Clinical Case Report

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Hyperthyroidism secondary to hysterosalpingography: an extremely rare complication

A case report

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Abstract

Rationale: Hysterosalpingography (HSG), a standard procedure for the evaluation of women with infertility and repetitive pregnancy loss, is associated with complications such as uterine perforation, infection, allergic reactions, syncope, hemorrhage and shock, and pulmonary or retinal embolus. However, hyperthyroidism has not been reported as one of its complications.

Patient Concerns and Diagnoses: We report the case of a 33-year-old euthyroid woman who presented to our hospital with palpitation, hand tremor, fatigue, and excessive sweating after HSG. Thyroid function tests revealed a thyroid stimulating hormone (TSH) level of 0.012 μIU/mL (range 0.38–4.34 μIU/mL), free T4 of 2.886 ng/dL (range 0.81–1.89 ng/dL), and free T3 levels of 9.4 pg/mL (range 1.80–4.10 pg/mL), and antithyroglobulin antibody of 31.78 IU/mL (range <115 IU/mL). The triiodothyronine uptake was 3.057 ng/mL (range 0.66–1.92 ng/mL). Serum iodine (SI) and urinary iodine (UI) levels: SI of 4717.748 μg/L (range 45–90 μg/L) and UI of 18069.336 μg/L (range 26–705 μg/L).

Interventions and Outcomes: The patient was diagnosed with iodine-induced hyperthyroidism (IIH), but was not treated with antithyroid drugs. She has spontaneously recovered and is pregnant currently.

Lessons: This is the first reported case of overt IIH caused by HSG in a euthyroid patient without risk factors. It suggests that HSG also leads to excessive iodine absorption, which induces secondary hyperthyroidism.

Abbreviations: AIT1 = type I amiodarone-induced thyrotoxicosis, AIT2 = type II amiodarone-induced thyrotoxicosis, HSG = hysterosalpingography, IIH = iodine-induced hyperthyroidism, SI = iodine, TSH = stimulating hormone, UI = urinary iodine, UIC = urinary iodine concentrations.

Keywords: hysterosalpingography, iodine contrast agent, iodine-induced hyperthyroidism, thyroid function

1. Introduction

Hysterosalpingography (HSG), a procedure used to examine uterine cavity and fallopian tubes after injection of an oil-soluble contrast medium through the cervical canals, was used to evaluate women with infertility and repetitive pregnancy loss. Complications of HSG are relatively uncommon, and include uterine perforation, infection, allergic reactions, syncope, hemorrhage and shock, pulmonary or retinal embolus, but not hyperthyroidism.[1]

2. Case presentation

A 33-year-old woman who was previously euthyroid presented to a local hospital with a complaint of infertility. HSG was performed on June 9, 2015, to determine whether the fallopian tubes were blocked. The patient is a nurse and a Chinese Han who was previously healthy without any family history of thyroid diseases. Indomethacin was administered for analgesia and the HSG outcome was favorable (Fig. 1). However, the patient started to develop vaginal bleeding after HSG, which may be caused by the high injection pressure with an estimated volume of 100 mL, sustained for almost 24 hours. One week later, the patient returned with complaints of palpitation, hand tremor, fatigue, excessive sweating, without any abnormal appetite, sleep disorders, weight changes, or changes in defecation or urination. Physical examination showed her blood pressure: 120/70 mm Hg, heart rate: 130 bpm, hand tremor, excessive sweating, no more positive findings. Thyroid function tests (June 25, 2015) revealed a thyroid stimulating hormone (TSH) level of 0.012 μIU/mL (range 0.38–4.34 μIU/mL), free T4 of 2.886 ng/dL (range 0.81–1.89 ng/dL), and free T3 levels

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GTM and RM contributed equally to this work.

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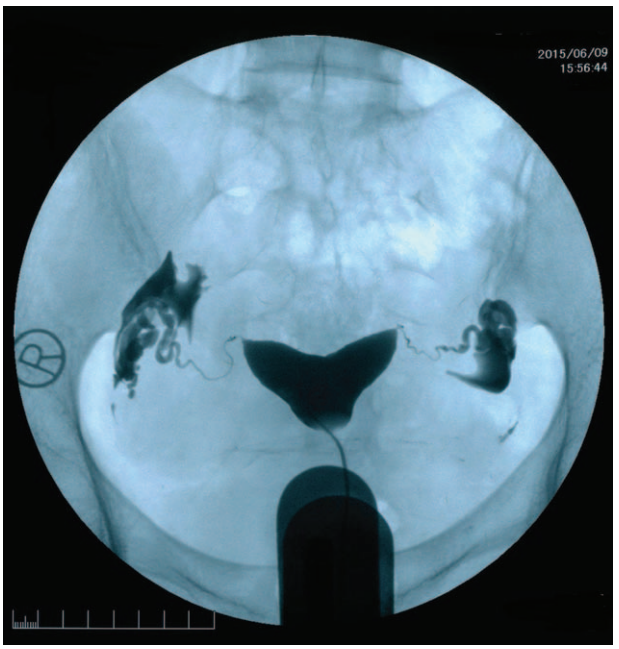

Figure 1. HSG (Jun 9, 2015) showed normal uterine cavity with filling, and unobstructed fallopian tubes.

of 9.4 pg/mL (range 1.80–4.10 pg/mL), and antithyroglobulin antibody of 31.78 IU/mL (range <115 IU/mL). The triiodothyronine uptake was 3.057 ng/mL (range 0.66–1.92 ng/mL). Thyroid ultrasound did not show any abnormality. Dynamic electrocardiogram showed sinus tachycardia (about 130 bpm). The ultrasonic cardiogram was normal. Further, liver function revealed an elevated ALT of 277 U/L (range 7–40 U/L). She was diagnosed with hyperthyroidism. We suspected that the hyperthyroidism was related to a history of HSG. Therefore, we tested serum iodine (SI) and urinary iodine (UI) levels: SI of 4717.748 μg/L (range 45–90 μg/L) and UI of 18069.336 μg/L (range 26–705 μg/L). The patient was treated with metoprolol to control her heart rate for 2 weeks until her HR reduced to 90 bpm. She was treated with glucuronolactone and phosphatidyl choline for 1 month to restore her liver function. In addition, no special measures were adopted to induce iodine excretion. During the follow-up, her heart rate recovered to nearly 75 bpm and other symptoms gradually improved except for tremor. We followed up with the patient regularly to monitor thyroid function (Fig. 2), serum and UI levels (Fig. 3). Thyroid function tests on March 11, 2016 revealed a TSH level of 1.918 mIU/mL, a free T4 level of 1.145 ng/dL, a free T3 level of 3.06 pg/mL and an antithyroglobulin antibody level of 33.43 IU/mL. Serum and UI values on March 24, 2016 were 257 and 1298.674 μg/L, respectively. The patient has recovered from transient hyperthyroidism and is currently pregnant.

3. Discussion

To the best of our knowledge, this is the first reported case of overt iodine-induced hyperthyroidism (IIH) caused by HSG in a patient without a history of thyroid disease and showing spontaneous recovery. Hemorrhage was the only event in this case following HSG. Excessive iodine absorbed into the blood may have induced hyperthyroidism. However, the possibility of lymphatic absorption still remains. Studies explored the effect of iodinated contrast used for HSG. A study of women with infertility who were divided into 3 groups based on the results of thyroid function before HSG included 180 in euthyroid status, 28 in subclinical hypothyroidism, and 13 in subclinical hyperthyroidism. The findings revealed a significantly increased risk of subclinical hypothyroidism following lipiodol treatment. Only 2 patients from the euthyroid group and 1 from the subclinical hypothyroidism group developed subclinical hyperthyroidism and spontaneously recovered. Nobody developed overt hyperthyroidism.[2]

The thyroid gland has intrinsic mechanisms that maintain normal thyroid function even in the presence of excessive iodine levels. IIH (the Jod–Basedow phenomenon) was first described in the early 1800s, when thyrotoxicosis was more common among patients with endemic goiter treated with iodine supplementation

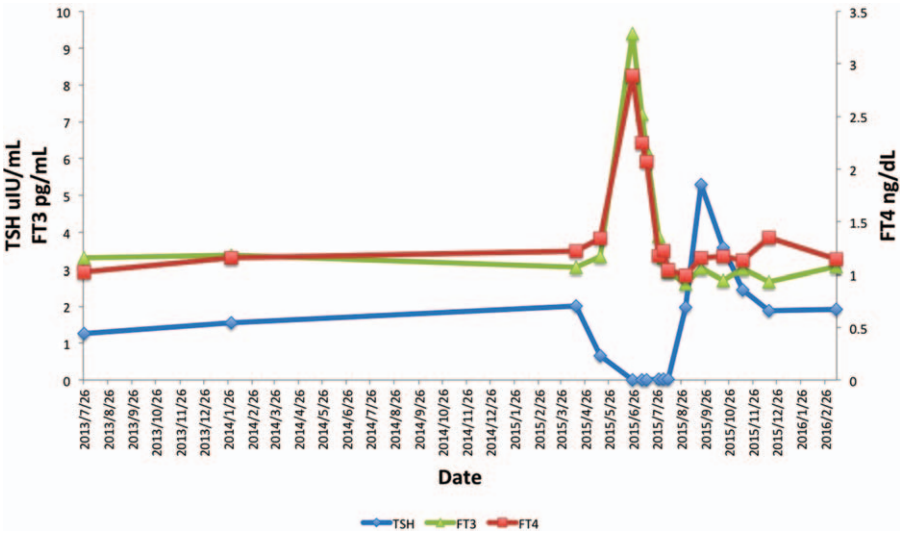

Figure 2. TSH, FT4, and FT3 levels were normal before HSG (July 26, 2013–May 15, 2015). Sixteen days after the HSG (June 25, 2015), TSH levels were reduced to 0.012 μIU/mL, which declined to the lowest level of <0.008 μIU/mL on July 7, 2015 until August 10, 2015, followed by a gradual increase to 5.298 μIU/mL on September 21, 2015. Finally, TSH gradually declined to the preoperative level. In contrast, FT4 reached a peak of 2.886 ng/dL and FT3 peaked at 9.4 pg/mL on June 25, 2015, followed by a decline in both values over the following days. The levels were restored to the preoperative level on July 29, 2015.

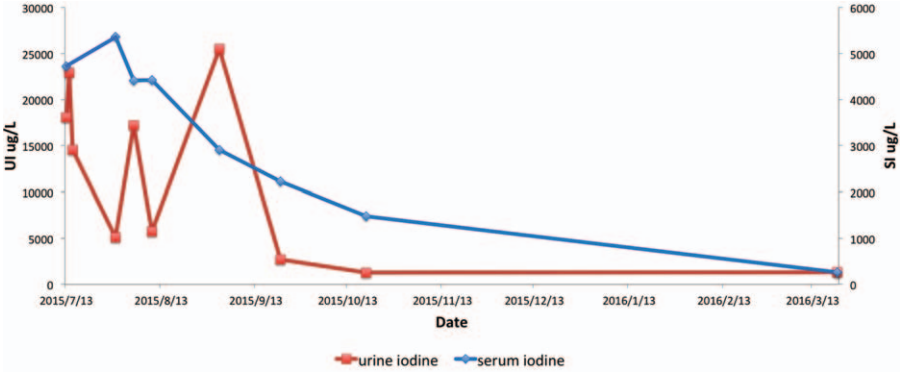

Figure 3. SI increased after the HSG to a peak of 5365.465 μg/L on July 29, 2015, and decreased gradually over the following days. The UI also increased after HSG, fluctuating in the range of 5101.471 to 25443.901 μg/L during the early stages (July 13, 2015–September 1, 2015), followed by a steady decline. The current UI and SI were higher than the normal levels.

than in individuals without goiter. Mutational events in thyroid cells lead to functional autonomy. The subject may become thyrotoxic following accumulation of abnormal cells and increased iodine levels.[3] Generally, 150 μg of iodine are required daily for thyroid hormone synthesis in adults.[4] Excessive iodine loads provide a rich substrate for increased production of thyroid hormones. IIH might be transient or permanent. The risk factors include nontoxic or diffuse nodular goiter, latent Grave disease, and chronic iodine deficiency, especially in older persons. Occasionally, IIH has been observed in euthyroid patients with a previous episode of postpartum thyroiditis or recombinant interferon-alpha induced destructive thyrotoxicosis.[5]

Iodide is absorbed in the stomach and duodenum and cleared by the kidneys and the thyroid. Seventy to 80% of the iodine content is located in the thyroid gland.[6] Organic binding of iodine in the thyroid is decreased when plasma iodide levels are elevated (acute Wolff–Chaikoff effect). Adaptation to this acute effect occurred in approximately 2 days, in the presence of constant high levels of iodide concentrations in plasma. Studies demonstrated that the escape was attributed to a decrease in iodide transported into the thyroid, lowering the intrathyroidal iodine content below a critical inhibitory threshold and allowing organification of iodide.[7] Thyroid clearance varies depending on iodine intake, ranging from 10% of absorbed iodide in healthy individuals to more than 80% in patients with chronic iodine deficiency.[6] Guitierrez-Repiso et al[8] observed that in an adult population with adequate and stable nutrition, iodine excretion in a random urine sample represented 70% to 80% of daily iodine intake. Therefore, median urinary iodine concentrations (UIC) are widely used as a biomarker of population iodine intake, with levels >300 μg/L considered excessive in children and adults, and levels >500 μg/L considered excessive in pregnant women.[5]

Large quantities of iodide occur in drugs, antiseptics, contrast media, and food preservatives. IIH induced by amiodarone is most commonly reported. The 2 mechanisms contributing to IIH are as follows: In type I amiodarone-induced thyrotoxicosis (AIT1), approximately 75 mg of excess iodine is released from each 200 mg tablet of amiodarone, which is several hundred-fold higher than the recommended daily intake of 150 μg in adults. In type II amiodarone-induced thyrotoxicosis (AIT2), an iodine-based drug moiety in the amiodarone molecule bearing structural resemblance to thyroxine (T4) induces destruction of the thyroid follicles and releases preformed hormones. Patients with type II thyrotoxicosis may develop permanent hypothyroidism due to fibrosis of the thyroid gland.[3,6,9] In severely ill patients, treating both AIT1 and AIT2 with anti-thyroid drugs and glucocorticoids with or without perchlorate reduces thyroid inflammation and also reduces the peripheral conversion of T4 to T3.[5,9,10]

The iodine contrast agent mainly includes aqueous and oleic solutions. Guidelines from the Contrast Media Safety Committee of the European Society of Urogenital Radiology only advocate monitoring high-risk patients for thyroid dysfunction following iodinated contrast use. There is no indication for routine pre- and post-CT thyroid function testing currently. Water-soluble iodinated contrast agents provide exposure to about 13,500 μg of free iodine during each CT imaging examination.[11] However, IIH induced by water-soluble iodinated contrast agents has also been observed. A study of 101 patients who underwent coronary angiography found a small increased risk of subclinical hyperthyroidism up to 8 weeks after iodine exposure.[12] In a large case–control study spanning over 20 years, patients without preexisting thyroid dysfunction who received a single iodinated contrast dose had a 2- to 3-fold increased risk of developing thyroid dysfunction at a median of 9 months following exposure, compared with patients who were not exposed to high iodine load.[13]

Inorganic iodine, occurring as iodide (I^-), is the available form of thyroid. The iodine contrast agent and amiodarone represent organic iodine. Most of the iodinated oil injected during HSG is discharged from vagina, a small amount of which enters the abdominal cavity and is slowly absorbed. In the previous studies, subclinical hypothyroidism in patients after HSG was attributed to Wolff–Chaikoff effect, while subclinical hyperthyroidism may be related to Jod–Basedow phenomenon.

This case study represents the first reported incidence of overt IIH after HSG. Hemorrhage after procedure possibly increases iodine absorption through blood stream, and induces IIH. However, the exact mechanism has yet to be elucidated.

4. Conclusion

This is the first reported case of overt IIH induced by iodinated contrast during HSG in a patient without any risk factors for hyperthyroidism. The patient recovered spontaneously and is currently pregnant. Our findings suggest that HSG leads to excessive iodine absorption, and secondary hyperthyroidism.

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