Twisted Ovarian Cyst, Galactorrhea and Pituitary Hyperplasia Misdiagnosed as Prolactinoma: An Overlooked Longstanding Overt Hypothyroidism from Hashimoto’s Thyroiditis

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Abstract:

We describe a 14–year–old girl who was referred for management of a prolactin–secreting pituitary adenoma as she had persistent milky discharge from her nipples, an elevated prolactin level and pituitary enlargement. Upon reviewing the medical history, it was noted that she had a history of secondary amenorrhea for 1 year, and had undergone an oophorectomy for twisted left ovarian cyst 5 months earlier. The physical examination found that she had a goiter, short stature and was relatively overweight. Based on these findings, it was thought that the patient likely had longstanding overt hypothyroidism. A thyroid function test (TFT) revealed a free thyroxine (FT4) level of 0.2 ng/dL and thyroid stimulating hormone (TSH) >100 mU/L, with high levels of antithyroid peroxidase (anti–TPO) and anti–thyroglobulin (anti–TG) antibodies, leading to the diagnosis of Hashimoto’s thyroiditis. After 8 months of levothyroxine treatment, the galactorrhea had disappeared, the pituitary enlargement had resolved and her menstruation had resumed normally, along with a 4–kg weight loss and 3–cm height gain. In summary, when evaluating a girl with ovarian cyst(s), especially if accompanied by other clinical findings like goiter, short stature, or menstrual irregularities, the physician should include hypothyroidism in the differential diagnosis. Early diagnosis and treatment of hypothyroidism can have a positive impact on the overall health and well–being of these patients, potentially preventing further complications related to both the thyroid disorder and ovarian cyst(s).

Keywords: Hashimoto’s thyroiditis, hyperprolactinemia, ovarian cyst, overt hypothyroidism, pituitary hyperplasia
Introduction

Hashimoto’s thyroiditis (HT), also known as chronic autoimmune/lymphocytic thyroiditis, is a common cause of goiter in children and adolescents with a reported prevalence of 1.2%1. The most common clinical presentation of HT is goiter with various thyroid functions at the time of diagnosis, i.e. euthyroidism (37–52% of cases), subclinical hypothyroidism (19–33%), overt hypothyroidism (8–22%), and transient hyperthyroidism (2–14%)2,3. There have been reports of wide fluctuations of thyroid function over time in HT patients with a tendency towards thyroid failure, and HT is known to be the most common cause of acquired hypothyroidism in children and adolescents4-6. One recent study reported that among children with severe overt hypothyroidism due to HT, the common symptoms were growth impairment, weight gain and goiter, while less frequent findings were menstrual irregularity, oligomenorrhea and secondary amenorrhea6. Ovarian cyst(s) including complications (e.g. twisted ovarian cyst), are rarely reported in pediatric HT patients and most of the reported cases were found to be longstanding untreated hypothyroidism7-9.

We herein report an adolescent girl who was referred due to misdiagnosis as pituitary prolactinoma. The medical review found that the girl had a history of a twisted ovarian cyst, secondary amenorrhea and later galactorrhea, and the physical examination revealed goiter, short stature and overweight, all of which led to the diagnosis of longstanding primary hypothyroidism from Hashimoto’s thyroiditis. As these clinical symptoms and signs are subtle, the diagnosis of acquired hypothyroidism from Hashimoto’s thyroiditis may be overlooked, and the delay in diagnosis and proper treatment can result in complications.

Case report

A 14-year-old girl presented at a local hospital with severe cramp-like pain at her left lower abdominal area. Her history taking at that time found that she had had a milky discharge from both nipples for 6 months. A whole abdominal computed tomography (CT) scan was performed to investigate the etiology of the severe abdominal pain which revealed a complex solid-cystic mass in the mid-pelvic cavity measuring 6.2x6.9x12 cm, compatible with a twisted left ovarian cyst. (Figure 1) After a left oophorectomy, the abdominal pain resolved but she still had milky discharge from both nipples. Laboratory investigations revealed a mildly elevated level of serum prolactin (PRL) at 38.1 ng/mL (normal 5–23). A pituitary magnetic resonance imaging (MRI) revealed a diffusely enlarged pituitary gland 1.5x1.3x1.0 cm in size. (Figure 2) She was then referred to Songklanagarind Hospital for further management of a pituitary prolactinoma.

At Songklanagarind Hospital, history taking found that she had had onset of menarche at 12 years of age and had experienced irregular menstruation during the first year, followed by no menstruation for 1 year. She had no symptoms of chronic fatigue, cold intolerance, constipation, visual disturbance or headaches, and no medication use. She had had a 4-kg weight gain but no height gain during the previous year. She had no family history of thyroid diseases or autoimmune disorders or precocious or delayed puberty. The physical examination found a short girl with a height of 144 cm (~2.35 standard deviation score, SDS) and she was relatively overweight with a weight of 51.7 kg (0.46 SDS) and BMI of 25 kg/m2. Her blood pressure was 104/65 mmHg and pulse rate 68/minute. She had a mildly puffy face and diffuse thyroid enlargement (6x3 cm). Her breast development was at Tanner stage V with milky discharge when breast compression was applied. She had no neurological deficits nor visual field defects. She had a midline surgical scar at the lower abdomen, and the ophthalmologic examination was unremarkable.

Laboratory investigations revealed very low levels of FT4 of 0.22 ng/dL (normal 0.90–1.60) and FT3 at 1.14 pg/mL (normal 2.00–4.40), and a very high level of
Figure 1 A whole abdominal computed tomography scan with contrast of the patient revealed a complex solid-cystic mass in the mid-pelvic cavity, measuring 6.2x6.9x12 cm, compatible with a twisted left ovarian cyst (A) coronal view (B) axial view

Figure 2 A contrast-enhanced fat-suppressed T1-weighted pituitary magnetic resonance imaging of the patient revealed a diffusely enlarged pituitary gland measuring 1.5x1.3x1 cm without optic chiasm compression (A) coronal view and (B) sagittal view
thyroid stimulating hormone (TSH) at >100 mU/L (normal 0.50–4.30), compatible with overt hypothyroidism. The serum PRL level was mildly elevated at 34.2 ng/mL (normal 5–20). Anti-thyroid peroxidase (anti–TPO) and anti-thyroglobulin (anti–TG) antibodies were elevated at 197 IU/mL (normal <26) and 67.9 IU/mL (normal <64), respectively. She was diagnosed as Hashimoto’s thyroiditis with long-standing primary hypothyroidism resulting in the earlier ovarian cyst (with complications), galactorrhea, and reactive thyrotroph and lactotroph hyperplasia.

The patient was started on levothyroxine 50 µg/day, which was increased to 100 µg/day after 4 weeks. After 4 months of treatment, her thyroid gland had decreased to 4x1 cm and her thyroid function test (TFT) returned to normal levels with FT4 of 1.51 ng/dL and TSH of 0.38 mU/L. Her menstruation resumed at 5 months after the levothyroxine treatment. A pituitary MRI performed at 6 months after the treatment found a normal size pituitary gland. She had a 4-kg weight loss and 3-cm height gain at 8 months after the beginning of treatment (her genetic height potential or midparental height was calculated to be 155 cm). Based on her bone age of 12.5–13 years, her predicted final adult height was 150–155 cm, indicating her genetic potential had been compromised after appropriate treatment.

Discussion

The patient’s symptoms began at the age of 13.5 years with acute severe abdominal pain, which was caused by a twisted ovarian cyst that necessitated an oophorectomy. Following the ovarian cyst surgery, the patient continued to have galactorrhea, along with an elevated prolactin level and pituitary enlargement. This combination of symptoms initially led to a diagnosis of a prolactinoma, a benign tumor of the pituitary gland. At our hospital, upon further examination and review of the patient’s medical history, it was found that she had a history of secondary amenorrhea and the physical findings including a goiter and short stature with relative overweight. Based on these additional findings, it was thought that the patient likely had longstanding overt hypothyroidism, most likely due to Hashimoto’s thyroiditis, the most common cause of acquired hypothyroidism in children and adolescents, which was confirmed by the TFT and presence of thyroid antibodies. The onset of hypothyroidism in this girl was estimated to be around 12–13 years of age, coinciding with a time when she had average height and started menstruating at age 12 (which is the average age of menarche for Thai girls). The galactorrhea observed in the patient, along with mildly elevated prolactin levels and pituitary enlargement, was simply explained by the loss of negative feedback due to very low levels of FT4, which led to increased production of thyrotropin–releasing hormone (TRH), which, in turn, stimulated both thyrotroph and lactotroph cells in the anterior pituitary gland10,11. This can result in elevated prolactin levels and associated symptoms like galactorrhea. The presence of an ovarian cyst in the patient was attributed to the high level of TSH, which can stimulate ovarian follicles as TSH shares structural similarities with gonadotropins.

An ovarian cyst is a benign condition in the adolescent age group. The exact incidence of ovarian cysts in adolescents is not well documented, but they are commonly found incidentally during abdominal ultrasound or other imaging studies for unrelated conditions. Most ovarian cysts in adolescents are functional cysts, including simple ovarian cysts, follicular cysts, or corpus luteal cysts, which are physiologically stimulated by gonadotropins during the normal menstrual cycle10,13. The majority of ovarian cysts are small, usually less than 5 cm, and often resolve spontaneously. Large ovarian cysts (>5 cm) can lead to complications such as rupture or torsion (twisting), which can cause acute abdominal pain15. Twisted ovarian cysts are rare in children and adolescents with an estimated incidence of 4.9 per 100,000 girls8. They typically present with acute abdominal pain in the pelvic area. The diagnosis
of a twisted ovarian cyst is confirmed through abdominal ultrasonography and oophorectomy is the most common management for this disorder. While most simple ovarian cysts are functional and resolve spontaneously, there have been many case reports of ovarian cysts in patients with longstanding hypothyroidism that were resolved after thyroxine treatment\(^1\), twisted ovarian cyst requiring oophorectomy\(^8\), and multiple enlarged cysts or ovarian hyperstimulation\(^3\). Therefore, it is important to consider a comprehensive approach in adolescent patients presenting with an ovarian cyst. This approach includes obtaining a detailed menstrual history, conducting a thorough physical examination including signs of hypothyroidism (goiter, short stature, overweight, puffy face/eyelids, and milky discharge from the nipples), and considering a wide range of potential causes and associated conditions to ensure accurate diagnosis and no delay in appropriate treatment to prevent complications or the progression of underlying conditions.

In overt hypothyroid Hashimoto’s thyroiditis patients, an enlarged pituitary gland (>10 mm) is commonly observed in magnetic resonance imaging or computed tomography studies\(^5\). One study found a significant proportion of pituitary enlargement in patients with TSH values greater than 50 mIU/L, and this proportion increased further for patients with TSH levels higher than 100 mIU/L\(^14\). Other studies have emphasized that it is important to distinguish between pituitary adenoma and pituitary hyperplasia because they may present with similar neuroimaging findings\(^10,11,14,15\). Differentiation between these conditions is important for appropriate management. In cases of pituitary tumors, particularly prolactinomas, prolactin levels are typically more than 250 ng/mL\(^15\). In our patient, she had a long duration of galactorrhea of at least 6 months with only mildly elevated prolactin levels, which made prolactinoma less likely as the diagnosis.

**Conclusion**

In summary, the patient’s complex presentation initially led to a misdiagnosis of prolactinoma, but a more comprehensive assessment of her medical history and clinical findings ultimately revealed that she had longstanding hypothyroidism due to Hashimoto’s thyroiditis. This underlying thyroid condition explained the galactorrhea, elevated prolactin levels, and pituitary hyperplasia. The presence of an ovarian cyst was linked to an elevated TSH level. It is probable that the misdiagnosis and delayed recognition of Hashimoto’s thyroiditis in our patient allowed these other conditions to persist and worsen over time.

**Ethics approval of research**

Ethical approval was obtained from the Institutional Review Board and Ethics Committee of Songklanagarind Hospital, Prince of Songkla University (REC. 66–233–1–4).

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SK, SJ, and TS performed the research. SK, SJ and TS wrote the paper. All authors read and approved the final manuscript.

**Conflict of interest**

There are no conflicts of interest to declare.

**References**


