37 \pm 4.1\%$ for females). The authors^{7, 8} surmise that all patients with Portuguese ascent should descend from a single mutant, the "sporadic" cases being the result of a low penetrance in females, an occasional late onset of symptoms, or the incomplete data on the families. They rejected an influence of environmental factors on the origin of the disease.

The cases here presented received the diagnosis of Andrade's familial amyloid neuropathy, by the genetic, clinical, laboratory, and pathological fea-

tures, as well as by the occurrence of Portuguese ascent in all patients. However, including all cases of amyloid neuropathy studied in our Department since 1957, the investigation could not show absolute uniformity. Some cases were examined some times only, while other patients were followed up for several years. As the richness of the symptomatology depends on the stage of the disease, one can easily understand the differences among the clinical pictures and the results of the laboratory and complementary examinations.

Concerning the epidemiology of the disease, the greater and earlier incidence in males (3:1, table 1)⁷, the onset of symptoms between 24 and 44 years of age^{3, 4, 7}, the familial involvement with a frequency consistent with a dominant autosomic inheritance^{4, 8}, the Portuguese places of origin of the patients or their families⁴, the course of the illness^{3, 8, 29}, and the independence on the social and economical level and profession (case 15 is a physician)^{4, 8, 45}, all agree with the literature^{3, 7}.

The analysis of the starting manifestations is also in agreement with previous studies, but it is worth to call attention to the facts that, usually, a multiple symptomatology opens the scene^{3, 37}, and gastrointestinal manifestations are the first symptoms in the female patients.

In the fully developed disease, the disorders of sensation fitted the classical picture of a progressive centripetal involvement⁸, more marked in the lower limbs and including all kinds of sensation, mostly and earlier the superficial forms, and mainly thermalgesia^{8, 18, 19, 37}. Like other authors^{3, 28, 37}, we found an impairment of vibration sense preceding the disorders of position sense sometimes for many years. Thomas & King⁵³ have recently observed, in the early stages, a preferential damage of non myelinated axons, thus explaining the significant impairment of thermalgesia and the marked autonomic involvement^{18, 19, 21}. The finding of hyposmia can not be duly interpreted, but hypoacusis was already found in neuroamyloidosis^{7, 16, 27, 54}.

Regarding motor and dystrophic manifestations, it seems a significant finding the possibility of all motor cranial nerves being injured. Involvement of the facial nerve is seldom recorded^{7, 27, 40}, but Andrade³, in his large series, did never find wasting of the facial muscles. In the present series pupillar abnormalities^{3, 7, 23, 27, 31, 37, 53} and involvement of the hypoglossus nerve⁷ were not found. Dysphonia (6 cases) is attributed to a pair of causal factors: deposition of amyloid substance (amyloid tumors²⁷) in the vocal cords²⁷, larynx^{6, 8, 15} and tongue^{6, 15, 27}, and the involvement of the muscles related to voice emission^{6, 10, 15, 29, 45}. Hypo or atonia of one or both vocal cords was found by laryngoscopy in some of our dysphonic patients; in one of them biopsy of the epiglottis was positive for amyloid material.

Digestive disorders, extremely severe in many cases and always present in the late stages of the disease, are responsible for the loss of weight and progressive cachexia⁸, in spite of Andrade's report³ on loss of body weight in the

absence of diarrhea. Anorexia, probably aggravated by the depressive state of the patients, increases the undernutrition.

Unlike the reports stating that the frequent electrocardiographic changes are not associated with clinical manifestations of heart failure ^{7, 27, 45}, in the present series a rather high incidence of dyspnea and edema of the lower limbs was noticed, and one of the deaths was due to an unequivocal congestive heart failure. For some authors ^{6, 14}, however, the absence of heart disease in neuroamyloidosis ^{3, 47} distinguishes this type from the cardiac amyloidoses.

As regards the autonomic disorders, present in almost half the cases of amyloid neuropathy reported by Henson & Urich ²⁷, we must emphasize the constant finding of impotence, without a primary loss of libido ^{8, 44, 50}. There is a double impotence: *coeundi*, owing to the autonomic involvement ⁵⁰, and *generandi*, owing to the deposition of amyloid substance on the testes ⁷, leading to a testicular atrophy ^{3, 23} and azoospermia ³. The disturbances of the menstrual cycle, amenorrhea, and the low levels of urinary gonadotrophins also recognize in their causation the storage of amyloid in the gonads ^{3, 7}.

Mental depression was evaluated by psychiatrist in only one patient, whose condition was extremely severe. Marked apathy and melancholy ³, however, seem to be an essential part of the clinical picture of almost every patient.

Concerning the laboratory and complementary examinations, it must firstly be emphasized that the electromyography showed fibrillations in 3 cases, evidencing the involvement of anterior horns ^{3, 8, 37}, but did not show myotonic phenomena in any case ³.

The electrocardiographic changes, so frequent in this disease ^{23, 47}, are the consequence of deposition of the amyloid substance on the conduction bundles and on the myocardial fibers ^{23, 52}.

The search for amyloid deposits on the vitreum was undertaken because some authors regard them as a pathognomonic sign of primary amyloidosis ^{33, 57}. But, unlike the findings in the other two types, it is seldom found in type I ^{4, 7, 27, 37}; its presence was doubtful in 1 case of this series.

Myelographic signs of arachnoiditis have already been recorded and marked involvement of the leptomeninges is a frequent finding at the postmortem examination ^{29, 30, 31} (it was present in our sole case of necropsy).

The radiological examination of the digestive tract corroborated the severe functional alterations suggested by the clinical picture. The results of the Schilling test, besides the evidence of low vitamin B₁₂ absorption — a condition which certainly aggravates the peripheral nerve damage ¹³ — also have shown an impairment of intrinsic factor secretion, thus indicating that the gastric mucosa is implicated in the malabsorption syndrome. The tests with labeled triolein gave more emphasis to both phenomena — deficient absorp-

tion and steatorrhea — peculiar to the digestive involvement in neuroamyloidosis.

The pathologic examination has frequently shown a double pancreatic involvement⁷: marked loss of secretory glands (atrophy of the pancreas³) plus amyloidosis of the fibers innervating the organ³. So, the pancreatic dysfunction should play an important etiologic role in the digestive syndrome. On the other hand, histopathological studies have demonstrated deposition of the amyloid substance on the mucosa^{27, 45}, the smooth muscles^{3, 7} and the autonomic fibers on the intestinal tract^{3, 21, 27, 31, 36, 45}. But there is still not an agreement of the authors on the degree of significance of these factors for the genesis of the digestive syndrome.

The finding of low blood protein contents in 6 cases was ascribed to the malabsorption syndrome and was due to the lowering of albumin. Alterations in the electrophoretic profile of the blood proteins are frequent but inconstant^{7, 11, 22, 27}. Several authors suggested an abnormal pike in the α_2 -globulins^{7, 11, 22, 48}, but it seems that there is not a specific pattern of abnormalities in neuroamyloidosis^{7, 23, 37}. Our results, showing marked variations, corroborate this viewpoint.

The frequent finding of high CSF protein concentrations^{3, 23} is explained by the early and conspicuous radicular involvement²¹. Lesions of the leptomeninges, leading to changes of the blood-brain barrier, shall concur to the increase of the protein. The values usually varies from 50 to 100mg/100ml²⁷, but one case with 240 mg/100ml has been reported⁵³. The cell count is normal. Our results agree with these findings. Concerning the fractionation of the CSF proteins, like it happened with blood proteins, no definite electrophoretic pattern could be demonstrated.

Congo red test, admitted as seldom positive in primary amyloidoses^{7, 22}, but recognized as important for the diagnosis, if positive^{3, 10, 16, 23, 35}, showed an increase of the tissue absorption of the dye in all cases submitted to this procedure.

The most effective method for the demonstration of amyloid deposition was the biopsy of lower limb nerves. Some authors admit that symptoms may precede for a long time the deposition of amyloid in the nerve fiber^{18, 37, 53}. Posterior roots seem to be involved earlier and would determine symptoms before deposits in the peripheral nerve trunks could be demonstrated^{10, 28}. Despite this, nerve trunks are the structures of choice for biopsy in neuropathic cases^{22, 29}.

The skin, mostly around hairs^{7, 45}, the rectal mucosa^{7, 22, 45, 53}, and the skeletal muscles are rather preserved tissues⁷, and in our series biopsies of them resulted negative for amyloid. The reverse is true for testicular biopsies, which were performed in patients with a negative nerve biopsy, and resulted positive in 3:5 cases.

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The authors intend, with this study, to pay homage to the unforgettable master of the Brazilian Neurology, Dr. Oswaldo Freitas Julião, whose pioner researches in the field of the neuro-amyloidoses have achieved international renown. We also acknowledge with thanks, Dr. Nelson Carvalho for the study of intestinal absorption with radioactive isotopes.

SUMMARY

The authors present a review of 21 cases with the diagnosis of type I amyloid neuropathy based on epidemiological data, clinical evolution and histopathological findings.

They call attention to the possibility of cranial nerves involvement (hyposmia, diplopia, masseterian hypotrophy, peripheral facial paralysis, hypacusis, dysphonia, laryngeal paralysis, dysphagia, and trapezium muscle hypotrophy), to the severeness of the digestive symptoms, to the precocity of the autonomic disorders, and to the rather high incidence (6 cases) of heart involvement.

The electromyography showed anterior horn involvement in 3 cases. The electrocardiography showed repolarization disorders in 11 cases, left ventricular overload in 6 cases and atrioventricular block in 5 cases. The serum proteins electrophoresis showed frequent abnormalities, but no typical curve could be obtained.

The barium-contrasted X-rays of the gastrointestinal tract showed no anatomical lesions, but functional abnormalities (hypo or hypermotility) were found in 14 examinations.

The Schilling test showed impairment of vitamin B12 absorption in 50% of the cases. However, with the concomitant administration of intrinsic factor (3 cases) there was improvement of its absorption. This proves that the gastric mucosa plays an important role in the disease malabsorption. The test with labeled-triolein showed slow absorption in 2 cases and steatorrhea in 3 (6 tests).

For the confirmation of the amyloid deposits, the best histopathological procedure was nerve biopsy. In men, when the nerve biopsy was negative, testicular biopsy has shown to be a good option.

RESUMO

Neuropatia amilóide primária tipo I (Andrade, Portuguesa): estudo clínico e laboratorial de 21 casos.

Os autores apresentam uma revisão de 21 pacientes com diagnóstico de neuropatia amilóide tipo I, firmado sobre os dados epidemiológicos, a evolução clínica e os achados histopatológicos.

Chamam a atenção para a possibilidade de comprometimento de vários nervos cranianos, para a gravidade do quadro digestivo, a precocidade dos distúrbios neurovegetativos e a incidência relativamente alta de sintomatologia cardíaca.

Constituem contribuição para o melhor conhecimento da afecção, os estudos sobre a síndrome digestiva feitos através de exames radiológicos e dos testes de absorção de vitamina B₁₂ e trioleína radioativas.

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