Endocrinopathies

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KEYWORDS

• Cushing disease • adrenal insufficiency • hypothyroidism • hyperthyroidism
• thyroid nodules • polycystic ovarian syndrome

KEY POINTS

- Important features of Cushing syndrome include purple abdominal striae, facial plethora, buffalo hump, proximal muscle weakness, central obesity, and diabetes mellitus.
- Primary adrenal insufficiency can present with hypotension, hyperpigmentation, fatigue, and gastrointestinal symptoms such as nausea and vomiting.
- Findings in patients with hypothyroidism can include goiter, weight gain, bradycardia, and delayed deep tendon reflexes.
- Patients with hyperthyroidism present with tremor, hyperreflexia, tachycardia, and orbitopathy.
- Patients with polycystic ovary syndrome present with oligomenorrhea, hyperandrogenism, and features of metabolic syndrome such as weight gain and diabetes mellitus.

CUSHING SYNDROME

Introduction and Definition

Cushing syndrome is caused by prolonged exposure to inappropriately elevated levels of plasma glucocorticoids. It can occur due to endogenous or exogenous sources. Endogenous sources can be either adrenocorticotropic hormone (ACTH) independent or ACTH dependent. ACTH-independent sources include cortisol-producing adrenal adenomas. ACTH-dependent sources include pituitary adenomas or ectopic ACTH-producing tumors. Exogenous sources can include prolonged systemic or topical corticosteroid use.

Discussion

Patients are screened for Cushing syndrome based on certain signs and symptoms. Some of the signs of Cushing syndrome, such as hyperglycemia and truncal obesity, overlap with those found commonly in the general population, and it is therefore important to perform a comprehensive history and physical examination in patients

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Med Clin N Am 106 (2022) 495–507
https://doi.org/10.1016/j.mcna.2021.12.010 **medical.theclinics.com**

suspected of having this syndrome. These patients typically have progressively worsening signs and symptoms over time.

Patients with Cushing syndrome can have findings such as central obesity that involves the face, neck, trunk, and abdomen. This appearance is different from generalized obesity, which is more common in the population. Other features of metabolic syndrome, including type 2 diabetes mellitus and hypertension, may also be present. A common finding in Cushing syndrome is rounding of the face due to fat accumulation in the cheeks, which is termed "moon facies." Patients may also develop facial plethora—a fullness of the face with a flushed appearing or reddish complexion. These patients often develop fat deposits over the thoraco-cervical spine (termed "buffalo hump") and in the supraclavicular fossae (**Fig. 2**).

Dermatologic manifestations of Cushing syndrome include a virtually pathognomonic sign of the presence of this syndrome which are purple, nonblanching striae that can be found on the abdomen, arms, and thighs. These striae are usually more than 1 cm in width and look different from the pale striae that occur in pregnant women or in the setting of rapid weight gain or loss (**Fig. 1**).[1] Women with Cushing syndrome can develop signs of hyperandrogenism because the adrenal glands are the main source of androgen production in women. These signs include hirsutism with particularly marked hair growth on the upper lip and chin. Other dermatologic findings include easy bruising as well as thinning of the skin due to prolonged corticosteroid exposure. Another feature of Cushing syndrome includes wrinkling of the skin on the dorsal surface of the hand, which results in a "cigarette paper" appearance known as Liddle sign.[1]

Musculoskeletal manifestations of Cushing syndrome include proximal muscle weakness involving the upper or lower extremities manifested by difficulty rising from a seated position, climbing stairs, or raising the hands above the head. Osteoporosis may occur resulting in bone loss followed by fragility and vertebral compression fractures and resultant loss in height.

The cardiovascular signs of hypercortisolism may include hypertension, and severe hypercortisolism can even cause a hypercoaguable state resulting in physical findings consistent with deep vein thrombosis or pulmonary embolism. **Table 1** lists some of the highest yield findings for Cushing syndrome.[2]

ADRENAL INSUFFICIENCY

Introduction and Definition

Adrenal insufficiency refers to glucocorticoid deficiency with or without concurrent mineralocorticoid deficiency and adrenal androgen deficiency and can be primary, secondary, or tertiary in origin. Primary adrenal insufficiency refers to disease that occurs in the adrenal cortex, whereas secondary adrenal insufficiency occurs due to pituitary disease leading to decreased secretion of ACTH. Tertiary adrenal insufficiency results from impaired release of corticotropin-releasing hormone from the hypothalamus, which then fails to stimulate the secretion of ACTH from the pituitary gland. The causes of primary, secondary, and tertiary adrenal insufficiency are summarized in **Boxes 1–3**.[3]

A key difference between primary adrenal insufficiency and secondary or tertiary adrenal insufficiency is that primary adrenal insufficiency results in mineralocorticoid deficiency, whereas secondary and tertiary adrenal insufficiencies do not. This is because aldosterone secretion is regulated by the renin-angiotensin-aldosterone system (RAAS) and not by the pituitary gland. In secondary and tertiary adrenal insufficiency, only glucocorticoid secretion from the adrenal gland is affected.

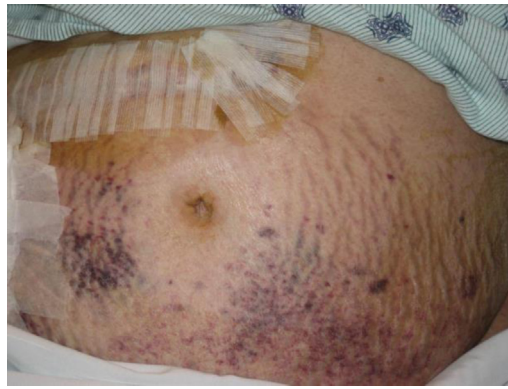

Fig. 1. Abdominal striae and bruising in a patient with Cushing syndrome (with permission from the collection of P. Aronowitz).

Discussion

Adrenal insufficiency can be chronic in nature or can present acutely, as an adrenal crisis, which is a life-threatening emergency. Chronic adrenal insufficiency presents with nonspecific signs and symptoms that can lead to a delay in diagnosis. Symptoms related to glucocorticoid deficiency include fatigue, weight loss, abdominal pain, nausea, and vomiting. Mineralocorticoid deficiency causes dizziness, orthostatic

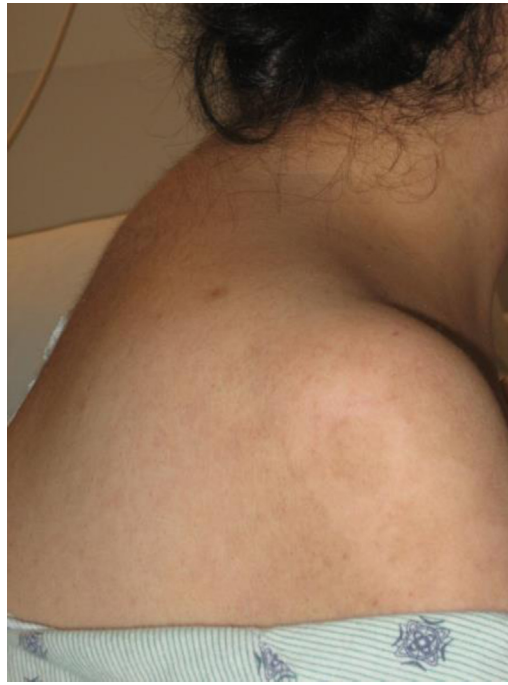

Fig. 2. Dorsocervical hump in a patient with Cushing syndrome (with permission from the collection of P. Aronowitz).

Table 1
Findings with increased likelihood ratios predicting the presence of Cushing syndrome

Physical Examination Finding	Likelihood Ratio if Finding Is Present
Skin thinning	115.6
Bruising	4.5
Central obesity	3.0
Facial plethora	2.7

hypotension, and, sometimes, salt craving. Adrenal androgen deficiency is more pronounced in women and can cause symptoms such as dry skin and loss of libido.

Patients with adrenal insufficiency may present with several key physical examination findings and are often relatively hypotensive with systolic blood pressures less than 100 mm Hg. Orthostatic hypotension due to mineralocorticoid deficiency may also be present. Weight loss due to volume depletion and anorexia are also often present. Patients with primary adrenal insufficiency may have skin hyperpigmentation, which occurs due to increased production of proopiomelanocortin, a prohormone that is cleaved into ACTH, melanocyte-stimulating hormone (MSH), and other hormones. The elevated MSH leads to increased melanin synthesis, which leads to hyperpigmentation. Brown pigmentation can be diffuse but tends to be more obvious in sun-exposed areas of the face, neck, and back of the hands. It also can be prominent in the palmar creases, on the inner surface of the lips, and the buccal mucosa.[1] Skin hyperpigmentation is an important distinguishing characteristic between primary and secondary adrenal insufficiency because it does not occur in patients with secondary adrenal insufficiency.

Primary adrenal insufficiency may occur in the context of autoimmune polyendocrinopathy syndromes. There are two predominant types of autoimmune polyglandular syndromes (APS type 1 and type 2). APS type 1 (abbreviated as APECED) is associated with Addison disease, chronic mucocutaneous candidiasis, ectodermal dystrophy, and hypoparathyroidism. It is caused by mutations in the *AIRE* gene and is

Box 1
Causes of primary adrenal insufficiency

Autoimmune adrenalitis caused by 21-21-hydroxylase autoantibodies hydro

APS type 1 (*AIRE* gene mutation)

APS type 2

Infectious adrenalitis (tuberculosis, HIV, fungal, and other infections)

Genetic disorders (adrenoleukodystrophy)

Adrenal metastases

Adrenal hemorrhage

Adrenal infarction

Medications (fluconazole, ketoconazole, phenytoin, etomidate, and others)

Congenital adrenal hypoplasia

Congenital adrenal hyperplasia

Familial glucocorticoid resistance

Box 2
Causes of secondary adrenal insufficiency

- Pituitary tumors
- Pituitary trauma
- Pituitary surgery
- Pituitary radiation therapy
- Infections or abscesses (tuberculosis and others)
- Infiltrative processes (sarcoidosis, lymphocytic hypophysitis, hemochromatosis, and others)
- Pituitary infarction
- Pituitary apoplexy
- Genetic mutations (eg, *HESX1* gene mutation)

inherited in an autosomal recessive fashion. Important physical examination findings in these patients are mucocutaneous candidiasis and less frequently, candidiasis affecting the esophagus and skin.[4] Ectodermal dystrophy refers to pitted nails and enamel hypoplasia.[4] Physical examination findings of hypoparathyroidism include features of hypocalcemia such as the presence of a Chvostek or Trousseau sign. Primary adrenal insufficiency can also occur in the context of APS type II, which is more common. APS type II is defined by a patient having two or more of the following: Addison disease, autoimmune thyroid disease, type 1 diabetes, primary hypogonadism, and other nonendocrine manifestations (such as myasthenia gravis).[4]

In patients with chronic secondary adrenal insufficiency, only glucocorticoid production is affected, and as a result, these patients have symptoms such as fatigue, anorexia, weight loss, nausea, and generalized abdominal pain. Hyperpigmentation is not present because ACTH production is decreased and hypotension usually does not occur because the RAAS system is intact. Manifestations of a pituitary or hypothalamic tumor may include anterior pituitary hormone deficiencies as well as headaches and visual field deficits if the tumor is causing increased intracranial pressure or compressing the optic chiasm.

Acute adrenal crisis is a medical emergency and needs to be treated immediately with high-dose corticosteroids. Patients with acute adrenal insufficiency present with complaints of fatigue, nausea, vomiting, and abdominal pain. Physical examination is often remarkable for the presence of hypotension, altered level of mentation,

Box 3
Causes of tertiary adrenal insufficiency

- Hypothalamic masses (craniopharyngiomas or metastases from distant primary cancer)
- Traumatic brain injury
- Hypothalamic surgery
- Hypothalamic irradiation
- Infections
- Infiltrative processes
- Glucocorticoid therapy (systemic, topical, or inhaled steroids)

and generalized abdominal tenderness. Patients may also have a fever due to an increased inflammatory response or the presence of an infection. Patients with acute adrenal insufficiency due to bilateral adrenal hemorrhage or infarction often present with hypotension, abdominal and flank tenderness, and decreased hemoglobin.

HYPOTHYROIDISM

Introduction and Definition

Hypothyroidism refers to thyroid hormone deficiency and can be classified as primary or secondary. In iodine-sufficient areas, the most common cause of primary hypothyroidism is autoimmune thyroiditis, more commonly known as Hashimoto disease. The most common causes of primary and secondary hypothyroidism are listed in **Boxes 4–6** and **Tables 2 and 3**.[5]

Discussion

The manifestations of hypothyroidism can affect all the organ systems. Some of the most common signs and symptoms of hypothyroidism include the following:

- *General:* weight gain, cold intolerance, and fatigue
- *Pulmonary:* dyspnea on exertion
- *Neurologic:* impaired memory and mood impairment
- *Gastrointestinal:* constipation
- *Endocrinologic:* menstrual dysfunction and manifestations of metabolic syndrome including hypertension and dyslipidemia
- *Musculoskeletal:* muscle weakness, muscle cramps, and arthralgias
- *Dermatologic:* coarse skin, alopecia, and brittle nails

Generalized physical examination findings of hypothyroidism include weight gain, bradycardia, and diastolic hypertension. In patients with Hashimoto thyroiditis, the thyroid gland may be firm or rubbery, and the thyroid examination may reveal a goiter in cases of severe hypothyroidism.

Dermatologic manifestations of hypothyroidism include pale, cool skin due to vasoconstriction and anemia. Hair loss, brittle nails, dry skin, and decreased sweating may be present in cases of severe hypothyroidism. Periorbital edema may occur, manifested as a puffy appearance around the eyes due to the accumulation of myxedematous tissue. Edema can also occur on the dorsa of the hands and feet as well as in the supraclavicular fossae.[6,7]

Box 4
Causes of primary hypothyroidism

Autoimmune thyroiditis (Hashimoto thyroiditis)

Iatrogenic (thyroidectomy, radiation)

Thyroiditis (painless thyroiditis, postpartum thyroiditis, and viral thyroiditis)

Drug induced (amiodarone, lithium, and checkpoint inhibitor therapy)

Iodine deficiency

Infiltrative diseases (sarcoidosis and hemochromatosis)

Thyroid malignancy

Metastases to the thyroid gland

Box 5
Causes of secondary hypothyroidism

Pituitary masses causing Thyroid stimulating hormone (TSH) deficiency

Hypothalamic disease causing Thyrotropin-releasing Hormone (TRH) deficiency

Resistance to TSH/TRH

The neurologic examination in the presence of hypothyroidism often reveals delayed relaxation of deep tendon reflexes, and in the elderly population, memory defects and lethargy can be present. Psychiatric manifestations, such as depression and other mood disorders, are frequently associated with hypothyroidism.

Patients with hypothyroidism due to thyroiditis may have characteristic findings on physical examination. Viral thyroiditis usually results in thyroid tenderness (and is often preceded by upper respiratory symptoms). Riedel thyroiditis is rare and occurs due to fibrosis of the thyroid gland, which extends into adjacent tissues. Riedel thyroiditis can present with an enlarged thyroid gland or goiter, which is hard, asymmetric, and fixed to adjacent tissues and muscles. These patients can have compressive symptoms such as hoarseness, shortness of breath, and dysphagia due to fibrosis involving surrounding structures such as the recurrent laryngeal nerve, trachea, and esophagus.

Patients with secondary hypothyroidism due to a pituitary tumor may present with other signs and symptoms of a pituitary adenoma. It is important to screen for coexisting anterior pituitary hormone deficiencies. Patients may also have visual field deficits due to compression of the optic chiasm from the enlarging pituitary tumor.

Box 6
Common causes of hyperthyroidism[8]

Thyrotoxicosis associated with normal or elevated radioiodine uptake

Graves' disease

Hashitoxicosis

Toxic adenoma

Toxic multinodular goiter

TSH-producing pituitary adenoma

HCG-mediated hyperthyroidism

Thyrotoxicosis associated with low radioiodine uptake

Subacute (DeQuervain, granulomatous) thyroiditis

Thyroiditis (lymphocytic thyroiditis and postpartum thyroiditis)

Amiodarone-induced thyroiditis

Thyroiditis induced by checkpoint inhibitors

Radiation thyroiditis

Iatrogenic thyrotoxicosis

Intentional ingestion of thyroid hormone

Struma ovarii

Table 2
Findings with increased likelihood ratios for the presence of hypothyroidism[2]

Physical Examination Finding	Likelihood Ratio if Finding Is Present
Hypothyroid speech (low voice, reduced range, low pitch)	5.4
Bradycardia	4.2
Coarse skin	3.4
Delayed ankle reflexes	3.4

HYPERTHYROIDISM

Introduction and Definition

Hyperthyroidism refers to increased thyroid hormone production by the thyroid gland. Signs and symptoms of hyperthyroidism can affect several organ systems and are listed as follows:

- *General:* weight loss
- *Eyes:*
  - Graves' eye disease can lead to proptosis, lid lag, dry eyes, conjunctival erythema, and irritation
- *Cardiovascular:*
  - Tachycardia, widened pulse pressure, systolic hypertension, and atrial fibrillation
- *Endocrine:*
  - Osteoporosis, dyslipidemia (low high-density lipoprotein), and hyperglycemia
- *Respiratory:*
  - Dyspnea
- *Gastrointestinal:*
  - Diarrhea (better described as soft, formed stools occurring several times each day)
- *Neurologic/psychiatric:*
  - Anxiety, agitation, depression, and psychosis
- *Skin:*
  - Warm skin due to increased blood flow; heat intolerance
  - Sweating, onycholysis, and vitiligo

DISCUSSION

Physical examination findings common to various forms of hyperthyroidism include weight loss due to the hypermetabolic effects of thyroid hormone, systolic hypertension, tachycardia, and irregular heart rhythm due to atrial fibrillation. Some patients

Table 3
Findings with clinically useful positive likelihood ratios for the presence of hyperthyroidism[2]

Physical Examination Finding	Likelihood Ratio if Finding Is Present
Eyelid retraction	33.2
Eyelid lag	18.6
Tremor	11.5
Warm, moist skin	6.8
Tachycardia	4.5

can have systolic hypertension. Neurologic examination often reveals a fine resting tremor, hyperreflexia, and proximal muscle weakness. Dermatologic examination shows warm, moist skin, hair loss, and onycholysis. Pretibial myxedema can occur in more serious cases of hyperthyroidism.

A common cause of hyperthyroidism is Graves' disease, which occurs due to thyroid autoantibodies, either thyroid-stimulating immunoglobulin or TSH receptor antibodies. Patients with Graves' disease have diffuse enlargement of the thyroid gland and a systolic bruit due to markedly increased blood flow to the gland, which may be heard when auscultating over the upper or lower poles of the thyroid gland, where the superior and inferior thyroid arteries enter the gland.[8] Sometimes, a thrill can also be palpated.

Graves' disease causes characteristic findings on eye examination, which include periorbital edema and conjunctival erythema, excessive tearing, and lid retraction, sometimes characterized as "thyroid stare." Examination of extraocular movements may reveal dysconjugate gaze and lid lag. In patients with lid lag, the upper lid lags behind the lobe, exposing more sclera when the patient looks downward or, similarly, when they look upward. Patients with Graves' orbitopathy can have proptosis and exophthalmos which can be measured by an exophthalmometer. Disease activity is assessed using a seven-point clinical activity score, with a score of 3 or more classified as being active disease.

Patients with a toxic adenoma have an autonomously functioning thyroid nodule, and on physical examination, patients may have a palpable thyroid nodule if it is greater than 3 cm in size.[9] Patients with toxic multinodular goiter have an overproduction of thyroid hormone due to multiple hyperfunctioning nodules; however, because these patients produce less thyroid hormone than those with Graves' disease, symptoms are usually milder in nature.[8]

Obstructive symptoms are more common in patients with toxic multinodular goiter than those in Graves' disease due to the characteristics of the thyroid gland.[8] Obstructive symptoms occur due to compression of surrounding cervical structures including the trachea, great vessels, and recurrent laryngeal nerve due to retrosternal extension of the thyroid. Compressive symptoms include dyspnea, dysphagia, hoarseness of voice, or vocal cord paralysis. In rare cases, Horner syndrome may occur due to compression of the cervical sympathetic chain. Toxic multinodular goiter is not usually accompanied by ophthalmologic manifestations and may be a sign of coexistent Graves' disease if also present.[8]

Another cause of hyperthyroidism is subacute thyroiditis which can occur in up to 5% of patients with thyroid disease.[10] Patients with subacute thyroiditis have thyroid pain, swelling, or both often following an upper respiratory infection. On palpation, part of the gland may be enlarged and often tender to palpation and the overlying skin may be warm and erythematous. Other features of a viral infection are commonly present, such as fevers, myalgias, and pharyngitis. Up to 50% of patients have symptoms of thyrotoxicosis.[10] Usually the symptoms are self-limited but can last for several months. In about 90% of patients, no residual deficiency in thyroid function remains after recovery.[8]

Struma ovarii occurs when thyroid tissue is present in ovarian teratomas. Thyrotoxicosis can occur in 8% to 10% of patients.[8] Patients generally present with lower abdominal pain or a mass and can occasionally have ascites. Findings on radioiodine scan indicate low uptake in the thyroid gland. Rarely, women who have a struma ovarii can present with a goiter, and these patients often have coexistent Grave disease.[11]

TSH-secreting adenomas are a rare cause of hyperthyroidism. A case series revealed that about 94% of patients with TSH-secreting pituitary adenomas have a

goiter.[12] These patients can have features of hyperthyroidism including palpitations, tremors, weight loss, and heat intolerance. They also have symptoms of a pituitary mass including headaches and visual field deficits such as bitemporal hemianopsia. Because TSH-secreting adenomas may cosecrete growth hormone and prolactin, it is important to assess for physical examination changes related to acromegaly and prolactinoma. In a case series with 255 patients with TSH-secreting adenomas, about 33% had menstrual disturbances and 28% had galactorrhea which are suggestive of prolactin excess.[12] Patients should be screened for findings of acromegaly including enlarged jaw, enlarged hands and feet, and coarse facial features, among other findings.

Hyperthyroidism can present differently in elderly patients as compared with younger patients. In one cross-sectional study, elderly patients had a higher prevalence of weight loss and shortness of breath but were less likely to have typical features of hyperthyroidism such as heat tolerance, anxiety, or tremors.[13] Apathetic hyperthyroidism refers to elderly patients who do not display the classic features of hyperthyroidism. These patients seem depressed or withdrawn and can be misdiagnosed as having psychiatric disorders such as depression or even suspected to have underlying malignancy. Patients with apathetic hyperthyroidism often have staring, placid faces, and weakness and muscle wasting are common in this disorder.[8]

THYROID NODULES

Introduction and Definition

Thyroid nodules are common and can be found in up to 65% of the population.[14] Thyroid nodules can be palpated by the patient, discovered on physical examination, or incidentally found on imaging studies such as computed tomography, magnetic resonance imaging, or ultrasound. Most thyroid nodules are benign, and the incidence of cancer ranges around 5%–10%.[14] Risk factors for cancer include previous head or neck irradiation, family history of thyroid cancer or thyroid cancer syndromes (such as multiple endocrine neoplasia type 2, familial adenomatous polyposis, or Cowden syndrome). Most patients with thyroid nodules are euthyroid and less than 5% of nodules cause hyperthyroidism or thyrotoxicosis.[14]

Discussion

Clinically, most patients with thyroid nodules are asymptomatic. Some patients with large thyroid nodules may complain of compressive symptoms such as dysphagia, dyspnea, dysphonia or hoarseness, whereas others may complain of a globus sensation (the feeling that something is stuck in the throat). Patients who have a globus sensation usually have a nodule greater than 3 cm, and the nodule is likely to be located close to the trachea.[14] Thyroid nodules that lead to dysphagia are located in the left lobe and extend posteriorly leading to compression of the esophagus.[14] Nodules that are increasing rapidly in size or have hemorrhage into them can cause pain. Thyroid nodules that are firm, fixed, rapidly growing, or associated with cervical lymphadenopathy must be evaluated promptly to rule out thyroid cancer.

Some patients with thyroid nodules will have a normal physical examination if the nodules are small or located posteriorly within the gland. On examination of the thyroid gland, it is important to note the size, number, and consistency of the nodules; the presence of multiple thyroid nodules can be a sign of multinodular goiter. Benign nodules tend to be smooth, soft, mobile, and generally do not cause obstructive symptoms. Suspicious nodules are generally hard, fixed, and irregular. When a patient presents with thyroid nodules, it is also imperative to examine the cervical lymph

Box 7
Rotterdam criteria to diagnose PCOS

Rotterdam criteria (Two of the following criteria are required to make the diagnosis):
- Oligo and/or anovulation
- Clinical and/or biochemical signs of hyperandrogenism
- Polycystic ovaries (by ultrasound)

node chains for evidence of lymphadenopathy as the presence of large, firm lymph nodes may indicate the presence of thyroid cancer. In addition to physical examination, thyroid nodules can be further evaluated with thyroid ultrasound.

In patients with obstructive symptoms due to a goiter or multinodular goiter, the examiner can ask the patient to perform the Pemberton maneuver. For this maneuver, the patient raises the arms vertically above the head for about 60 seconds. This test is considered positive (Pemberton sign) if the patient's neck veins become more distended or if the patient develops facial plethora, cyanosis, or dyspnea due to impaired venous return from the neck and face due to compression of the great vessels by the goiter.

POLYCYSTIC OVARY SYNDROME

Introduction and Definition

Polycystic ovary syndrome (PCOS) is an endocrinopathy affecting women and is characterized by a constellation of signs and symptoms. It is characterized by oligomenorrhea, hyperandrogenism, and symptoms of metabolic syndrome. The Rotterdam criteria are used to make a diagnosis of PCOS (**Box 7**).

Discussion

Women with PCOS frequently have oligomenorrhea or amenorrhea, so it is important to take a detailed menstrual cycle history. They often have features of hyperandrogenism such as hirsutism which is characterized by thick terminal hair in a male distribution pattern (upper lip, chin, and periareolar area). Hair growth can be characterized using the Ferriman–Gallwey score to evaluate hirsutism. Women with PCOS also have androgenic alopecia or hair loss pattern seen in men. In rare cases, patients can develop acne, clitoromegaly, deepening of the voice, and oily skin. If women present with these symptoms, other serious causes of hyperandrogenism (such as adrenal or ovarian tumors) should be excluded.

Women who have PCOS can develop insulin resistance leading to hyperglycemia or diabetes mellitus. The insulin resistance can lead to obesity and associated

Fig. 3. Acanthosis nigricans on the neck of a patient with PCOS.[18] (With permission from the collection of S. Karakas).

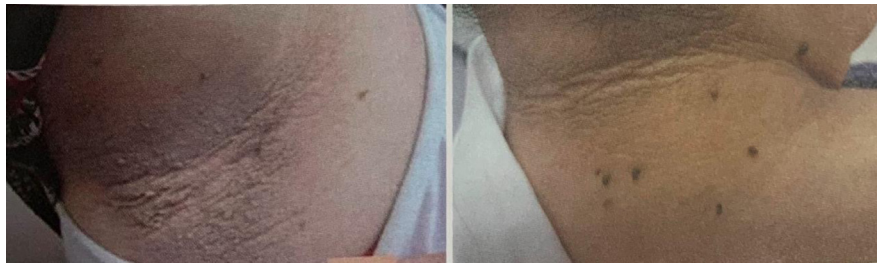

Fig. 4. Skin tags on a patient with PCOS. (With permission from the collection of S. Karakas).

comorbidities of hypertension and dyslipidemia. It is important to check patient's weight, body mass index (BMI), and blood pressure at every visit. A recent study found that women with PCOS are more likely to develop hypertension beginning in early adulthood (by age 35), independent of BMI.[15,16] The study concluded that PCOS was independently associated with 37% greater risk of hypertension when compared with women without PCOS.[15]

Body fat distribution can be assessed by checking waist and hip circumference. Women with PCOS often have a BMI of 30 or higher. Due to increased insulin resistance, patients develop dark skin patches in the axillae, neck, and thighs known as acanthosis nigricans as well as skin tags in these same regions (**Figs. 3** and **4**). Insulin resistance can also lead to nonalcoholic fatty liver disease; it is therefore important to assess for liver size which may be suggestive of hepatomegaly from evolving liver disease.

It is important to screen for obstructive sleep apnea (OSA) in patients with PCOS. One meta-analysis concluded that patients with PCOS are about 9.7 times more likely to develop OSA.[17] Although the exact mechanism of how PCOS leads to OSA has not been elucidated, one important link seems to be the presence of obesity. Obesity can lead to increased fat deposition around the pharynx and decreased thoracic compliance. Patients should be asked about symptoms of sleep apnea such as excessive daytime sleepiness or snoring during sleep.

Finally, women with PCOS can develop psychiatric or mood disorders such as anxiety or depression. Screening for these disorders using a Patient Health Questionaire 9 (PHQ-9) questionnaire should be part of the evaluation for women with PCOS.

CLINICS CARE POINTS

- Cushing syndrome should be considered when there is the presence of violaceous striae.
- Adrenal crisis is a medical emergency that can present similar to septic shock and should be treated with high dose corticosteroids.
- Thyroid nodules are present in up to 65% of the population, however, 90-95% of these nodules are benign.
- Polycystic ovarian syndrome should be considered in women with oligomenorrhea, clinical signs of hyperandrogenism and insulin resistance.

DISCLOSURE

The authors have nothing to disclose.

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