Acta Clin Croat 2023; 62:551-555
doi: 10.20471/acc.2023.62.03.18

Case Report

ACUTE PAINFUL THYROIDITIS AND THYROTOXICOSIS AFTER PCI – A CASE STUDY

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SUMMARY – Destructive thyroiditis is a self-limited disease characterized by acute release of preformed thyroid hormones. We present a patient with extremely rare acute painful thyroiditis after percutaneous coronary intervention (PCI) in acute myocardial infarction without ST-elevation. The acute onset of thyroid pain and increase of fT3, fT4 and parameters of inflammation were compatible with acute destructive thyroiditis. Such acute thyroiditis probably resulted from local inflammation induced by a large amount of iodine given to the patient *via* iodinated contrast media used during PCI. Because of the increasing number of patients referred to cardiac catheterization, invasive cardiologists should be aware of the potentially serious thyroid dysfunction that can result from iodinated contrast use. The aim of our paper is, in the light of the patient presented, to discuss the pathophysiology, clinical presentations, therapy and potential preventive measures in patients that develop thyroid dysfunction after PCI.

Key words: *Acute thyroiditis; Thyrotoxicosis; Percutaneous coronary intervention; Acute coronary syndrome; Iodinated contrast agent*

Introduction

Destructive thyroiditis is a self-limited disease which occurs upon acute release of preformed thyroid hormones. It can present in two forms, i.e., as painful acute thyroiditis or as painless acute thyroiditis. It usually presents as hyperthyroidism resulting in heart rhythm disturbances, loss of body weight, ophthalmopathy, and other adrenergic symptoms. Elevated levels of serum free tetraiodothyronine (fT4) and free triiodothyronine (fT3) with low concentration of thyroid stimulating hormone (TSH) can be found by laboratory tests[1].

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Received October 13, 2016, accepted June 26, 2017

The most common causes of hyperthyroidism are autoimmune diseases of the thyroid gland (such as Graves' disease), toxic multinodular goiter, and functional adenoma. Hyperthyroidism can also be induced by local inflammation of the thyroid exposed to excessive amounts of iodine. Iodinated contrast media used during cardiac catheterization contain large amounts of iodine that can induce thyroid inflammation resulting in various forms of thyroid dysfunction[2].

In this case study, we present a patient with acute painful thyroiditis after percutaneous coronary intervention (PCI) in acute myocardial infarction without ST-elevation (NSTEMI).

Case Report

A 76-year-old male patient was admitted to our facility with chest pain, palpitation, and dyspnea. His

previous medical history showed hypertension and cholecystectomy he had undergone 8 years before. Clinical examination on admission revealed high blood pressure (170/100 mm Hg). Electrocardiogram showed atrial fibrillation with ventricular response of 120/min without any signs of ischemia. Slightly elevated levels of troponin (0.27 ug/L) and C-reactive protein (6.5 mg/L) were also detected. On the day of admission, the patient underwent coronary catheterization. The procedure depicted subtotal stenosis of the mid part of the circumflex artery. A technically challenging angioplasty with placement of a bare-metal intracoronary stent was performed. The patient received 250 mL of contrast dye (Visipaque, GE HealthCare, Marlborough, USA) and intracoronary unfractionated heparin during catheterization. Optimal medical therapy for NSTEMI was also administered and included clopidogrel, acetylsalicylate, perindopril combined with amlodipine, atorvastatin and bisoprolol. Two days after the procedure, the patient developed severe neck pain radiating to his ears. The pain was exacerbated with swallowing. Further clinical and laboratory evaluation revealed markedly depressed levels of serum thyroid stimulating hormone (TSH) (0.00 mU/mL). The levels of fT3 and fT4 were elevated (fT4 29.4, normal range 11.5-22.7 pmol/L; fT3 10.8, normal range 3.5-6.5 pmol/L). Thyroid antibodies anti-TPO and anti-Tg were in the normal range. White blood cell count was slightly elevated ($10x10^9$/L) with C-reactive protein level of 89 mg/L. Thyroid ultrasonography showed a normal-sized thyroid with inhomogeneous focal substrates in both lobes, and a nodular formation in the right lobe. Fine needle biopsy was done and the endocrinologist was consulted. Under the first clinical impression of thyrotoxicosis due to destructive thyroiditis the endocrinologist decided to start the patient on prednisone 5 mg daily and thiamazole 10 mg bid (*bis in die*). A needle biopsy finding depicted a mixed nodular goiter. No microbes were identified from the culture test of either blood or thyroid gland samples.

A week after therapy initiation, the patient was discharged in good condition with optimal medical therapy including prednisone 5 mg daily for 3 days and thiamazole 10 mg bid at first, then 5 mg bid after 7 days.

A month later, the levels of TSH were still markedly suppressed, while the levels of fT3, fT4 and parameters of inflammation were within the normal range. Prednisone therapy was stopped, and the dose of thiamazole was halved.

At the last endocrinological check-up, 12 months after the PCI, thyroid hormone levels were completely normalized. Thiamazole therapy was continued in its previous dose and further endocrinological follow-up was scheduled. The patient was free from chest pain and palpitations while taking the usual therapy for patients with established coronary disease.

Discussion

The recommended daily iodine intake is 150 μg in adults who are not pregnant or lactating. Exposure to greater amounts of iodine is generally well-tolerated[4]. However, in susceptible individuals, including those with pre-existing thyroid disease, the elderly, fetuses and neonates, or patients with other risk factors, the risk of developing iodine-induced thyroid dysfunction might be increased[5]. Hypothyroidism or hyperthyroidism as a result of supraphysiological iodine exposure might be either subclinical or overt, and the source of excess iodine might not be readily apparent[6].

Iatrogenic causes of increased iodine intake could be a result of iodine-containing medication ingestion, intravenous application of iodine contrast media, or local application of iodine agents. Thyroid gland can regulate hormone synthesis and secretion in the presence of excessive amounts of iodine. This has been described as the Wolff-Chaikoff effect. This effect is based on a decrease in the expression of the sodium-iodide symporter on the membrane of thyroid cells. Reduced expression of that transport protein leads to a decreased transport of iodide into the thyroid cell which preserves normal gland function. However, exposure to supraphysiological levels of iodide may overwhelm regulatory capacity and precipitate hyperthyroidism *via* so-called Jod-Basedow phenomenon. This phenomenon has been seen with as little as 300 to 500 μg of iodide daily exposure[3]. Both diagnostic and interventional medical procedures using iodine-containing contrast media expose the patients to the amount of iodide that exceeds the aforementioned number several times[5-7]. Jod-Basedow is classically described in patients with underlying thyroid disease. Among them are patients with autoimmune thyroid disease and patients with autonomous nodular goiters (especially older patients among whom the prevalence of nodular disease is high). Although controversial, iodine-induced thyrotoxicosis has been reported in patients without underlying thyroid disease[8,9].

The complete mechanism of iodine-induced hypothyroidism remains unclear. It is believed to represent a failure to adapt to the acute Wolff–Chaikoff effect. This failure could be a result of a previously damaged thyroid[4].

Currently used conventional contrast media are chemical modifications of the 2,4,6-tri-iodinated benzene ring. They are classified on the basis of their physical and chemical characteristics, including their chemical structure, osmolality, iodine content, and ionization in the solution[10]. Classification based on osmolality, because of the probable relation between osmolality and contrast induced nephropathy, is most widely used. Contrast induced nephropathy and allergic reactions to contrast media are adverse reactions that are very well known and recognized by interventional cardiologists.

On the other hand, contrast induced thyroid dysfunction is much less studied. Hence, the usual knowledge on that particular problem is rather insufficient and studies considering this clinical entity are relatively scarce. Two studies in Germany and the USA showed that only a small proportion of patients after coronary angiography or computed tomography scan develop subclinical hypothyroidism[11,12]. It is usually established approximately 1 week after the examination. One of the most rigorous studies that examined the association between iodinated contrast use and thyroid dysfunction was a large case-control study from two hospitals in Boston. It was conducted over a period of 20 years in patients without clinical signs of thyroid dysfunction. It showed that exposure to contrast dye increased the risk of developing incident hyperthyroidism 2-3 fold over a period of 9 months following exposure. No association between contrast exposure and incident hypothyroidism was observed[3].

As mentioned earlier, medical procedures using iodine-containing contrast media expose the patients to the large amount of iodine. Those amounts exceed the ones known to be related to thyroid dysfunction several times. In our case, we used Visipaque contrast that contains 320 mg of iodine *per* milliliter[13]. The patient received a total iodine load of 80 g during the procedure. For comparison, the normal dietary iodine intake in the United States is 150-300 μg daily and the amount known to exert Jod-Basedow phenomenon has been described with as little as 300-500 mcg[3]. This high amount of iodine alone could be responsible for hyperthyroidism. Older patients, such as our patient, are also known to have a high prevalence of clinically silent nodular thyroid disease which is a known risk factor for hyperthyroidism with excessive iodine exposure[14]. However, its clinical presentation was quite surprising. Acute painful thyroiditis as a result of iodine excess is extremely unusual in the setting of acute NSTEMI PCI[15].

The most common cause of painful destructive thyroiditis is post-viral subacute thyroiditis. Considering the clinical presentation and absence of viral infection together with extremely fast onset of symptoms, post-viral subacute thyroiditis was not likely. The received amount of radiation during the procedure could also be considered as a cause but radiation thyroiditis is generally not painful[16]. Other causes of painful destructive thyroiditis include malignant pseudothyroiditis (due to primary thyroid malignancies or malignancies metastatic to the thyroid), acute suppurative thyroiditis, painful autoimmune subacute thyroiditis, and amiodarone induced thyrotoxicosis, especially type 2 (destructive thyroiditis)[17]. All of the above was highly unlikely in the presented case considering the results of the extensive clinical work-up performed[18,19].

Treatment of our patient consisted of prednisone with thiamazole as recommended by the endocrinologist, despite the undefined role of corticosteroids in acute myocardial infarction. Prednisone is used in the treatment of most forms of thyroiditis (viral, amiodarone-induced) because of its anti-inflammatory effects, as well as its potential to partially block the T_4 to T_3 conversion[20,21]. Thiamazole was administered to control the symptoms of hyperthyroidism.

There are no strict recommendations, such as those for contrast induced nephropathy, for monitoring thyroid function in patients undergoing PCI or other procedures with iodine contrast. Routine monitoring of thyroid function in patients with normal thyroid function and undergoing cardiac catheterization is currently not recommended. Patients at risk of developing thyroid dysfunction after contrast injection are those with Graves' disease and those with multinodular goiter, especially elderly ones. Such patients should be carefully monitored by endocrinologists after procedures in which iodine contrast is used. Prophylaxis is not generally recommended in these groups, although it may offer some protection in selected high-risk individuals[5]. Various regimens have been suggested for prophylaxis, as follows: for elective contrast media administration: sodium perchlorate, 300 mg 3 times daily

(beginning the day prior to examination and continuing for 8-14 days) and/or thiamazole, 30 mg once daily (beginning the day prior to examination and continuing for 14 days); for emergency contrast media administration: sodium perchlorate, 800 mg directly prior to examination and continue with 300 mg 3 times daily for 8-14 days and/or thiamazole, 30 mg once daily directly prior to examination and continue for 14 days[22].

Finally, we believe that our patient developed an extremely rare form of thyroid dysfunction as a result of the PCI procedure that was performed. It was potentially precipitated by the underlying thyroid dysfunction. Although in this case, as in any case of acute coronary syndrome, we would not defer interventional treatment to evaluate thyroid function, there are possibly some groups of patients that should undergo such evaluation. This is especially true for older patients undergoing elective procedures. Such abrupt clinical course of hyperthyroidism as seen in our patient could even potentially be life-threatening, especially if unrecognized for a longer period of time.

It is important to raise awareness of invasive cardiologists of the possible, unexpected and clinically aggressive forms of iodinated contrast effects on the thyroid gland function. Recommendations for thyroid screening are inconsistent and are not generally accepted[23]. The US Preventive Services Task Force does not recommend routine TSH screening[24]. Screening costs could be significant when applied at the population level, but without clear benefit. It seems reasonable to determine TSH level in patients with nonspecific complaints, positive family or personal history of thyroid disease, presence of thyroid antibodies, radiation therapy to the head, neck or chest, other autoimmune diseases, therapy with lithium, amiodarone or iodine, and in the elderly[25].

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Sažetak

AKUTNI BOLNI TIREOIDITIS I TIREOTOKSIKOZA NAKON PCI – STUDIJA SLUČAJA

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Destruktivni tireoiditis samoograničavajuća je bolest obilježena akutnim otpuštanjem tireoidnih hormona. Prikazujemo bolesnika s akutnim bolnim tireoiditisom nastalim uslijed perkutane koronarne intervencije (PCI) u akutnom koronarnom sindromu bez ST elevacije. Nagla pojava boli u predjelu štitnjače, povećanje vrijednosti fT3 i fT4 te parametara upale bili su konkluzivni s dijagnozom akutnog destruktivnog tireoiditisa. Navedena bolest vjerojatno proizlazi iz lokalne upale izazvane velikom količinom joda apliciranog kao jodni kontrast tijekom PCI. Zbog sve većeg broja bolesnika podvrgnutih koronarnoj angiografiji invazivni kardiolozi trebali bi biti svjesni potencijalne opasne disfunkcije štitne žlijezde nastale upotrebom jodnog kontrasta. Cilj našeg rada je, kroz konkretan klinički slučaj, prikazati i raspraviti o patofiziologiji, kliničkoj prezentaciji, terapiji i preventivnim mjerama u bolesnika koji razviju poremećaj rada štitnjače nakon PCI.

Ključne riječi: *Akutni tireoiditis; Tireotoksikoza; Perkutana koronarna intervencija; Akutni koronarni sindrom; Jodni kontrast*