Other potential changes in this syndrome include pre-
excitation syndrome, left ventricular hypertrophy, dilated
cardiomyopathy¹, retinal macular dystrophy, intestinal
pseudo-occlusion, neuropsychiatric changes, lactic acidosis,
and complications during pregnancy (prematurity, placenta
accreta).⁶

Diagnosis is based on molecular studies which look for the
mtDNA mutation. Two techniques may be used, sequencing
and PCR-RFLP.

Treatment consists of the administration of coenzyme
Q10, an electron transporter of the respiratory chain which
acts as an antioxidant, protecting cell membrane phos-
pholipids and low density lipoprotein cholesterol from the
oxidative damage caused by free radicals. Administration of
Q10 at a dosage of 150 mg/day for three years delays the
occurrence of insulinopenia and hearing loss and decreases
post-exercise lactate levels.⁹ However, other authors have
not supported these findings.¹⁰ Statins should be used with
care because they decrease coenzyme Q10 levels. Other
treatments used in other mitochondrial syndromes include
arginine, L-carnitine, and multivitamin complexes.

In conclusion, although the prevalence of mitochondrial
diabetes in the diabetic population is low, its diagnosis is
important because it has a different prognosis and treat-
ment. It should be suspected in the presence of a personal
and/or family history of diabetes and deafness or microvas-
cular complications that do not correlate with diabetes
duration, and in slim diabetic patients with negative pan-
creatic autoimmunity.

References

1. Maassen JA, Jahangir RS, Janssen GM, Raap AK, Lemkes HH,
t’Hart LM. New insights in the molecular pathogenesis of the
maternally inherited diabetes and deafness syndrome.
2. Salles JE, Kasamatsu TS, Dib SA, Moises RS. Beta-cell function in
individuals carrying the mitochondrial tRNA leu (UUR) mutation.
Molecular mechanisms and clinical presentation. Diabetes.
4. Guillausseau PS, Bassin P, Dubois-LaForgue D, Timsit J, Virally M,
Gin H, et al. Maternally inherited diabetes and deafness:
a multicenter study. Ann Intern Med. 2001;9:
721–8.
5. Uimonen S, Moilanen JS, Sorri M, Hassinen IE, Majamaa K.
Hearing impairment in patients with 3243A>G mtDNA muta-
tion: phenotype and rate of progression. Hum Genet.
6. Jansen JJ, Maassen JA, van der Woude FJ, Lemmink HA,
Van den Ouwereland JM, t’Hart LM, et al. Mutation in mitochon-
drial tRNA(leu(UUR)) gene associated with progressive kidney
7. Majamaa-Voltti L, Peuhkurinen K, Kortalaainen ML, Hassinen IE,
Majamaa K. Cardiac abnormalities in patients with mitochon-
drial DNA mutation 3243A>G. BMC Cardiovasc Disorders. 2002;
2:12.
8. Hosono T, Suzuki M, Chiba Y. Contraindication of magnesium
sulfate in a pregnancy complicated with late-onset diabetes
mellitus and sensory deafness due to mitochondrial myopathy.
et al. The effects of coenzyme Q10 treatment on maternally
inherited diabetes mellitus and deafness, and mitochondrial
DNA 3243 (A to G) mutation. Diabetologia. 1998;41:584–
8.
10. Silvestre-Aillaud P, Vendan D, Paquis-Fluckinger V, Pouget J,
Pelissier JF, Desneeuve C, et al. Could coenzyme Q10 and
L-carnitine be a treatment for diabetes secondary to 3243 muta-

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Lupus, graves’ disease, and vasculitis.
A case report

Lupus, enfermedad de graves y vasculitis.
A propósito de un caso

Autoimmune thyroid disease (AITD), characterized by the
presence of antibodies against thyroid antigens, is associ-
ated with a number of non-organ-specific rheumatological
disorders such as systemic lupus erythematosus (SLE),
rheumatoid arthritis, and Sjögren’s syndrome.¹² For exam-
ple, while the prevalence of subclinical hypothyroidism
(SCH, normal T4 with elevated TSH) is 4.3% in the general
population,³ it is increased to 11–13% in patients with SLE.⁴,⁵
Similarly, the prevalence of anti-thyroid peroxidase antibod-
ies (anti-TPO) is 10–12% in the general population,³,⁶ but
17–23% in SLE patients.⁴,⁵ Clinical or subclinical hypothy-
roidism is usually common in patients with SLE and accounts
for more than 87.5% of thyroid function changes in these
patients.⁵,⁷ As regards Graves’ disease (GD), it is less com-
mon in both the general population (0.5%)³ and patients with
SLE (1.7%).¹

Antithyroid drugs are associated with adverse events,
and most of them are mild and uncommon (less than 5%),
but, in some cases, they may cause severe autoimmune
disorders such as vasculitis, polyarthritis, or drug-induced
lupus.⁸ Vasculitis associated with antithyroid drugs usually
consists of a combination of polyarthralgia and skin lesions.
However, it may affect other organs such as kidney, lung,

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gastrointestinal tract, or brain. We report the case of a female patient recently diagnosed with SLE and renal impairment who showed GD and worsening of lupus nephritis due to vasculitis associated with the use of dipyrone after being symptom-free for three years.

A 24-year-old female patient with an unremarkable clinical history was admitted to hospital for the recent onset of a nephrotic syndrome (24-h proteinuria, 8.75 g/day) and moderate renal failure (glomerular filtration rate, 80 mL/min). The result of a renal biopsy was consistent with class V lupus nephritis (diffuse membranous glomerulonephritis). Positive ANA and anti-DNA tests completed the diagnostic criteria. Treatment was therefore started with prednisone 60 mg/day and bimonthly intravenous cyclophosphamide pulses. The clinical course was characterized by the remission of proteinuria, asymptomatic SLE, and the occurrence of iatrogenic Cushing syndrome.

Three years later, the patient reported fine hand tremor, heat intolerance, palpitations, and weight decrease. Physical examination showed exophthalmos, diffuse goiter (60 g), and hyperreflexia. Laboratory test results included TSH 0.042 µIU/mL (normal, 0.3–5), free T4 6.85 ng/dL (normal, 0.8–2), and total T3 415 ng/dL (normal, 86–190). Anti-TPO antibodies were positive, and iodine uptake was 60% at 24 h (normal, 15–35). Anti-TSH receptor antibodies were not measured. These results confirmed the diagnosis of GD, and treatment was started with dipyrone 20 mg/day and propranolol 40 mg three times daily. After one week of treatment, the patient experienced malaise, fatigue, joint pain, and generalized edema. A repeat 24-h urine protein test showed a value in the nephrotic range. In our department, it was assumed that renal impairment was secondary to vasculitis induced by antithyroid drugs, and dipyrone was therefore discontinued. No repeat renal biopsy or measurement of antineutrophil cytoplasmic antibodies (ANCA) was performed. The disease activity index for SLE (SLEDAI) was consistent with moderate disease. However, serum complement levels and platelet and WBC counts were normal. The patient continued to receive propranolol and prednisone. After one week, she was administered 12 mCi of 131I. The clinical course was favorable. Massive proteinuria disappeared, SLE remained asymptomatic, and the patient developed hypothyroidism, which was treated with levothyroxine 50 µg daily.

Up to 25% of patients with SLE may have thyroid dysfunction, which most commonly occurs as SCH and the presence of anti-thyroid antibodies. Anti-thyroid antibodies may even appear before thyroid dysfunction in 70% of SLE patients. On the other hand, 30% of patients with AITD have an associated systemic autoimmune disease, particularly patients with Hashimoto’s thyroiditis. Rheumatoid arthritis is the most commonly associated autoimmune disease.

This event may be related to polyautoimmunity, a condition in which autoimmune diseases with different phenotypes occur in the same person or familial groups. These diseases may share common pathophysiological mechanisms such as genetic factors, cross-reactivity between their autoantibodies, T cells autoreactive to different autoantigens, or similar variations in their cytokine patterns.

Systemic autoimmune diseases could also accelerate the occurrence of anti-thyroid antibodies in susceptible subjects. The prevalence of anti-TPO in the general population over 18 years of age is approximately 10%, but may be increased to 30% in women older than 70 years. Thus, the progression of the thyroid autoimmune process (the presence of autoantibodies, SCH, hypothyroidism) could be accelerated.

GD, as a variant of AITD, is less common, but these patients may spontaneously evolve to hypothyroidism. In addition, autoantibodies, which stimulate and block the action of antineutrophil cytoplasmic antibodies (ANCA) in vasculitis induced by antithyroid drugs, and dipyrone was not dose-dependent. This condition is usually characterized by renal impairment, arthritis, skin ulcers, and respiratory symptoms. Thionamides have been shown to accumulate in neutrophils, where they induce the production of toxic substances which finally act as immunogens.

In our patient, the administration of dipyrone triggered a generalized inflammatory process characterized by proteinuria and SLE exacerbation. The discontinuation of the triggering agent and the use of glucocorticoids resulted in a significant improvement.

In conclusion, frequent evaluation of the thyroid profile and the presence of anti-thyroid antibodies is recommended in patients with SLE.

References


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