ATYPICAL GRAVES’ DISEASE SYMPTOMS

Rhabdomyolysis, Weight Gain, Hives, EAC, and other Atypical Symptoms

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Besides the typical symptoms associated with hyperthyroidism, patients with Graves' disease are also at risk for a number of different atypical symptoms.

Predominant Symptoms

Graves' disease is a condition of autoimmune hyperthyroidism, which typically causes one or more predominant symptoms related to excess thyroid hormone, such as nervousness, anxiety, and palpitations. Graves' disease can also cause extrathyroidal (away from the thyroid) manifestations, including pretibial myxedema, which primarily causes swelling and scaling of the lower legs, and the eye condition Graves' ophthalmopathy. In addition, Graves' disease can also cause several atypical symptoms such as erythema annulare centrifugum (EAC), vitiligo, hives, and weight gain. This article describes these atypical symptoms. It's important to recognize that these symptoms can be part of the Graves' disease spectrum rather than indications of a newly emerging illness.

Dermal Symptoms

Patients with Graves' disease can develop hypersensitivity reactions resulting in hives, urticaria (itching), and angioedema, a type of swelling that often occurs on the neck, face, or hands. A condition of urticaria-related angioedema can also occur. Although common allergens and insect bites are often implicated, the cause of the hypersensitivity reaction can't always be determined.

The condition erythema annulare centrifugum (EAC), which is classified as one of the figurate or gyrate erythemas (redness) can also occur. The rash in EAC is characterized by a scaling or non-scaling, reddened eruption which spreads from the edges outward while the center area clears. An exact trigger hasn't been determined for the hypersensitivity reaction in EAC. In scaling lesions, a trail of scales may follow the rash's periphery as it spreads.

There are several varieties of EAC, some associated with itching and some with no symptoms other than rash. EAC tends to recur in times of stress and the condition may persist for several months to many years. Besides its association with Graves' disease, EAC may occur in patients with liver disease, hypereosinophilic syndrome, appendicitis, systemic lupus erythematosus (SLE) and Sjogren’s syndrome.

About 7 percent of patients with Graves' disease may also develop white or blanched patches of skin in a condition known as vitiligo.
Acropachy, a condition of soft tissue swelling that primarily affects the fingers and toes, causing a condition resembling elephantiasis, rarely occurs in patients with Graves' disease. Acropachy is most likely to occur in patients who have been treated with radioiodine ablation and also have pretibial myxedema. Acropachy is also considered a rheumatological disorder because it can cause an associated joint pain.

Skin and mucous membrane blisters and erosions can also occur in co-existing conditions of autoimmune bullous skin disease, especially herpes gestationis, which can occur in pregnancy and during the postpartum period. In Graves' disease it may be confused with a anti-thyroid drug reaction.

**Metabolic Symptoms**

Hypoglycemia, a condition of low blood sugar, can occur as a transient condition in patients with Graves' disease. The hypoglycemia that occurs in patients with Graves' disease is caused by insulin antibodies that cause a condition of insulin autoimmune syndrome.

Hyperglycemia, a condition of elevated blood sugar can occur in patients with Graves' disease as part of a hyperglycemic hyper-osmolar state, similar to dehydration.

Weight gain occurs in 10-15 percent of patients with Graves' disease, usually younger patients. The reasons are unclear but appear to be due to inflammation and to deficiencies of free fatty acids. Sedentary changes related to fatigue may also be responsible.

Rhabdomyolysis, a potentially fatal condition of muscle destruction typically seen in cocaine and amphetamine overdoses, has been reported to rarely occur in patients with Graves' disease. In Graves' disease, rhabdomyolysis is caused by increasing energy consumption associated with depletion of muscle energy and muscle substrate stores.

Hypokalemia, a condition of low potassium, may occur in patients with Graves' disease, especially Asian males, and lead to thyrotoxic periodic paralysis. This condition leads to muscle weakness and temporary paralysis and tends to be exacerbated by the ingestion of alcohol and foods with a high sugar content.

**Circulatory Changes**

A small number of patients with hyperthyroidism caused by Graves' disease are reported to have increased Factor VIII activity, which can cause increased clotting and cerebral venous thrombosis.

Patients with Graves' disease are more likely than other people to have antiphospholipid or anticardiolipin antibodies, which cause increased clotting. Antiphospholipid syndrome is the primary cause of miscarriages and strokes in young women.
Neurological Changes

A condition known as rapid consciousness disturbance, which is similar to dementia, can occur in Graves' disease, especially in elderly patients. Apathy is a similar presentation in the elderly Graves' patient.

Headache is a rare occurrence in Graves' disease and when it occurs it can be an early warning sign of cerebral venous thrombosis. Six reports of cerebral venous thrombosis have been reported in Graves' disease patients and appear to be related to recurrent inflammation. Of these six patients one was a male, and the other five were females, all of whom were using oral contraceptives.

Hashimoto's encephalopathy has been reported to occur in a small number of patients with Graves' disease, primarily middle-aged and elderly patients. Seizures and a condition of multifocal motor status epilepticus have also been reported in a small number of patients with Graves' disease.

Eye Changes

Besides the typical symptoms of thyroid eye disease (TED) associated with either abnormal thyroid hormone levels or the autoimmune process, a small number of patients with Graves' disease may develop a temporary condition of unilateral edema, affecting the upper eyelid of only one eye. Unilateral edema is a sign of hyperthyroidism and typically resolves as thyroid hormone levels return to the normal range.

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