Radioactive Iodine Therapy in Papillary Thyroid Carcinoma with Moyamoya Disease

Andrew Dominic S. Kalaw, MD and Leandro C. Manalaysay, MD
Section of Nuclear Medicine and PET/CT, Cardinal Santos Medical Center, Greenhills West, San Juan City

ABSTRACT

Papillary thyroid carcinoma is the most common histological subtype of thyroid carcinoma. Management is surgical with post-operative radioiodine therapy to ablate thyroid tissue remnants. Although the management of uncomplicated papillary thyroid carcinoma is well established, treatment of patients also affected with Moyamoya disease is limitedly described. There are concerns with regards to doing radioactive iodine therapy, which might affect the diseased arteries in Moyamoya disease. We report a case of a 36-year-old male with Moyamoya disease, who was subsequently diagnosed to have papillary thyroid carcinoma. After total thyroidectomy, the patient underwent radioactive iodine therapy with 5.7 GBq (155.0 mCi). Post-ablation scan with SPECT of the pelvis showed functional thyroid tissue remnants in the lower anterior neck with suspicious tracer-avid focus in the sacrum. There were no complications such as radiation-induced arteritis encountered with the patient's Moyamoya disease during post-operative high-dose radioiodine ablation and no subjective complaints even on follow-up after almost one year.

Keywords: *papillary thyroid carcinoma, Moyamoya disease, radioactive iodine therapy*

For correspondence:
Andrew Dominic S. Kalaw, MD
E-mail: andrewkalawmd@gmail.com

INTRODUCTION

One of the most common endocrine malignancies is thyroid cancer, with 2.0 to 3.8 in women and 1.2 to 2.6 in men per 100 individuals' annual incidence. It has the highest mortality rate than all other endocrine cancers combined [1]. Greater than 90% of all thyroid cancers are of the papillary and follicular subtypes [2]. These subtypes are well-differentiated and majority are able to concentrate radioiodine, and therefore amenable to radioiodine therapy [3].

Moyamoya disease is defined as an idiopathic occlusion of bilateral vessels of the circle of Willis. In this condition, there is progressive stenosis of the distal internal carotid arteries (ICAs), usually bilaterally, but there are cases wherein only one side is affected, and is aptly called unilateral Moyamoya disease. Its etiology is unknown to date, but it is usually associated with a familial history, ethnic predilection for Asians, and various environmental factors [4].

Existing but limited data associate Moyamoya disease with thyroid pathologies. Concurrent disease risks and predilection are implicated in the link between the two pathologies. There are already reported relationships, although limited, between Moyamoya disease and Graves' disease, but very rare cases of Moyamoya disease associated with thyroid carcinoma. Herein, we describe a case of a patient diagnosed with Moyamoya disease who developed papillary thyroid carcinoma and was subjected to post-surgical radioactive iodine therapy as part of the treatment management.

CASE DESCRIPTION

J. A., a 36-year-old male, felt progressing weakness, right arm numbness, and right-sided facial asymmetry while playing in a basketball game in June 2012. He was then brought to another hospital and subsequently admitted for observation and management. On the day of admission, his neurologic symptoms improved. CT angiogram of the brain was done, revealing

Moyamoya pattern of involvement (Figure 1). Upon improvement of his condition, he was sent home and given clopidogrel, atorvastatin, and amlodipine for maintenance medications.

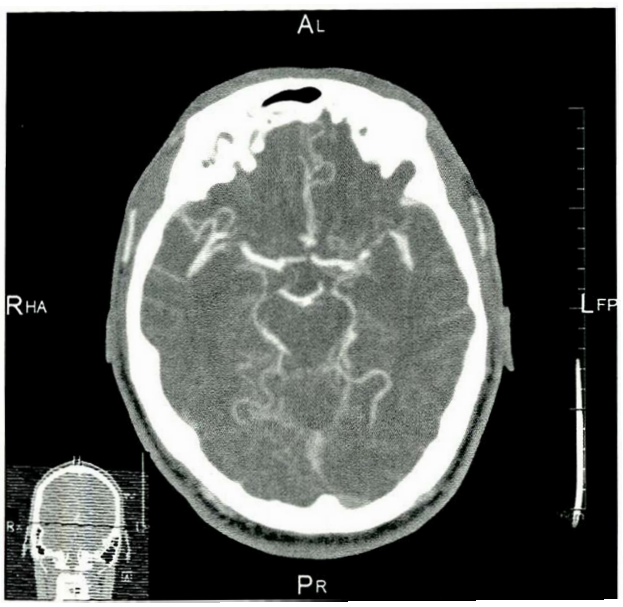

Figure 1 CT angiogram revealing mild stenosis of the distal left internal carotid artery and severe focal stenosis versus occlusion of the proximal left middle cerebral artery. There has been development of lenticulostriate collaterals as may be seen with Moyamoya pattern of involvement.

Patient was apparently well until February 2015, when he noticed a lump on his anterior neck with no other complaints noted. He consulted a specialist and thyroid function tests (TSH, FT3, FT4) were done with normal values. Ultrasound of the anterior neck was also done which revealed two nodules in the left thyroid lobe, which were considered benign at the time of examination. No other diagnostic procedures were done.

It was not until February 2016 when he noticed that the anterior neck mass was enlarging. He then sought consult and biopsy was done, revealing findings consistent with papillary thyroid carcinoma on the left thyroid mass and positive for metastatic papillary thyroid carcinoma on the left supraclavicular node. TSH and FT4 were within normal values. Surgery was performed in March 2016. Histopathology of the mass showed "multifocal papillary thyroid carcinoma, left thyroid gland, classical, follicular and columnar variants, with extrathyroidal spread and lymphovascular space invasion. Papillary thyroid microcarcinoma in the isthmus, classical variant, and positive for metastasis: all two perithyroid lymph nodes, ten of twenty-one lymph nodes labeled as left, level 2; all two lymph nodes labeled as left, level 3; two of four labeled as left, level 4; and six of seven lymph nodes labeled as neck, level 6. Extracapsular spread and tumor deposits present. AJCC/UICC 7th edition pathologic stage: I (pT3 pN2 Mx)." During the surgery, chyle leak was reported that required the patient to apply additional pressure on the surgical site every time change of dressing was done. Patient tolerated the procedure well and was eventually discharged.

Upon follow-up with his endocrinologist, the patient was advised post-surgical radioactive ablation. Due to his Moyamoya disease, he was asked to be cleared by his neurologist before undergoing radioiodine therapy. After being cleared, he was then referred to our institution for radioiodine therapy one-month post-surgery. Thyroid function test was done, showing TSH to be elevated at >100.0 µIU/mL (N.V. 0.27–3.75 µIU/mL), low FT3 at 1.06 pmol/L (N.V. 2.5–5.8), and low FT4 at 2.16 pmol/L (N.V. 11.5–23.0 pmol/L). The patient received 155.0 mCi of I-131 capsule per orem. There were no complications reported. Post-ablation scan with SPECT of the pelvis was done 7 days after the radioactive iodine therapy (Figure 2). He was prescribed levothyroxine 50 mcg tablet daily, and was advised short-interval follow-up to document the course of the disease.

DISCUSSION

Moyamoya disease affects the distal internal carotid arteries (ICAs) and their major branches, causing progressive stenosis and occlusions. There is growth of small collateral vessels in the lower part of the cerebrum which accompany the vascular stenosis/occlusion, which was described as a "puff of smoke in Japanese," hence the term Moyamoya [4]. Clinical presentations vary widely, from being asymptomatic,

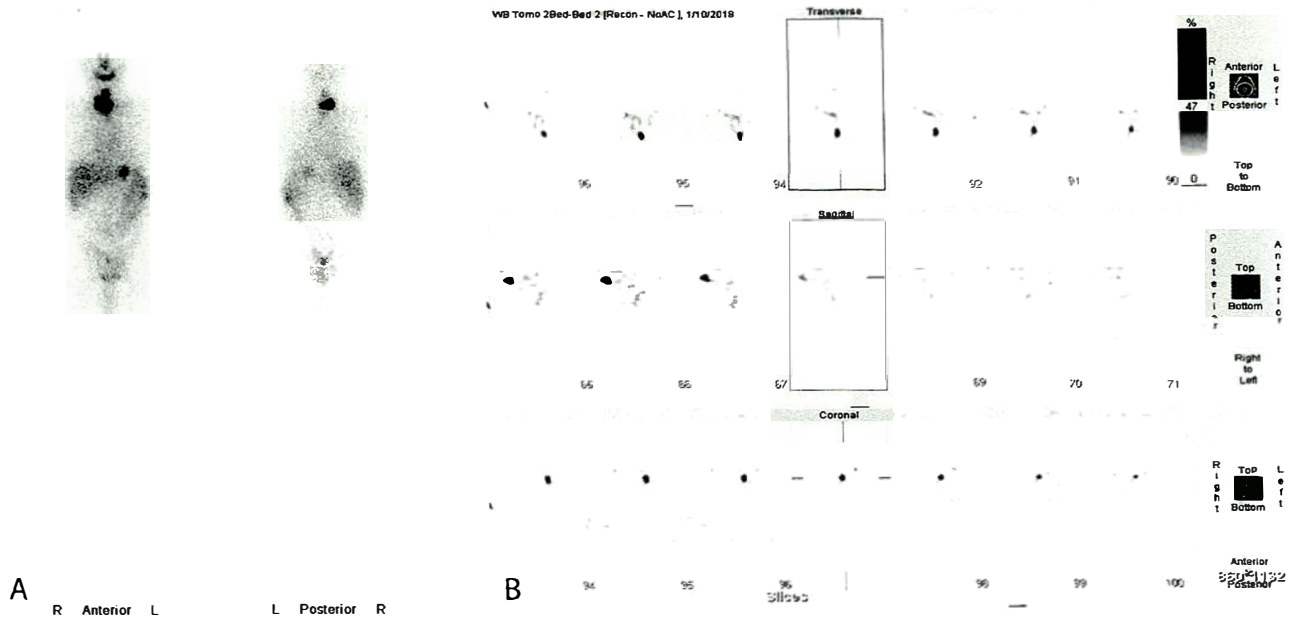

Figure 2 Whole body images taken seven (7) days after radioiodine therapy showing functioning thyroid tissue remnants in the lower anterior neck and moderately intense tracer activity in the sacrum (A), which is better localized on SPECT (B).

to manifesting transient events, to causing severe neurologic deficits. In some cases, hemorrhage or ischemic events occur. Pharmacologic management has been disappointing. Therapy is directed more at the complications of the disease. Hypertension is controlled along with anticoagulation or antiplatelet agents to prevent further strokes [5].

Our patient was diagnosed with Moyamoya disease in 2012, after presenting with facial asymmetry and weakness, and was maintained on anti-hypertensives, anti-platelets, and cholesterol-lowering agents. After the initial incident, there were no other neurologic complications that followed, as the patient claimed that he has been compliant with his maintenance medications.

Papillary thyroid carcinoma (PTC) is the most common histopathologic type of differentiated thyroid malignancy (70%). It often spreads via the regional lymphatic vessels, but can also spread hematologically as well, usually in the bone and lungs [6]. The cause of the cancer is also idiopathic; a genetic defect may be involved. Exposure from high-dose radiation increases the risk of developing thyroid cancer. Thyroid function tests are usually normal in patients with thyroid cancer, as in this patient's case. Characteristic cytologic features include psammoma bodies, cleaved nuclei with an "orphan-Annie" appearance caused by large nucleoli, and the formation of papillary structures [7]. Treatment options include surgery, radioiodine therapy, and pharmaceuticals.

There have been few documented cases of Moyamoya disease associated with thyroid pathologies, specifically Graves' disease. However, Moyamoya disease associated with papillary thyroid carcinoma is rarely reported [4]. Interestingly, in some documented patients, symptoms of ischemic stroke or transient ischemic attack (TIA) presents along with elevated thyroid hormone levels and suppressed thyroid stimulating hormone consistent with a thyrotoxic state. Thyroid antibodies including thyroid peroxidase antibody and thyroid gland antibody are elevated in these patients.

Several studies mentioned the relationship between Moyamoya disease and Graves' disease where elevated thyroid antibodies are frequently observed.

Based on the study by Ni et al., those patients who presented with ischemic stroke and/or TIA were in a thyrotoxic state, leading them to hypothesize that cerebrovascular hemodynamic changes due to thyrotoxicosis might be responsible for ischemic attacks [8]. Another prospective study states that increased sympathetic nervous system sensitivity brought about by thyrotoxicosis may involve the formation of abnormal vessels. Another study pointed that a possible link is T-cell dysregulation, which is related to cellular proliferation and vascular dysregulation in Moyamoya disease and immunologic stimulation of the thyroid in Graves' disease [9].

In one of the studies which reported the association between Moyamoya disease and thyroid carcinoma, thyroid function test was consistent with a euthyroid state, but thyrotropin receptor antibody (TRAb) was elevated. It is important to take into account that the said patient in the study had thyroid carcinoma first and was already treated surgically and with radioactive iodine therapy ten years before developing Moyamoya disease. The study suggested that long-term TRAb elevation may be correlated with development of Moyamoya disease. In a recent prospective study, it was demonstrated that there were elevated thyroid autoantibodies in patients with Moyamoya disease, suggesting a possible underlying thyroid autoimmune process. Therefore, in patients developing Moyamoya vessels, thyroid carcinoma must be considered [4]. The unique aspect of our case is the fact that the patient already presented with Moyamoya disease even before developing papillary thyroid carcinoma, which is not yet reported in the literature.

The surgical recommendation for our patient was total thyroidectomy and gross removal of all primary tumors, as indicated in most literatures [2]. This approach was based on data suggesting that total thyroidectomy would improve survival, decrease recurrence rates, allow for routine use of radioactive iodine ablation, and facilitate detection of recurrent/persistent disease upon follow-up [2]. According to the 2015 American Thyroid Association (ATA) management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer, AJCC/UICC staging is recommended for all patients with differentiated thyroid carcinoma (DTC), based on its utility in predicting disease mortality. Using the ATA 2009 Risk Stratification System with Proposed Modifications guidelines, the patient's condition was then classified as ATA intermediate risk [2].

After the surgery, it was decided that the patient undergo radioactive iodine therapy because this was necessary to eliminate remaining normal thyroid tissue and to treat any residual tumor cells in DTC patients [10]. Upon post-ablation scan of the whole body, there were functioning thyroid tissue remnants in the lower anterior neck and moderately intense tracer activity in the sacrum. Applying the ATA 2009 Risk Stratification System with Proposed Modifications guidelines, the patient's condition was now classified as ATA high risk [2].

Up to date, very limited reports are seen where papillary thyroid carcinoma is treated post operatively with radioactive iodine therapy when there is concurrent Moyamoya syndrome. A coordinated approach involving the endocrinologist, neurologist, surgeon, and nuclear medicine specialist is vital for an optimal treatment outcome.

One of the concerns that must be considered is the possibility of radiation induced-arteritis in our patient that could worsen the condition of the patient because he is already presenting with stenotic carotid arteries due to his Moyamoya syndrome. Subjecting the patient to radioiodine therapy could possibly result in worsening of the pathology in his carotid arteries, given the proximity to the thyroid bed. Although there is no literature stating that carotid arteritis could occur from radioactive iodine therapy if given in high doses for papillary thyroid cancer patients with Moyamoya syndrome, there are reports of radiation-induced occlusive vasculopathy in large arteries from irradiation for cranial tumors. It is documented that one of the known causes of acquired Moyamoya disease is cranial irradiation. One report even stated development of Moyamoya disease four months after irradiation [11]. Radiation-induced injuries to large arteries that result in stenotic and/

or occlusive vasculopathy have been considered to be relatively rare. It is recommended that follow-up studies be done to document the state of the carotid arteries involved to determine occurrence [11].

CONCLUSION

There is still no definite pathogenesis associating papillary thyroid carcinoma with Moyamoya disease. In our case, the patient was already diagnosed with Moyamoya disease four years before being diagnosed with papillary thyroid carcinoma. With coordinated planning from neurology, endocrinology, surgery, and nuclear medicine services, the patient had a successful surgery and radioiodine ablation without complications. He is currently asymptomatic and is able to return to his daily activities.

REFERENCES

Eary J, Brenner W. Nuclear medicine therapy. New York: Informa Healthcare. 2007; 4: 45–66.

2. Haugen B, Alexander E, Bible K, Doherty G, Mandel S, Nikiforov Y et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016;26(1):1–133.
3. Mettler F, Guiberteau M. Essentials of nuclear medicine imaging. Philadelphia: Elsevier/Saunders; 2012.
4. Chen J, You C. Moyamoya disease associated with thyroid carcinoma. eurosurgery Quarterly. 2016;26(2):148–150.
5. Phi J, Wang K, Lee J, Kim S. Moyamoya syndrome: a window of Moyamoya disease. J Korean Neurosurg Soc. 2015;57(6):408.
6. Schneider DF, Mazeh H, Lubner SJ, Jaume JC, Chen H. Cancer of the endocrine system. Abeloff's Clinical Oncology. 5th ed. Philadelphia, PA: Elsevier Saunders; 2014: chap 71.
7. Kasper D, Fauci A, Hauser S, Longo D, Jameson J, Loscalzo J. Harrison's principles of internal medicine. New York : McGraw Hill Education; 2008.
8. Ni J, Zhon LX, Wei YP, Li ML, Xu WH, Gao S, Cuj LY. Moyamoya syndrome associated with Graves' disease: a case series study. Ann Transl Med 2014;2(8):77. Doi:10.3978/j.issn.2305–5839.2014.08.03
9. Kim S, Heo K, Shin H, Bang O, Kim G, Chung C et al. Association of thyroid autoantibodies with Moyamoya-type cerebrovascular disease: a prospective study. Stroke. 2009;41(1):173–176.
10. Ziessman H, O'Malley J, Thrall J, Fahey F. Nuclear medicine. Philadelphia, PA: Elsevier Mosby; 2014.
11. Al-Amro ASchultz H. Moyamoya vasculopathy after cranial irradiation–a case report. Acta Oncologica. 1995;34(2):261–263.
12. Aoki S, Hayashi , Abe O, Shirouzu I, Ishigame K, Okubo T et al. Radiation-induced arteritis: thickened wall with prominent enhancement on cranial MR images–report of five cases and comparison with 18 cases of Moyamova disease. Radiology. 2002;223(3):683–688.