50 Gy) are required.[9] Chemotherapy has been used in adjuvant or neo-adjuvant protocols, as well as in combination with radiotherapy, but the overall result is not good.[3]

Taking into account that tumour growth depends on the formation of new vessels, other studies have investigated new lines of treatment, such as drugs that target the vascular endothelial growth factor (VEGF) pathway and its receptor (VEGFR), as well as tyrosine kinase inhibitors with activity against VEGFR, without encouraging results according to the data available to date.[9,10]

Conclusions

Publications in recent years have shown that, despite its low frequency, there are more and more cases of thyroid angiosarcoma being described in non-alpine regions. For this reason, this condition must be taken into account in the differential diagnosis of malignant thyroid disease. The presence of bleeding could make us suspicious. However, no effective treatment is currently available.

Conflicts of interest

None of the authors have any conflict of interest to declare.

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Role of plasmapheresis in the management of severe amiodarone-induced hyperthyroidism refractory to conventional medical treatment

Papel de la plasmaféresis en el manejo del hipertiroidismo severo inducido por amiodarona y refractario a tratamiento médico convencional

Amiodarone is a class III antiarrhythmic drug widely used in our setting for the treatment of cardiac arrhythmias. It is a benzofuran derivative with high iodine content, which can have a bearing on thyroid function at different levels (hypophysis, thyroid and peripheral receptors). In many cases, it can modify the circulating concentrations of thyroid hormones and be accompanied by both hypo- and hyperthyroidism, although the majority of patients remain euthyroid.[1,2]

The first-line treatment of amiodarone-induced hyperthyroidism is fundamentally medical with synthetic antithyroid drugs In the case of Type 1 thyrotoxicosis (iodine induced), or with glucocorticoids in type II (owing to glandular destruction). Other less conventional drugs include potassium perchlorate and cholestyramine.[3,4] Plasmapheresis has occasionally been used in cases of intolerance to antithyroid drugs, refractory hyperthyroidism, and to achieve euthyroidism prior to thyroidectomy, though clinical experience is scant.[5]

We present the case of a patient with structural cardiopathy with severe amiodarone-induced hyperthyroidism refractory to medical treatment which required a high number of plasmapheresis cycles prior to definitive treatment with thyroidectomy.

53-year-old male with Arterial hypertension, dyslipidaemia, obesity, sleep apnoea syndrome, and persistent anticoagulated atrial fibrillation, owing to which he had received treatment with amiodarone (200 mg/day) over 3

years, with the suspension thereof in the 2 months prior to admission, at which time it was replaced by bisoprolol.

The patient was admitted for a preferential coronary angiography owing to chest pain with elevated markers of cardiac damage, which turned out to be normal. A study with transthoracic echocardiography was completed, showing a severely dilated right ventricle and data on severe pulmonary hypertension, as well as the existence of a superior sinus venosus atrial septal defect, with indication of non-urgent surgical closure. During admission, a severe overt hyperthyroidism was discovered (TSH < 0.01 μIU/mL, normal range [NR]: 0.35–5.0; Free T4 [FT4] 10.03 ng/dl, NR: 0.7–1.98, and Free T3 [FT3] 9.3 pg/mL, NR: 2.3–4.2) one week before the catheterisation was to be performed, without having previously presented exposure to iodised contrast agents. Clinically, he did not report palpitations, tremor, nervousness, or any other symptom of thyroid hyperfunction. He presented with good blood pressure and heart rate control with beta blockers. A grade 2 goitre, with no nodules was palpable. The thyroid echography showed a normal-sized gland with decreased vascularisation. The thyroid autoimmunity study was negative and the Interleukin-6, normal (<2.7 pg/mL, NR: 0.0–4.4). In light of these findings and suspected amiodarone-induced hyperthyroidism, treatment was started with metimazol (30 mg/day) and prednisone (60 mg/day). During admission, the patient presented increasing serum levels of thyroid hormones, which made it necessary to increase the dose of metimazol (45 mg/day) and prednisone (90 mg/day) (Fig. 1). Acholestyramine (16 g/day) and potassium perchlorate (800 mg/day) were also associated. Despite this and, after supervising the proper adherence to the treatment, after three weeks the severe hyperthyroidism persisted (TSH < 0.01 μIU/mL, FT4 11.92 ng/dl and FT3 9.76 pg/mL) with the diagnosis of severe amiodrone-induced hyperthyroidism refractory to high doses of metimazol, corticosteroids, cholestyramine and potassium perchlorate being established, owing to which total thyroidectomy was proposed as definitive treatment. After discussing the case in a multi-disciplinary session with Cardiac Surgery, Cardiology, Anaesthesia, General Surgery and Endocrinology, it was decided to first perform a total thyroidectomy and, secondly, the closure of the ASD. With the aim of reducing perioperative cardiovascular risk, treatment with plasmapheresis was initiated with the aim of achieving euthyroid status.

The plasmapheresis sessions consisted of mixed plasma exchanges of albumin/plasma of 1.5 volumes in each session, performed by the Haematology Department using an apheresis machine. By way of complications, the patient presented various episodes of skin rash which required prophylactic antihistamine treatment with each exchange. During the procedure, a slight tendency towards anaemisation was observed (nadir of haemoglobin 11.2 g/dl, NR: 12.0–17.0 g/dl; after the 11th session of plasmapheresis, 13 days after its commencement) which required no treatment. An asymptomatic hypocalcaemia was also observed, despite intravenous supplementation with calcium gluconate (nadir of 7.6 mg/dl; NR: 8.7–10.3 mg/dl). All of these complications were resolved after concluding the plasmapheresis.

Given the difficulty to attain a reduction in circulating thyroid hormones, a total of 17 were performed prior to surgery. At no time was the additional medical treatment suspended, although the dose of prednisone was reduced to 40 mg/day. Serum levels of thyroid hormones were also determined on 5 occasions before and after the session of plasmapheresis, achieving a reduction of their levels in the extraction sample immediately post-plasmapheresis (FT4 pre- vs. post-plasmapheresis 7.89 ± 2.48 vs. 4.58 ± 1.35 ng/dl, $P = .009$; reduction of 41.9% and FT3 pre- vs. post-plasmapheresis 8.60 ± 2.46 vs. $8{,}24 \pm 2.17$ pg/mL, $P = .157$; reduction of 4.1%), with a further increase on the day after plasmapheresis (FT4 following day 6.73 ± 1.07 ng/dl, $P = .001$; increase of 46.94% and FT3 following day 8.25 ± 2.15 pg/mL, $P = .950$; increase of 0.1%).

Finally, total thyroidectomy was performed 40 days after the initial diagnosis of hyperthyroidism, without incident. The thyroid profile prior to surgery was TSH 0.01 μIU/mL, FT4 4.33 ng/dl and FT3 4.95 pg/mL. On the day immediately after, a reduction in the FT4 to 3.88 ng/dl was noted, falling to values of 1.98 ng/dl 3 days after the intervention. Given the absence of post-surgical complications, and the rapid normalisation of the thyroid hormones, the patient was discharged with hormone replacement therapy with 150 μg of levothyroxine a day.

Therapeutic plasma exchange (TPE) Is a treatment rarely used for the control of hyperthyroidism. The Blood Bank (Haematology and Haemotherapy Department) was responsible for its implementation, requiring for the procedure afferent and efferent lines connected to the apheresis equipment. Its usefulness is based on the binding of T3 and T4 to plasma proteins that are eliminated. By decreasing their plasma concentration, the hormonal concentration is reduced (principally T4, with a lower free fraction). Additionally, by using fresh plasma as replacement fluid, these proteins are applied allowing the binding of the free hormone.[6]

Its indication in hyperthyroidism is not clearly established. Some authors consider that TPE could be useful in the thyrotoxic storm, in cases of intolerance or refractoriness to conventional treatments, and as preoperative preparation,[7] its most frequent indication being Graves' disease, followed by amiodarone-Induced hyperthyroidism.[8] Its complications include bleeding, infection, arterial hypotension, hypocalcaemia and skin reactions. The most serious correspond to disseminated intravascular coagulation or pulmonary thromboembolism, with a mortality <1%.[9,10] In our patient, all the complications were mild and self-limiting.

Although there are studies in which 4–6 TPE sessions were necessary for normalising thyroid hormones[5,11] in our case, this rose to 17. The analytical alteration was clearly more pronounced in the other series, with exposure to the iodinated contrast agents of the catheterisation also possibly making control more difficult. After reviewing the literature, this case would seem to be the greatest number of plasmapheresis that have been received before definitive treatment. Moreover, each session significantly reduced the FT4, practically without affecting the FT3; however, this reduction was transient, with a significant increase after 24 h, which justified the repetition of sessions. During the evolution, it was difficult to discern the net effect of the drug therapy and the plasmapheresis in controlling the hyperthyroidism. Although there was no reduction in thyroid

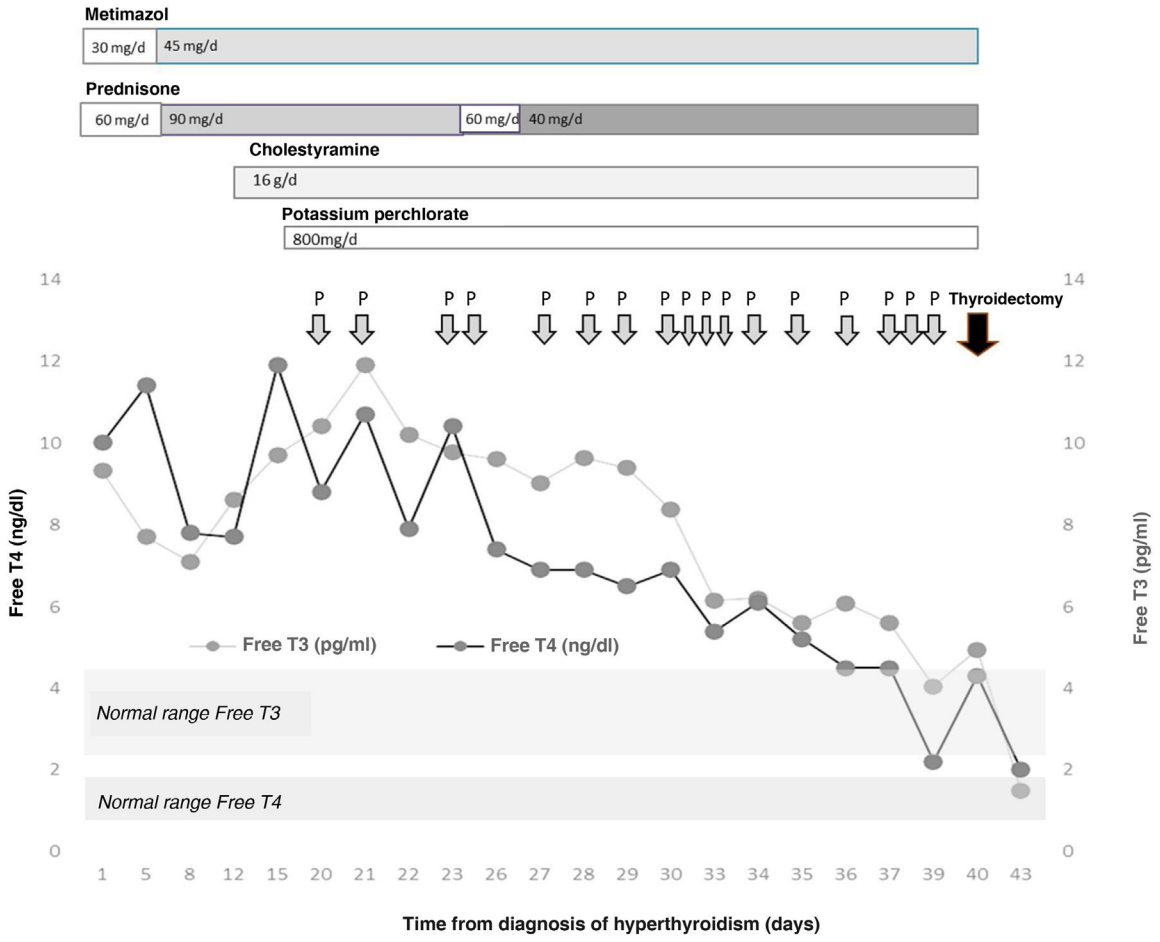

Figure 1 Response of the circulating levels of thyroid hormones after the diagnosis of severe refractory amiodarone-induced hyperthyroidism after 17 sessions of plasmapheresis.
d: day; P: plasmapheresis.

hormones until the TPE was started, which could reflect the efficacy of this technique.

In conclusion, plasmapheresis would seem to be an effective alternative in those cases of severe amiodarone-induced hyperthyroidism refractory to conventional medical treatment at maximum doses as preparation for definitive treatment with surgery.

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Refeeding syndrome: What to expect when you're not expecting

Síndrome de realimentación: qué esperar cuando no estás esperando

A 54-year-old woman in a precarious socioeconomic situation, with a history of anorexia nervosa and chronic alcoholism, with multiple episodes of acute alcohol intoxication, as well as a history of Wernicke's encephalopathy two years before, was admitted with acute alcoholic hepatitis. On admission, a prognosis score showed no severity criteria (Glasgow score 7 points [poor prognosis if score $\geq$ 9 points], Maddrey 9 points [poor prognosis if score $\geq$ 32 points] and MELDNa + 13 points [90-day mortality < 2% if score < 17 points]) and the electrolyte values were normal. She was started on fluid therapy, oral thiamine supplementation (100 mg/day) and prophylaxis of withdrawal syndrome with oxazepam (15 mg every 8 h). A mini nutritional assessment score evidenced the presence of malnutrition (score of 10 points [malnutrition if < 17 points]), confirmed as severe malnutrition, according to GLIM criteria (body mass index [BMI] of 14.5 kg/m^2 [weight 39.4 kg; height 165 cm] and reduced food intake).[1] In this context, oral nutritional supplementation (520 kcal) was initiated on day 4 in the ward, in addition to the hospital culinary diet, adding up to a total daily intake of 2620 kcal (66 kcal/kg/day). The day after, the patient developed gait ataxia, dysarthria and nystagmus, suggestive of Wernicke's encephalopathy, cerebrovascular event excluded. Intravenous supplementation of thiamine was started (500 mg every 8 h), and the nutritional plan maintained. However, in the following hours, the patient developed shock and ventilatory failure, requiring aminergic support and invasive mechanical ventilation. The study highlighted severe hypophosphataemia (0.07 mmol/l [0.87–1.45]), hypomagnesaemia (0.53 mmol/l [0.60–1.10]) and hypokalaemia (2.6 mmol/l [3.5–5.0]), without worsening cytocholestasis or coagulopathy. Other causes of shock, such as infection, pulmonary thromboembolism or acute coronary event were excluded. A transthoracic echocardiogram showed signs of stress cardiomyopathy. This clinical presentation was assumed in the context of refeeding syndrome and Wernicke's encephalopathy, and electrolyte replacement and organ dysfunction support were started in an intensive care unit. The electrolytes normalised and feeding was restarted at a slower rate, starting at 600 kcal per day (15 kcal/kg/day). The patient gradually improved, allowing for the suspension of aminergic and ventilatory support, with progressive resolution of the remaining condition, so she was transferred to a general ward. A progressive improvement in functional status was observed after reinforcement of motor rehabilitation, allowing her to be discharged one month after admission, under oxazepam, thiamine, pyridoxine and folic acid supplementation. She was advised to maintain a culinary diet, without enteral supplementation and to maintain alcohol abstinence. At the time of discharge, she presented a BMI of 14.5 kg/m^2 (weight 39 kg), with no neurological symptoms or signs, electrolyte or liver profile disorders. Two months later she had completely recovered her functional status, presenting a BMI of 15 kg/m^2 (weight 41 kg) and a daily caloric intake of 1100 kcal (27 kcal/kg/day), with an alcohol consumption of 10 g per day, and she was motivated to maintain a progressive weight increase.

Malnutrition is directly associated with the ability to respond to disease, leading to potential medical and surgical complications, extended hospitalisation and higher healthcare costs.[2] Therefore, nutrition screening tools have been widely adopted in order to quickly identify and intervene in patients at higher nutritional risk.[2] However, vigorous oral, enteral or parenteral refeeding in malnourished patients can be fatal.[3–5] Refeeding syndrome is a rare and potentially fatal condition, caused by the shift in fluids and electrolytes that may occur after the reintroduction of feeding in malnourished patients.[3,4] Elderly people and alcoholic, oncologic and anorexic patients are the major risk groups in developed countries.[5] The underlying mechanism of this condition rests on the rise of insulin levels caused by refeeding, promoting cellular glucose and phosphorus uptake for the production of phosphorylated compounds.[6] This leads to a sharp decline in phosphorus levels, already depleted in malnourished patients, making hypophosphataemia the hallmark characteristic of this syndrome.[6] It may also feature hypokalaemia, hypomagnesaemia and thiamine deficiency, due to underlying malnutrition and consumption of