



SELECTIVE EMBOLIZATION OF THYROID ARTERIES AS AN ALTERNATIVE TREATMENT OF AMIODARONE - INDUCED HYPERTHYROIDISM



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Abstract: Background: A selective embolization of thyroid arteries (SETA) is a rarely performed procedure. Although 35 years have passed since the first description of the SETA application, only about 150-200 procedures have been published so far.

Case presentation: We present the case of a patient successfully treated for amiodarone-induced hyperthyroidism using the SETA method. Patient had a history of paroxysmal atrial fibrillation (PAF), diagnosed three years earlier, treated with an anticoagulant – rivaroxaban. During 35 months, amiodarone was used as a method for treating the PAF. During the treatment, the patient developed hyperthyroidism. The patient was treated with thiamazole, propranolol and sodium perchlorate. After obtaining euthyrosis, SETA was performed. The patient underwent selective embolization of the left superior and right inferior thyroid arteries with a sclerosing agent – polyvinyl alcohol with good clinical effect. A thyrostatics agents were discontinued.

Conclusions: This case demonstrates difficulties in differential diagnosis of the type of amiodarone-induced hyperthyroidism. Normal ultrasound image of the thyroid gland and absence of antithyroid antibodies suggests type II of amiodarone-induced hyperthyroidism. While, a good, fast response to thyrostatics – type I. It seems, therefore that the diagnosis of the mixed type of amiodarone-induced hyperthyroidism is justified. Further research are also required to assess the safety and efficacy of SETA in amiodarone-induced hyperthyroidism in larger groups of patients.

Key words: embolization, hyperthyroidism, amiodaron, thyroid arteries, sodium perchlorate.osis.

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Introduction

Selective embolization of thyroid arteries (SETA) is a rarely performed procedure. Although 35 years have passed since the first description of the SETA application, only about 150-200 procedures have been published so far [1, 2]. This is most likely due to the availability of traditional forms of thyroid disease treatment options: pharmacotherapy, radioactive iodine treatment (RIT) and surgery. Each of the above methods has its limitations and is not always acceptable by both the patient and the physician. It seems that treatment of amiodarone-induced hyperthyroidism may be a special indication for the use of SETA. Pharmacological treatment with thyrostatics is associated with the possibility of allergic reactions, liver and bone marrow injury and secondary agranulocytosis and thrombocytopenia. Administration of RIT is not useful due to blockade of iodine uptake by long-term use of amiodarone. Surgical treatment may be particularly dangerous due to frequent comorbid cardiac arrhythmias, exacerbation of heart failure, and the possibility of bleeding complications [3, 4]. We present the case of a patient successfully treated for amiodarone-induced hyperthyroidism with the use of the SETA method.

Case report

Fifty-nine years old patient has been under the care of the Department of Endocrinology and Isotope Therapy of the Military Medical Institute for 3 months. The patient was referred due to hyperthyroidism non-reactive to a thyrostatic treatment with thiamazole. Patient had a history of paroxysmal atrial fibrillation (PAF), diagnosed three years earlier, treated with an anticoagulant – rivaroxaban. In addition, the patient had also a history of benign prostatic hypertrophy and degenerative spine disease. Amiodarone had been used for 36 months as a method for treating the PAF. Subsequently, the drug was discontinued due to poor tolerance of physical effort, increased palpitations, hand tremors and symptoms of NYHA class II heart failure. In the ECHO exam, moderate enlargement of the left atrial area (LAA) – 26 cm², borderline size of the right atrium and right ventricle was found. In addition, borderline thickness of left ventricular muscle was described, without segmental contractility disturbances, with left ventricular ejection fraction (LVEF) of 63%. Heart valves were without abnormalities. Chest X-ray was normal. Ultrasound examination revealed a non-enlarged, normal, echogenically homogeneous thyroid, with right lobe dimensions: 18x25x48 mm, left

lobe 20x21x51 mm, with normal vascular flow in the entire gland. A single, isoechogenic, solid-cystic focal lesion of 7x7 mm, with a peripheral type of vascularization, was visualized in the superior pole of the right lobe. No abnormalities were found in the regional cervical lymph nodes. In the additional tests, thyrotropin (thyroid stimulating hormone – TSH) concentration was <0.005 uIU/ml (0.27–4.2 uIU/ml), free triiodothyronine (FT3) – 8.14 pmol/l (3.2–6.9 pmol/l), free thyroxine (FT4) 54.83 pmol/l (12–22 pmol/l). Neither the TSH receptor antibodies TRAb, thyroglobulin, nor thyreoperoxidase antibodies were found. Due to confirmed thyrotoxicosis, thiamazole was increased to 60 mg/day, beta-blocker – propranolol 240mg/day and sodium perchlorate in a dose of 4x10 drops, as an equivalent of 800–1000 mg sodium perchlorate per day, were started. Additional tests were performed after 7 days. No abnormalities were found in the peripheral blood morphology. There was an improvement in free hormone concentrations: FT4 decreased to 37.08 pmol/l, FT3 to 5.51 pmol/l. After 14 days of treatment, a significant further reduction of FT4 to 32.12 pmol/l, and FT3 to 4.28 pmol/l was achieved with the accompanying improvement in well-being, resolution of palpitations and improvement of physical performance. After 3 weeks of treatment, further improvement, in FT4 concentrations to 26.07 pmol/l, was observed. The patient was qualified for selective embolization of the thyroid arteries due to the possibility of only short-term use of sodium perchlorate, up to a maximum of 4 weeks. Initial selective arteriography of the superior and inferior thyroid arteries was performed from the incision of the right femoral artery, using the Seldinger method, under local anesthesia (1% procaine). The examination revealed narrow arteries: inferior left and superior right thyroid arteries. The decision about the extent of the embolization procedure was made based on the angiographic and clinical data. The patient underwent selective embolization of the left superior and right inferior thyroid arteries with a sclerosing agent – polyvinyl alcohol (PVA) (Figure 1A, 1B and 2A, 2B). The procedure was carried out without complications.

In the next days of follow up, the patient did not report any symptoms. There was no pain in the neck area. Laboratory tests showed a temporary reduction in total calcium concentration to a minimum value of 8.3 mg/dl (8.6–10.2 mg/dl), with no typical symptoms of tetany. In laboratory tests further reduction of FT3 to 2.8 pmol/l and FT4 to 22.76 pmol/l was found 3 days after SETA. The patient was discharged from the Endocrinology and Isotope Therapy Department on the fourth day after the procedure, in good clinical condition, with the recommended use of thiamazole in a dose of 20 mg/day and propranolol 4x120 mg. Four weeks after SETA, clinical euthyreosis was found with TSH concentration of 1.56 uIU/ml, FT3 – 2.36 pmol/l, FT4 – 16.25 pmol/l. Thiamazole dose was gradually reduced, and after 4 weeks the medication was discontinued. After achieving euthyreosis, electrical cardioversion was performed, which proved to be ineffective. After 3 weeks of electrical cardioversion, atrial fibrillation recurred.

Discussion

The presented clinical case requires a detailed discussion. Diagnosis of the disease and determination of the

cause of hyperthyroidism raise doubts. Long-term history of amiodarone treatment makes it easier to diagnose amiodarone-induced hyperthyroidism. However, it is difficult to differentiate between type I and II of the disease, which have completely different pathogenesis and treatment options [5].

Normal ultrasound picture of the thyroid gland – no nodular goiter with non-increased vascular flow, and the absence of antithyroid antibodies suggest the diagnosis of type II amiodarone-induced hyperthyroidism. This is mostly a self-limiting disease, responding to glucocorticosteroid treatment. It is believed that it is possible to distinguish the type of amiodarone-induced hyperthyroidism on the basis of color flow Doppler sonography (CFDS) even in 80% of cases [6]. The CFDS method is effective, especially if the tests are performed sequentially, but it is not useful in case of earlier application of thyrostatic drugs, what happened in the case discussed. Here, normal CFDS has made differential diagnosis difficult. Discontinuation of amiodarone did not inhibit thyrotoxicosis, but on the contrary, exacerbated the course of the disease. The patient was admitted with symptoms of heart failure, with atrial fibrillation, fast ventricular rate of 160/min, lack of clinical response to thyrostatic and beta-blocker therapy in full doses. Prednisone was not started due to concerns about the possible side effects of glucocorticosteroids (GSK), especially the increase in the volume of body fluids and its implications. In addition, according to available literature, the efficacy of oral glucocorticosteroids at FT4 concentrations exceeding 50 pmol/l is limited [7, 8]. Sodium perchlorate (Irenat®) treatment, at a dose of 1000 mg/day was included for the rapid control of hyperthyroidism symptoms. Sodium perchlorate competitively inhibits the sodium-iodide symporter, thereby blocking the iodine uptake system by thyroid follicular cells. In addition, it inhibits thyroid peroxidase, thereby reducing the incorporation of iodine into organic compounds. An additional effect of sodium perchlorate is the elimination of a follicular iodine pool not bound to thyroglobulin from the cell, and blockage of reutilization of iodine released from thyroid hormones; as a result, renal iodine excretion increases [9]. The drug after oral administration binds to albumin, it is not metabolized, and is excreted in an unchanged form by the kidneys. Sodium perchlorate is active very quickly and for a short time period. The effect of sodium-iodide symporter inhibition lasts up to several hours and even shorter in case of concurrent hyperthyroidism. The administration of sodium perchlorate with thiamazole enhances clinical effects, which was used in this case. The application of sodium perchlorate resulted in a relatively rapid achievement of euthyreosis. This drug, however, should not be used for more than 4 weeks. Its toxicity increases, especially to the bone marrow (significant risk of agranulocytosis) and to the kidneys [9, 10].

That good response to the treatment with thyrostatic medications on the contrary suggests the diagnosis of type I amiodarone-induced hyperthyroidism. Not standard plasmapheresis may be considered in the absence of response to thyrostatic drugs in order to achieve rapid euthyreosis [13]. After achieving euthyreosis, a method has been sought that would stabilize the clinical effect. Surgical treatment was postponed because of prophylactic treatment with new oral anticoagulant (NOAC) – ri-



Figure 1A. Selective arteriography the superior right thyroid artery before effective embolization with PVA.



Figure 1B. Selective arteriography the superior right thyroid artery after effective embolization with PVA.



Figure 2A: Selective arteriography the inferior left thyroid artery before effective embolization with PVA.



Figure 2B: Selective arteriography the inferior left thyroid artery after effective embolization with PVA.

varoxaban, high risk of hemorrhagic complications, and lack of patient's consent for proposed thyroidectomy [11, 12].

Thus, it was decided to perform SETA. Procedures of embolization of the thyroid arteries have already been described already in 1984. The first treatments concerned patients with parathyroid glands who were disqualified from surgery due to difficulties in surgical access [13]. Procedures of embolization of the thyroid arteries can be effectively performed as a rescue treatment after iatrogenic damage of thyroid vessels. Successful own experience of the Endocrinology and Isotope Therapy Department, as well as the available results of clinical trials, prompted to qualify the patient for embolization of the thyroid arteries. Since 2004, about 30 SETA procedures have been performed at the Department of Endocrinology and Isotope Therapy of the Military Institute of Medicine. In the years 2004-2005, we conducted the clinical trial that assessed SETA effectiveness. Fifteen patients were included in the study, among which one patient suffered from amiodarone-induced hyperthyroidism. In 67% of cases, two of the four thyroid vessels were embolized, most often the inferior right and left thyroid artery. After 12 weeks, euthyresia was obtained in 75%. Only 3 patients required substitution treatment with L-thyroxine [14]. Adverse events were rare. Most often it was a slight pain in the neck area and a temporary decrease in the total calcium blood concentration without clinical symptoms [15]. Similar results were obtained by other groups [16]. The patient discussed was qualified for SETA on the basis of promising examination results. The procedure turned out to be effective, safe and minimally invasive.

To summarize, the presented case demonstrates difficulties in differential diagnosis of the type of amiodarone-induced hyperthyroidism. Normal ultrasound image of the thyroid gland and absence of antithyroid antibodies suggests type II of amiodarone-induced hyperthyroidism. While a good, fast response to thyrostatics – type I. It seems therefore that, the diagnosis of the mixed type of amiodarone-induced hyperthyroidism is justified. Further research are also required to assess the safety and efficacy of SETA in larger groups of patients with amiodarone-induced hyperthyroidism in larger groups.

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