NEUROLOGICAL MANIFESTATIONS IN THYROIDITIS

MIHAELA LUNGU¹, AURELIA ROMILA², AUREL NECHITA³, DANA TUTUNARU⁴, BACAREA ANCA⁵
¹Lecturer, MD., PhD., Faculty of Medicine and Pharmacy, “Dunarea de Jos” University of Galati, Head of Neurological Department, Emergency Clinical Hospital, Galati
²Associate Professor, MD., PhD., Faculty of Medicine and Pharmacy, “Dunarea de Jos” University of Galati, Center for Research on Medical - Pharmaceutical, Head of Geriatrics Department, Emergency County Hospital, Galati
³Professor, MD., PhD. Faculty of Medicine and Pharmacy, “Dunarea de Jos”, University of Galati, Head of Geriatrics Department, Emergency Hospital of Pediatrics, Galati
⁴Professor, MD., PhD. Faculty of Medicine and Pharmacy, “Dunarea de Jos”, University of Galati, Head of Pediatric Department, Emergency Hospital of Pediatrics, Galati
⁵Associate Professor MD., PhD., University of Medicine and Pharmacy Targu-Mures, Pathophysiology Department

ABSTRACT

Introduction: A five years prospective study was conducted with the aim to observe the neurological manifestations in acute, subacute and chronic thyroiditis.

Materials and methods: A study on 26 patients was carried out over the span of 5 years. Clinical and paraclinical examinations were carried out every three months. The paraclinical exam included hormone dosing, ultrasound exams, thyroid scintigraphy, biopsies, brain computed tomography and blood biochemistry tests.

Results: A large amount of detailed data was collected over a relatively long span of time.

Conclusions: The collected data largely corresponds to the reference literature. It is often the case that patients first address the neurologist, who has to diagnose the thyroid disease and its neurological manifestations.

Keywords: thyroiditis, neuropsychiatric manifestations.

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Introduction

Thyroiditis represents the inflammation or infection disorders of the thyroid parenchyma, with complex etiology and occurring in patients that previously presented an urging thyroid or a preexistent goiter (Struma).

The evolution of this disease can be acute, subacute or chronic.

We conducted a clinical study supported by laboratory examinations which had the purpose to determine the neurological manifestations of thyroiditis, referring to frequency, clinical and therapeutic response of neurological determinations in this type of thyroid pathology, and revealing the diagnostic difficulties of the damage done to the nervous system by thyroiditis.

Materials and methods

The research followed the recommended methodology for conducting the prospective clinical and epidemiological studies.

The study focused on a group of 26 patients with thyroiditis who were examined in the neurology and endocrinology sections in Galati Emergency Hospital, followed for a period of five years. Patients were examined clinical and paraclinical every 3 months.

Clinical examination was associated with paraclinical tests. Paraclinical data were recorded in the observations sheets. For the clinical diagnosis of hyperthyroidism, the Newcastle index was used, and in the clinical assessment of the hypothyroidism the Billewicz index was used.
For the paraclinical endocrinological diagnosis we used: hormone dosage T3 (triiodothyronine), FT3 (free serum triiodothyronine), T4 (thyroxine), FT4 (free serum thyroxine), TSH (adenohypophysis thyrotropin hormone), thyroid ultrasound exam and thyroid scintigraphy with 99m (Technitium isotope), in doses of 2mCi, thyroid biopsy with thin needle puncture, sella turcica radiography, CT (computed tomography) brain scan or mediastinum scan, brain magnetic resonance imaging (MRI), biochemical usual tests of blood and urine: cholesterol, Hb (hemoglobin), Ht (hematocrit), number of WC (white cells) and PMN-polymorphonuclears, ESR (erytrocytes sediment rate) liver test, CPK (creatine phosphokinase), total proteins, bilirubin, alkaline phosphatase, immunoassay, immunoelctrophoresis, lupus cells, C-reactive protein, complement serum, circulating immune complexes, antithyroglobulin antibody, bone scan, electrocardiography.

For the study of neurological damage the following were used: electroneuromyography data, VCM (motor conducting velocity), VCS (sensory conducting velocity), ocular fundus exam, electroencephalography (EEG), nervous and muscular biopsy with microscopic evaluation, anatomopathological exam of some parts gathered after brain excision, lung x-ray, mediastinum x-ray, bone x-ray, Doppler exam and cerebrospinal fluid exam.

Statistical analysis
Statistical data analysis was performed using specialized software. We calculated central tendency indicators (mean and standard deviation), structural indicators and frequency indicators (prevalence).

The specific objectives of the clinical trial of patients with thyroiditis were:
• Detecting the main neurological manifestations;
• Evaluating the frequency of such cases;
• Identify the response of the neurological manifestations to treatment regarding this thyroid pathology.

No major sources of error have been identified in the process of data collection and analysis.

Results
In the study group we examined 26 cases of acute, subacute and chronic thyroiditis.

Out of all the cases of thyroiditis, there were recorded (fig. 1).

Fig. 1: Structure of the study group - based on the thyroiditis onset: acute, subacute and chronic.
• Acute thyroiditis - 4 cases (15.38% of the cases of thyroiditis in the study group);
• Subacute thyroiditis - 12 cases (46.15% of the cases);
• Chronic thyroiditis - 10 cases (38.46% of the cases).

Acute thyroiditis
These are rare disorders, representing 0.5% of thyroid pathology.

In the study group, they represented 0.64% of the pathology, data comparable to other similar studies conducted.

There were 4 cases of acute suppurative thyroiditis, probably of microbial etiology, present in 100% in women within the age range 20-29 years, coming from urban environment.

There were no other associations registered regarding other immune disorders or affections of other nature.

The clinical diagnosis was supported by the presence of a thyroid enlarged in volume, with redness of the superjacent teguments, local pain either spontaneous or on palpation, associated with signs of general distress: fever, cough, dysphagia, as well as headache, dizziness, myalgia, physical asthenia. The symptoms started suddenly.

Clinical examination: painful thyromegaly was associated in all cases.

Paraclinical
• Blood samples - were characteristic of an infectious status: increased ESR, leucocytosis with polymorphonuclear neutrophils predominance;
• Thyroid ultrasound showed in all 4 cases specific hypoechoic areas;
• Thyroid scintigraphy, performed in 2 cases revealed hypo- and affixation areas.

Since the symptoms and clinical signs resolved under antibiotic treatment, ABC (fine nee-
dle puncture biopsy) wasn’t practiced (method of choice in diagnosis, which allows detection of germs and antibiogram making).

The electroencephalogram was normal in all of the cases.

The neurological manifestations encountered in patients from the study group, with acute thyroiditis were not specific, without neurological signs, manifesting only through subjective phenomena.

Thus, in the studied cases, there were present, in sequence (fig. 2): headache - 2 cases; dizziness - 2 cases; myalgia - 4 cases, syncope - 1 case, anxiety - 2 cases, physical asthenia - 4 cases.

Table 1: Neuropsychiatric manifestations in acute thyroiditis.

<table>
<thead>
<tr>
<th>Case nr.</th>
<th>Identification data of the patient</th>
<th>Endocrinemanifestations</th>
<th>Neuropsychiatric and muscular manifestations</th>
<th>Thyroid ultrasound exam</th>
<th>Thyroid scintigraphy</th>
<th>Biological probes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Fem, 34 years</td>
<td>Painful thyromegaly</td>
<td>Headache</td>
<td>Thyroid lobes increased in size, hypoechoic structure</td>
<td></td>
<td>Thyroid increased in size, hypo and affixation areas.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Fever</td>
<td></td>
<td>ESR-100mm/1h WC-12000/mm PMN-90%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Fem, 27 years</td>
<td>Painful thyromegaly</td>
<td>Myalgia</td>
<td>Thyroid lobes increased in size, hypoechoic structure</td>
<td></td>
<td>ESR-90mm/1h WC-9800/mm</td>
</tr>
<tr>
<td>3</td>
<td>Fem, 24 years</td>
<td>Painful thyromegaly</td>
<td>Headache</td>
<td>Thyroid lobes increased in size, hypoechoic structure</td>
<td>Inhomogeneous capture of both the lobes, with areas of hypofixation in the right one</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Fem, 22 years</td>
<td>Painful thyromegaly</td>
<td>Dizziness</td>
<td>Thyroid lobes increased in size, hypoechoic structure</td>
<td></td>
<td>ESR-95mm/1h WC-9200/mm PMN-78%</td>
</tr>
</tbody>
</table>

Fig. 2: Neurological manifestations in acute thyroiditis.

Subacute thyroiditis

In the patient group with thyroid pathology there were 12 cases of subacute thyroiditis, representing 46.15% of the total cases of thyroiditis of the group.

Gender distribution

More affected were the females, the age distribution being:
• 30-39 years 2 cases;
• 40-49 years 2 cases;
• 50-59 years 2 cases;
• 60 years and over - 1 case (fig. 3).

Urban - rural distribution

• 10 cases - came from urban environment;
• 2 cases - came from rural environment (fig. 4).

Associations with other pathologies

• Hypochromic anemia - 2 cases;
• Diabetes - 1 case, in this case the patient associated left external oculomotor nerve paralysis trough diabetic neuritis.
There was one noted case with acute infection of the superior air ways in the recent pathologies of the patient.

**Clinical endocrinological diagnosis**

The patients initially presented local inflammatory phenomena, associated with an aspect that resembled the flu, the thyrotoxicosis phase being represented trough sweating, limb tremor, tachycardia, and hypothyroidism trough bradycardia, sleepiness and adynamia.

Painful thyromegaly was found in 2 cases and painless thyromegaly also found in 2 cases.

Low fever states appeared in 4 patients and cough was present in 2 cases.

Neuropsychiatric manifestations in patients with subacute thyroiditis from the study group included (fig. 5).

- Headache - 2 cases;
- Physical asthenia - 6 cases;
- Adynamia - 6 cases;
- Suffocating - 6 cases;
- “lump in the throat” – 4 cases;
- Dysphagia - 2 cases;
- Insomnia - 4 cases;
- Palpitations - 4 cases;
- Tearfulness - 2 cases;
- Vertigo - 10 cases;

In none of the cases were there any neurological focal signs found.

There had been situations in which patients with subacute thyroiditis presented themselves initially in the neurologic service with intense training headache, associated with vertigo. The clinical exam detected thyromegaly, the patient being sent to endocrinology section, where the diagnosis was confirmed.

Laboratory tests: we registered in all the cases:
- C reactive protein - +++;
- Fibrinogen - over 600mg/ml;
- ESR - over 80ml/h;
- Thyroid hormones - had values depending on the stage of hyperthyroidism or hypothyroidism in which the patient was in that moment of gathering biological probes: in the state of thyrotoxicosis there were 3 cases registered (increased T3 and T4 with decreased TSH), 2 cases presenting suggesting values of thyroid hormones for hypothyroidism (T3, T4 - decreased, TSH - increased). The other patients were in euthyroid state.

**Antithyroid antibodies - tested on 4 patients were in normal limits.**

Thyroid ultrasound examinations - initially presented inhomogeneous thyroid aspect, with limited hypoechoic areas - in 10 cases with better ultrasound aspect in the latest examinations.

Thyroid scintigraphy - done in 4 cases has shown projective areas of thyroid lobes increased in volume with hypocaptation areas (fig 6).

![Fig. 5: Neuropsychiatric manifestations in subacute thyroiditis.](image)

Fig. 5: Neuropsychiatric manifestations in subacute thyroiditis.

![Fig. 6: Thyroid scintigraphy - Patient N.E. 47 years old.](image)

Fig. 6: Thyroid scintigraphy - Patient N.E. 47 years old.

Thyroid capture much reduced, with the projection areas of the thyroid lobes still sketchy. Large amount of radiotracer free in circulation.

There was no fine needle puncture thyroid biopsy done on any of the patients.

**Neuroimaging**

In one of the cases, because of the persistence of headache under treatment there was a CT brain exam done which was in normal limits.

**Chronic thyroiditis**

The study group included 10 cases of chronic thyroiditis out of which 4 cases of atrophic chronic thyroiditis and 6 cases of lymphocytic chronic Hashimoto thyroiditis (fig. 7).

Chronic thyroiditis represented 38.46% of all the thyroiditis cases.
Distribution based on age range

- 30-39 years - 2 cases;
- 40-49 years - 2 cases;
- 50-59 years - 6 cases (fig. 8).

All the patients came from urban environment.

Associations with other pathologies

- myxedematous heart - 2 cases;
- paroxysmal rhythm disturbances - 2 cases;
- ischemic brain lacunas - 2 cases;
- bilateral cochlear neuritis - 2 cases;
- psoriasis - cases;
- hypocalcemic tetany.

Clinical endocrinological diagnosis

All the patients presented asymmetric thyromegaly with progressive evolution, dysphagia in 3 cases existing latero-cervical adenopathy.

Neuropsychiatric manifestations encountered in the cases of chronic thyroiditis from the studied group included

- vertigo - 4 cases;
- slowness in ideation - 2 cases;
- physical asthenia - 2 cases;
- hemicranias - 4 cases;
- retrieval disorders - 2 cases;
- sleepiness - 2 cases;
- dysphagia - 2 cases;
- lower limb sensory neuropathy - 3 cases - fig. 9.

Sensory neuropathy was confirmed through laboratory tests in one case, the other 2 cases being clinically diagnosed through the existence of superficial hypoesthesia and profound vibrating hypoesthesia in the distant third of the lower limbs.

Since through the laboratory tests at disposal we didn’t detect any other causes for the peripheral nervous suffering we interpreted these modifications as being determined by the same autoimmune mechanism as chronic thyroiditis.

The laboratory endocrinological diagnosis included

- thyroid hormone dosage which showed a euthyroid stage in 7 cases, hypothyroidism in 2 cases and hyperthyroidism - 1 case;
- antithyroglobulin antibodies and antiperoxidase antibodies were very much increased over the normal values;
- thyroid ultrasound registered hypoechoic aspects with increased size of the thyroid lobes;
- thyroid scintigraphy revealed the following aspects:
  - free radiotracer in circulation - 4 cases;
  - “cold” scintigraphic nodule - 2 cases;
  - hypocaptation - 4 cases;
  - excess captation under the form of hyperthyroidism (fig.10).

Neurological manifestations in chronic thyroiditis

Fig. 9: Neurological manifestations in chronic thyroiditis.

Fig. 10: Thyroid scintigraphy - very reduced thyroid captation with projecting areas of the thyroid lobes poorly sketched.
**Histopathologic exam**

The histopathologic diagnosis of chronic thyroiditis - Hashimoto form or atrophic form was previously established. One case of chronic Hashimoto thyroiditis was detected in the endocrinological department of the Galati Emergency Hospital. This allowed obtaining the following slides, using optical microscopy. The histopathologic exam of the probes gathered through fine needle puncture biopsy of the thyroid (fig. 11, 12, 13, 14).

![Histopathologic exam](image)

**Fig. 11:** Thyroid biopsy, O.C. x10, OB x10/ x20, H.E. coloration, fem., 51 years old: Atrophic thyroid follicles limited by eosinophilic cells, abundant lymphocytic inflammatory infiltrate, colloid intensely eosinophilic.

**Fig. 12:** Thyroid biopsy, O.C. x10, OB x10/ x20, H.E. coloration, fem., 51 years old: Atrophic thyroid follicles limited by eosinophilic cells, abundant lymphocytic inflammatory infiltrate, colloid intensely eosinophilic.

**Fig. 13:** Thyroid biopsy, O.C. x10, OB x10/ x20, H.E. coloration, fem., 51 years old: Atrophic thyroid follicles limited by eosinophilic cells, abundant lymphocytic inflammatory infiltrate, colloid intensely eosinophilic.

- Electroencephalogram - registered traces without any changes in cases with headaches.

**Neurological laboratory diagnosis included**

- Ocular fundus exam - without any specific modifications;

- Electroencephalogram - registered traces without any changes in cases with headaches.

**Electromyographic exam and determining the conducting speed.**

**Fig. 14:** Thyroid biopsy, O.C. x10, OB x10/ x20, H.E. coloration, fem., 51 years old: Atrophic thyroid follicles limited by eosinophilic cells, abundant lymphocytic inflammatory infiltrate, colloid intensely eosinophilic.

**Discussions**

In the acute thyroiditis clinical picture, there were no neurological characteristic signs, predominately existing complaints regarding the general infectious picture.

These data are consistent with the ones existing in the specialized literature, where there are no neurological characteristic changes mentioned regarding acute thyroiditis\(^1\).

The frequency of subacute thyroiditis in the studied group was smaller than the one found in specialized literature: 5-6% of the thyroid pathology\(^1\).

We manage to state that most of the cases of subacute thyroiditis were found in patients between 40-59 years old, data which corresponds to other studies\(^2\).

In none of the subacute thyroiditis were there any signs of neurological focal signs. This data corresponds to those existing in other studies\(^1\,^2\), according to which there aren’t any specific neurological determinations in subacute thyroiditis.

Subacute thyroiditis in the studied group was less frequent than in the data gathered from other studies.

In none of the cases were there registered specific neurologic manifestations, nor neurological focal signs.

Predominant were the neuropsychiatric accusations of headache, vertigo, sleep disorders.

Among the chronic thyroiditis patients there were no cases of focal thyroiditis or postpartum thyroiditis.

The pathology was present only in women.

We have not encountered any other associations with autoimmune pathologies (type 2 dia-
betes, vitiligo, systemic lupus erythematosus etc.), mentioned in other studies\(^1\) in the chronic thyroiditis group.

In chronic thyroiditis patients it is to be remarked the fact that the paresthesia accuses decreased after the treatment was given for thyroid pathology, fact that sustains the etiological idea previou In other studies, Duyff et al.\(^{\text{4}}\) mentions a case of Hashimoto thyroiditis associated with multifocal motor neuropathy with conductive block.

In the patients from the study group we did not encounter any type of motor pathology of the peripheral nerves, as another study concludes\(^{\text{5}}\).

In specialized literature there is mentioned a particular neurological manifestation associated to Hashimoto thyroiditis: Hashimoto encephalopathy (Steroid Responsive Encephalopathy Syndrome)\(^{\text{6}}\). It is a rarely encountered clinical status (there are 20 known cases), clinically manifested through confusion, myoclonus, epileptic seizures, hemiparesis, ataxia, psychosis, tremor, aphasia and coma in patients with antithyroglobulin antibodies, antimicrosomal -MAK and antithyroperoxidase -TAK with altered or normal thyroid function. Liver function can also be altered and in CSF(cerebrospinal fluid) there can be pleiocytosis, hyperproteinorachia, and there are oligoclonal bands present\(^{\text{7}}\). There is a form of apoplectic vasculitis with epileptic seizures, neurological focal deficits, coma and an insidious progressive form with focal seizures or generalized seizures, confusion, myoclonus, ataxia and even dementia\(^{\text{8}}\).

In the studied lot, we have not encountered any such neurological manifestation.

Also, we haven’t encountered in any of the followed patients chronic thyroiditis associated with myasthenia gravis, fact cited even in other studies.

Conclusions

In acute thyroiditis, the predominant symptoms are those of a generalized infection, with unspecific neurological accuses such as headaches and vertigo.

Both in acute and subacute thyroiditis there were unspecific accuses predominant, especially of psychiatric order.

The same neurological aspect was also observed in subacute thyroiditis, in which we did not encounter focal neurological signs or peripheral nervous system damage. Like in acute thyroiditis, subjective disorders were present in the subacute variety. These disorders include: headache, vertigo, sleep disorders, physical fatigue and adynamia.

Sensory neuropathy was detected in 30% of the cases, only one of which was confirmed through electrophysiological exam, the other ones being clinically diagnosed.

We have not encountered any cases of motor neuropathy.

In the chronic thyroiditis group, no neurological manifestations were detected.

Chronic thyroiditis had the same type of neuropsychiatric accuses. Also worth mentioning is sensory neuropathy of lower limbs, confirmed through electrophysiological exams. Neuropathy probably has the same autoimmune mechanism as the thyroid disease.

There were no registered cases of myasthenia gravis associated with the thyroid pathologies in the studied group.

Chronic headache and vertigo determined the neurologist to proceed to neuroimaging evaluation.

The patient first addressed the neurologist due to neuropsychiatric symptoms, who discovered the thyroid disease.

References

Corresponding author
AURELIA ROMILA
Geriatrics Department, University of Medicine and Pharmacy
“Dunarea de Jos”
Vadu Sacalelor, no.1, bl. Pescarus, ap. 8
Galati,
(Romania)