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Association of Graves' Disease and Systemic Lupus Erythematosus

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Abstract

Summary of Lupus and Basedow Disease Association: The association lupus auto-immune thyroid disease is well known. Lupus is most commonly associated with Hashimoto's thyroiditis. As for Graves' disease, it is most often associated with pernicious anaemia, vitiligo, idiopathic purpura and myasthenia gravis. To our knowledge, we report the first case of lupus associated with Graves' disease in sub-Saharan Africa. Observation: A female patient of 52 years old has been followed since February 2010 for systemic lupus diagnosed on biological and immunological clinical ACR criteria. There was no skin ailment and kidneys involved. Combined treatment with high-dose corticosteroids early and rapid decrease and hydroxychloroquine was established with good clinical and biological evolution. One year later the patient developed thyrotoxicosis syndrome and vascular goitre without exophthalmos associated with the presence of antibodies anti receptor of TSH leading to the diagnosis of Graves' disease. The patient has been treated with synthetic anti-thyroid and beta blocker allowing the regression of clinical symptoms and the normalization of thyroid hormones. Since then, the patient had not shown other signs of systemic affection. Conclusion: Systemic diseases are often associated with autoimmune thyreopathies. But association of lupus with Graves' disease has been rarely described in the literature. One should always watch out for the occurrence of thyroid disease in front of any systemic disease and vice versa.

Keywords

Lupus, Graves' Disease, Autoimmune, Dakar

1. Introduction

Autoimmune thyreopathies such as Graves' disease and more frequently Hashimoto thyroiditis can be associated with other auto immune systemic or organ specific diseases. The more frequently reported associations in these

autoimmune thyreopathies are Biermer anaemia, vitiligo, myasthenia, Sjogren disease or rheumatoid polyarthritis. Graves' disease is very often associated with Biermer disease, vitiligo, idiopathic purpura thrombopenic and myasthenia [1]. There is a possible association with lupus. Systemic lupus is more frequently associated with auto immune hypothyroidisms. The association with Graves' disease and systemic lupus is rarely described in the literature. We are reporting the first observation in Senegal.

2. Observation

A 52-year-old woman was followed on an outpatient basis since February 2010, in an internal medicine department of the University Hospital of Dakar, for systemic lupus diagnosed according to the ACR criteria modified, non-erosive rheumatoid arthritis and non-deforming small joints (hands, wrists and feet), unilateral serofibrinous pleurisy without cutaneous signs. On interrogation, the history was unremarkable. There were no other systemic affections.

A full blood count showed leukopenia with bicytopenia at 3000/mm^3 and anaemia (normocytic normochromic) haemolytic to 9.2 g/dl with direct Coombs test positive and anti Sm antibodies were positive at 2.9 (normal < 0.9). There were no other serous or visceral affections. The 24-hour proteinuria was zero.

The patient was put under corticosteroids (Prednisone) 1 mg/kg for one month, followed by a rapid reduction in 4 weeks of dosing, in increments of 10 mg in combination with hydroxychloroquine 400 mg/day for 6 months. The outcome was favourable with regression of signs of arthritis, loss of pleurisy and normalization of hematologic biological signs after 6 months of treatment.

In November 2011 (*i.e.* 22 months after taking hydroxychloroquine), she presented a syndrome of thyrotoxicosis combining weight loss despite keeping up of appetite, feelings of tachycardia with palpitations, non-neurological trembling of extremities, thermophobia, physical asthenia and vascular goitre without exophthalmia. There were no other signs of thyrotoxicosis.

Hormone check-up showed a collapsed TSHus rate (less than 0.005 IU/L). Anti TSH antibodies were strongly positive 124.8 IU/L (normal < 1.5).

The thyroid Doppler ultrasonography objectivised a homogeneous diffuse goitre hyper vascular. The patient was put under Carbimazole 5 mg: 45 mg/day and propranolol 120 mg/day associated with their previous treatment 10 mg/day corticosteroid and hydroxychloroquine 400 mg/day for two months, followed by 20 mg/day maintenance therapy of Carbimazole. Currently it has a maintenance involving 5 mg of Carbimazole 5 mg of Prednisone daily and 200 mg morning and evening of hydroxychloroquine treatment.

The evolution was favourable with no evidence of thyrotoxicosis signs. The thyroid check-up was also normalized. Only the rate of anti TSH receptor antibody remained still high at 27 IU/L after 14 months of treatment. There was no recurrence of signs or other systemic affections.

3. Discussion

We report a case of lupus associated with Graves' disease. The diagnosis of systemic lupus was placed before clinical criteria (a non-deforming non-erosive rheumatoid arthritis of the small joints, unilateral serofibrinous pleurisy) biological (a bicytopenia with leukopenia 3000/mm^3 and haemolytic anaemia to 9.2 g/dl with direct Coombs test positive) and immunologic (positivity of anti Sm). Graves' disease occurred almost two years after diagnosis of treated lupus disease.

The diagnosis of Graves' disease was based on manifestations of hyperthyroidism on the one hand and on the other hand autoimmunity events [1]. The thyroid autoimmunity in Graves' disease typically causes a homogeneous diffuse vascular goitre, Graves' orbitopathy and the presence of anti TSH receptor antibody. Goitre is present in the majority of patients while exophthalmos occurs in half of the cases. The development of antibodies to the anti TSH receptor is a main characteristic of Graves' disease [2]. In our observation the patient had more signs of hyperthyroidism, a vascular goitre and a high level of antibodies anti receptor of the TSH to 124.8 IU/L allowing the diagnosis despite the absence of exophthalmos. This rate remained still high after 14 months of treatment.

Several authors have stressed the frequency of the association of systemic disease and autoimmune thyreopathies, but their actual number is unknown. In a study conducted by Gaches *et al.* [3], analysing 218 patients suffering from autoimmune thyreopathy, 30 patients, *i.e.* 13.76% had one or more other autoimmune diseases associated with autoimmune thyreopathy. In the UK, Boelaert *et al.* [4] have studied the prevalence of the association autoimmune thyreopathy and system disease in 3,286 Caucasian subjects. They were distributed as fol-

lows, 2791 cases of Graves' disease and 495 cases of Hashimoto's thyroiditis. The prevalence of another autoimmune disease was 9.67% in Graves' disease and 14.3% in case of Hashimoto's thyroiditis.

The most common associations in autoimmune thyroid disease were the Gougerot syndrome, Biermer disease, and primitive biliary cirrhosis. Graves' disease is very often associated with Biermer disease, vitiligo, idiopathic purpura, and myasthenia [1]. The association systemic lupus-Graves' disease is a clinical entity rarely described in the literature.

In fact, systemic lupus is more usually associated with autoimmune hypothyroidism. Appenzeller *et al.* [5] have followed 524 patients affected by lupus: 32 of 524 patients (6.1%) were suffering from thyroid autoimmune diseases of which 28 with an hypothyroidism. In another study Mzebi *et al.* [6], in which 97 patients affected by lupus were followed, 9 patients had thyroid dysfunction with hypothyroidism. Toujani [7] has described a case of lupus associated with Graves' disease. Mokhtar [8] has reported two cases. For the first case, it was systemic lupus associated with Graves 'disease and for the second Graves' disease associated with anti-phospholipids syndrome. Baili [3] has also described the association as well as Baleva [9], in 4 cases of systemic lupus erythematosus.

The terms of the lupus-Basedow disease association are variable. Lupus can precede Graves' disease that was the case in this observation. This same observation was made by Mokhtar [8]. In other cases lupus can occur after the diagnosis of Basedow disease as Toujani observed [7] and Baleva [9]. It is also possible that these two conditions are concomitant as observed by Baili. [10]

In the series of Gaches *et al.* [3] for 17 cases (56.8%), the diagnosis of systemic disease associated was increased concomitantly with that of autoimmune thyroid disease; in 5 patients (16.6%) system disease has preceded thyroid disease and in 8 patients (26.6%) thyroid disease was revealing.

These results require a clinical, biological and immunological monitoring of thyroid function in all patients followed for lupus or other systemic disease.

This association between two autoimmune diseases guides discussions around dysimmune mechanisms. A review of the literature allows considering a common pathogenetic link. There is a genetic field predisposing to the onset of single or multiple dysimmune diseases [3]. However, each of these two conditions has a peculiarity. It is usual to distinguish the specific organ auto-immunity and systemic auto-immunity. In the first case, the loss of self-tolerance are only vis-à-vis one or more molecules of that organ, while in the other case it is recognized that excessive polyclonal activation lymphocyte B leads to the production of many varieties of antibodies and immune pathological lesions of different organs. However, the boundary between these two forms of auto-immunity is often difficult to trace; it is not clear that different mechanisms are involved [11].

Graves' disease presents a clear female predominance in the literature [1]. Severe forms of lupus disease are indicative of early high-dose corticosteroid therapy for several weeks or months. The recommended dose of prednisone varies between 0.5 mg kg/day and 1.5 mg to 2 kg/day during the first month, preceded by intravenous glucocorticoid methylprednisolone assaults at a dose of 1 g/24 hours for three days. Currently many authors, in case of renal active impairment proliferative, prescribe right away immune suppressants. It is either mofetil per os associated with a high dosage of corticoid therapy, or oral intravenous cyclophosphamide once a month for the first six months [12]. In our case, the patient had a blood dyscrasias without renal and neurological involvement. She was put under corticosteroid 1 mg/kg associated with synthetic antimalarial. The postoperative course was uneventful with a regression of joints' pain, pleurisy and normalization of blood counts and that is when the Graves' disease appeared.

Treatment of Graves' disease is based on the prescription of synthetic anti thyroid loading dose, allowing a rapid normalization of thyroid hormone levels, followed four weeks after by a maintenance dose to be administered [13]. The objective of maintenance therapy is to maintain a euthyroid state for extended periods. This allows the reduction of the auto-immune process and therefore the title of antibodies receiver until they disappear, thus promoting the remission of the disease. This treatment should be continued for 18 to 24 months. The remission rate is above 50%. The occurrence of relapse after discontinuation of medical treatment occurs in the majority of cases quickly enough [14]. In our patient the long-term treatment with synthetic anti-thyroid and propranolol led to a disappearance of clinical signs of thyrotoxicosis and normalization of thyroid hormones. However the anti-receptor antibody levels remains positive at 32 which predisposes to a possible relapse.

4. Conclusion

The autoimmune thyroid diseases are often associated with systemic diseases. Lupus is most frequently seen in

autoimmune hypothyroidism. However, Graves' disease is rarely associated with lupus. This is the first observation reported in Sub-Saharan Africa. A systematic examination of the thyroid should be practiced regularly in front of any systemic disease.

References

[1] Groussin, L. and Bertherat, J. (2007) Pathologie thyroidienne. *Revue Francophone des Laboratoires*, **2007**, 34-36.

[2] Prabhakar, B.S., Batin, R.S. and Smith, T.J. (2003) Current Perspective in the Pathogenis of Graves' Disease and Ophtalmopathy. *Endocrine Reviews*, **24**, 802-835. http://dx.doi.org/10.1210/er.2002-0020

[3] Gaches, F., Delaire, L., Nadalon, S., Loustau Ralli, V. and Vidal, E. (1988) Fréquence des maladies auto immunes chez 218 patients atteints de pathologie thyroïdienne auto-immunes. *Revue de Médecine Interne*, **19**, 173-179. http://dx.doi.org/10.1016/S0248-8663(97)80716-3

[4] Boelaert, K., Newby, P.R., Simmonds, M., Holder, R.L., Carr-Smith, J.D., Heward, J.M., Manji, N., Alahabadia, A., Armitage, M., Chatterjee, K.V., Lazarus, J.H., Pearce, S.H., Vaidya, B., Gough, S.C. and Franklyn, J.A. (2010) Prevalence and Relative Risk of Other Autoimmune Diseases in Subjects with Autoimmune Thyroid Disease. *The American Journal of Medicine*, **123**, 183.e1-9.

[5] Appenzeller, S., Pallone, A.T., Natalin, R.A. and Costallat, L.T. (2009) Prévalence of thyroïd dysfonction in systemic lupus erythematous. *Journal of Clinical Rheumatology*, **15**, 117-119. http://dx.doi.org/10.1097/RHU.0b013e31819dbe4c

[6] Mzabi, A., Ben Ismaïl, F., Mrad, B., Karmani, M., Toumi, S., Ahiri, H.H. and Laouani Kechrid, C. (2011) Lupus érythémateux systémique et dysthyroïdies. *Thyroïde/Annales d'Endocrinologie*, **72**, 388.

[7] Toujani, W., Berriche, O., Zantour, B., Alaya, W. and Sfar, M.H. (2011) Association lupus érythémateux systémique et maladie de Basedow. *Thyroïde/Annales d'Endocrinologie*, **72**, 395.

[8] Mokhtar, M., Ben Kacimi, N., Hamida, F., Amrandi, A. and Bouafia, M.T. (2013) Basedow et maladies auto immunes: 2 observations rares. *Thyroïde/Annales d'Endocrinologie*, **4**, 353.

[9] Baleva, M., Nikolov, R., Manov, E., Stoikou, A., Shaboni, R., Dourmishev, L. and Nikolov, M. (2013) The Coexistence of Systemic Lupus Erythematous and Thyrotoxicosis: The Diagnostic Value of Anti. *International Journal of Immunopathology and Pharmacology*, **26**, 217-222.

[10] Baili, L., Rachdi, I., Ben Dhaou, B., Aydi, Z., Boussein, F., Ketari, S. and Rokbani, L. (2011) Association d'un lupus érythémateux systémique et d'une maladie de Basedow. Etiopathogénie croisée ou association fortuite? *Thyroïde/Annales d'Endocrinologie*, **72**, 391.

[11] Brouet, J.C.L. (1998) Auto-immunité: Mécanismes-physiopathologie. *Revue Française des laboratoires*, **302**, 49-51. http://dx.doi.org/10.1016/S0338-9898(98)80086-3

[12] Meyer, O. (2005) Lupus érythémateux systémique. *EMC—Rhumatologie-Orthopédie*, **2**, 1-32. http://dx.doi.org/10.1016/j.emcrho.2004.08.005

[13] Kaguelidou, F., Carel, J.C. and Lager, J. (2005) Grave's Diseases in Children. *Best Practice and Research Clinical Endocrinology and Metabolism*, **28**, 233-243.

[14] Léger, J. (2010) Pathologie auto-immune thyroïdienne. *Archives de Pédiatrie*, **17**, 595-596. http://dx.doi.org/10.1016/S0929-693X(10)70014-2