

Antithyroid psychosis

Manuel Menéndez
González

Hospital Álvarez-Buylla, Mieres, Spain.

Corresponding author:

 manuelmenendez@gmail.com

Abstract

The association of thyroid disorders and thyroid-related treatments with psychiatric disorders is well known. What is not recognized yet is if antithyroid antibodies may cause psychosis in the absence of encephalopathy and thyroid dysfunction. I report here the cases of 4 patients who developed *de-novo* psychosis where I found they had high titers of antithyroid antibodies, both antithyroglobulin and anti-TPO antibodies. All the four patients were women aging 39-64 years old, without history of psychiatric disorders until they started with an isolated and flourished picture of psychosis. Remarkably, thyroid function was normal. All four cases showed positive CSF thyroid antibodies and recovered after steroid therapy.

I propose to coin the term “antithyroid psychosis” to denote cases of *de-novo* psychosis with antithyroid antibodies in the absence of encephalopathy. The main importance of diagnosing these cases is that it is a tractable disorder. Screening for antithyroid antibodies should be considered in all patients with *de-novo* psychosis or postpartum psychosis.

Key words: autoimmune thyroid disease, Hashimoto, antithyroid psychosis, *de-novo* psychosis, postpartum psychosis, EAATD, SREAT.

Introduction

The association of thyroid disorders and thyroid-related treatments with psychiatric disorders is well known. For instance, the relationship between antithyroid medications and psychosis has been described time ago [1, 2]. “Thyrotoxicpsychosis”, that is, the presence of psychoses associated with thyrotoxicosis has been described more than 150 years ago. Basedow first described a psychotic illness in a patient with “exophthalmic goitre” [3] and several recent series have confirmed this association [4].

The association of encephalopathy with Hashimoto's thyroiditis [5], known as "Hashimoto encephalopathy", today named steroid-responsive encephalopathy associated with autoimmune thyroiditis (SREAT) or encephalopathy associated with autoimmune thyroid disease (EAATD) is also a classic syndrome [6]. Clinical manifestations of EAATD include a mixture of encephalopathic features such as seizures, behavioral and psychiatric manifestations, movement disorders, and coma. Although it has been linked to cases of Hashimoto's thyroiditis or thyroid dysfunction, the most common immunological feature of EAATD is the presence of high titers of antithyroglobulin or anti-TPO (antimicrosomal) antibodies.

What is not recognized yet is if antithyroid antibodies may cause psychosis in the absence of encephalopathy and thyroid dysfunction.

Cases report

In the last times I have had 4 patients who developed de-novo psychosis and I found they had high titers of antithyroid antibodies, both antithyroglobulin and anti-TPO antibodies. All the four patients were women aging 39-64 years old, without history of psychiatric disorders until they started with an isolated picture of psychosis in the 16-6 months before I first visited them. The clinical picture was flourished, with delusions, paranoia and hallucinations. I found no neurological deficits at examination other than bradypsychia and mild tremor, probably due to high doses of antipsychotic drugs they were taking. There were no signs of encephalopathy.

Laboratory findings were similar in the four cases: all patients have high titers of thyroid antibodies (1:690; 1:1250, 1:1250 and 1:10240; reference range, < 1:100), and the TPO antibody titer was (242 IU/mL; 318 IU/mL, 234 IU/mL and 415 IU/mL; reference range, <20 IU/mL).

Remarkably, thyroid function was normal; only one patient had mild thyroid failure (serum sensitive TSH, 5.1-15.6 mIU/L with normal T3 and T3). Erythrocyte sedimentation rate was mildly to moderately elevated in 2 cases (34 mm/h, 37 mm/h). The CSF was analyzed in the four patients: no infectious origins were identified, the protein level was elevated in 2 patients (55mg/dL and -61 mg/dL; reference range, <45 mg/dL) and one case had mild lymphocytic pleocytosis (white blood cell count, 13 cells/ μ L). The CSF IgG index was normal in all 4 cases, and the CSF IgG synthesis rate was elevated in 1 case. All four cases showed positive CSF thyroid antibodies although titration was not technically possible (probably due to very low titers).

All patients underwent EEG studies, of which 2 showed generalized, unspecific slowing activity while the other 2 were normal. We found no signs of focal slowing, triphasic waves or epileptic form abnormalities. One patient had a normal routine EEG result. Cranial MRI was performed in the four patients and all had normal brain imaging other than nonspecific white matter abnormalities consistent with mild small-vessel disease.

All four patients were put on intravenous methylprednisolone, 1 g/d for 5 days followed by oral steroid therapy 1 mg/Kg leading to clinical and EEG improvement within 3-6 weeks in all patients.

Discussion

Misdiagnosis of EAATD at presentation is common. Recent case reports showed that the clinical, laboratory, and radiologic findings associated with EAATD are more varied than previously reported [7, 8], but psychosis alone has not been described as a manifestation of autoimmune thyroiditis yet. These four cases I present here would be consistent with the diagnosis of EAATD if they had other clinical or elec-

troencephalographic signs of encephalopathy; but they did not. Therefore I prefer to name this picture “antithyroid psychosis”.

A similar condition is “postpartum psychosis”. Postpartum psychosis is a rare disorder affecting women who become psychotic in the first months after delivery. Autoimmune thyroid disease is present in a significantly high proportion of patients with postpartum psychosis [9]. It is well known that in women with a dysfunctional immune system (the autoimmune diseases, such as multiple sclerosis, rheumatoid arthritis, and autoimmune thyroiditis), the autoimmune symptoms are generally greatly ameliorated during pregnancy. However, this time of relatively low autoimmune activity is followed in the post-partum period by a “rebound” with greatly increased symptoms and greater autoantibody titers measured in the serum. Therefore, screening for antithyroid antibodies should be considered in patients with *de-novo* psychosis or postpartum psychosis.

Until recently, it was unclear whether antithyroid antibodies in EAATD represent an immune epiphenomenon or they are really associated with pathogenic mechanisms of the disorder. However, today

there are several evidences supporting this hypothesis. First, antithyroid antibodies and circulating immune complexes (CIC) were found in the CSF of EAATD, and the synthesis of autoantibodies and CIC was seen to be intrathecal [10, 11]. Second, the responsiveness of EAATD to immunosuppressant therapies and plasmapheresis also supports the hypothesis that this is a disorder that involves immune pathogenic mechanisms. Relapses are usually controlled with steroids and maintenance therapy was reported successful with rituximab, intravenous immunoglobulin (IVIg), azathioprine, mycophenolate mofetil and methotrexate [8].

Conclusion

In resume, I propose to coin the term “antithyroid psychosis” to denote cases of *de-novo* psychosis with antithyroid antibodies in the absence of encephalopathy. The main importance of diagnosing these cases is that it is a tractable disorder. Screening for antithyroid antibodies should be considered in all patients with *de-novo* psychosis or postpartum psychosis.

References

- Hedley, AJ., Bewsher, PD. Psychosis and antithyroid drug therapy. *Br Med J.* 1969; 3 (5670): 596-597.
- Vita, R., Mazzi, V., Antonelli, A., Benvenga, S. Antithyroid medications and psychosis. *Expert Opin Drug Saf.* 2013; 12 (6): 865-72.
- Greer, S., Parsons V. Schizophrenia-like psychosis in thyroid crisis. *British Journal of Psychiatry* 1968; 114: 1357-62.
- Brownlie, BE., Rae, AM., Walshe, JW., Wells, JE. Psychoses associated with thyrotoxicosis - 'thyrotoxic psychosis'. A report of 18 cases, with statistical analysis of incidence. *Eur J Endocrinol.* 2000; 142 (5): 438-44.
- Hashimoto, H. Zur Kenntniss der lymphomatosen Veränderung der Schilddrüse (Struma lymphomatosa). *Arch Klin Chir.* 1912; 97: 219-48.
- Schiess, N., Pardo, CA. Hashimoto's encephalopathy. *Ann N. Acad Sci.* 2008; 1142: 254-65.
- Castillo, P., Woodruff, B., Caselli, R. et al. Steroid-Responsive Encephalopathy Associated With Autoimmune Thyroiditis. *Arch Neurol.* 2006; 63 (2): 197-202.
- Olmez, I., Moses, H., Sriram, S., Kirshner, H., Lagrange, AH., Pawate, S. Diagnostic and therapeutic aspects of Hashimoto's encephalopathy. *J Neurol. Sci.* 2013; 331 (1-2): 67-71.
- Bergink, V., Kushner, SA., Pop, V., Kuijpers, H., Lambregtse-van den Berg, MP., Drexhage, RC., Wiersinga, W., Nolen, WA., Drexhage, HA. Prevalence of autoimmune thyroid dysfunction in postpartum psychosis. *Br J Psychiatry.* 2011; 198 (4): 264-8.
- Ferracci, F., Moretto, G., Candeago, RM., Cimini, N., Conte, F., Gentile, M., Papa, N., Carnevale, A. Antithyroid antibodies in the CSF: their role in the pathogenesis of Hashimoto's encephalopathy. *Neurology.* 2003; 60 (4): 712-4.
- Gini, B., Lovato, L., Cianti, R., Cecotti, L., Marconi, S., Anghileri, E., Armini, A., Moretto, G., Bini, L., Ferracci, F., Bonetti, B. Novel autoantigens recognized by CSF IgG from Hashimoto's encephalitis revealed by a proteomic approach. *J Neuroimmunol.* 2008; 196 (1-2): 153-8.

Comment on this article:



<http://medicalia.org/>

Where Doctors exchange clinical experiences, review their cases and share clinical knowledge. You can also access lots of medical publications for free. **Join Now!**

Publish with iMedPub

<http://www.imedpub.com>

Archives of Medicine encompasses all aspects of medical science and clinical practice and cooperates closely with *Archivos de Medicina*, a Spanish-language open access journal.

Submit your manuscript here:

Archives of Medicine

<http://www.archivesofmedicine.com>

Archivos de Medicina

<http://www.archivosdemedicina.com>