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THE ORIGIN OF SHEEHAN SYNDROME ETIOPATHAGENESIS AND METHODS OF TREATMENT WITH MODERN METHODS

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Annotation: Sheehan syndrome is a rare condition involving injury to your pituitary gland following extreme blood loss during childbirth. With Sheehan syndrome, severe blood loss deprives your pituitary gland of the oxygen it needs to work properly. As a result, some of the tissue in your pituitary gland dies.Damage to your pituitary gland can have widespread effects on your body because it's a "master gland." Not only does your pituitary gland secrete hormones that spur important processes in your body, but it also tells other glands to secrete hormones. Your pituitary gland helps regulate processes that impact your brain, skin, energy, mood, reproductive organs, growth and more.

Key words: Sheehan syndrome, hormone , energy, blood, inflammation .

Sheehan's syndrome, also known as postpartum pituitary gland necrosis, occurs when the pituitary gland is damaged due to significant blood loss and hypovolemic shock (ischemic necrosis) usually during or after childbirth leading to decreased functioning of the pituitary gland (hypopituitarism).[1] The pituitary gland is an endocrine organ, meaning it produces certain hormones and is involved in the regulation of various other hormones.[2] This gland is located in the brain and sits in a pocket of the sphenoid bone known as the sella turcica.[3] The pituitary gland works in conjunction with the hypothalamus, and other endocrine organs to modulate numerous bodily functions including growth, metabolism, menstruation, lactation, and even the "fight-or-flight" response.[2] These endocrine organs release hormones in very specific pathways, known as hormonal axes. For example, the release of a hormone in the hypothalamus will target the pituitary to trigger the release of a subsequent hormone, and the pituitary's released hormone will target the next organ in the pathway.[2] Hence, damage to the pituitary gland can have downstream effects on any of the aforementioned bodily functions.

The various signs and symptoms in Sheehan's syndrome are caused by damage to the pituitary, thereby causing a decrease in one or more of the hormones it normally secretes. Since the pituitary controls many glands in the endocrine system, partial or complete loss of a variety of functions may result.[4] Many of the signs and symptoms of Sheehan's are considered "nonspecific" in the medical community; in other words these signs and symptoms are seen in a number of different disease processes, and are not specific to a singular disease or syndrome.[5]

In some cases, a woman with Sheehan syndrome may be relatively asymptomatic initially; therefore, the diagnosis would not be made until years later when features of hypopituitarism become evident.[6] In rare instances this syndrome can present acutely with unstable vital signs, dangerously low blood glucose levels, heart failure, or even psychosis.[7][8] Hypopituitarism can lead to an interruption in any of the following hormone pathways: thyroid disorder (secondary hypothyroidism), adrenal gland (adrenal insufficiency due to glucocorticoid deficiency), sex hormone (gonadotropin deficiency), prolactin (a hormone responsible for lactation), growth hormone, or rarely anti-diuretic hormone deficiency (central diabetes insipidus).[2] Since damage to the pituitary can cause a deficiency in more than one of these hormone pathways simultaneously, it is possible to have a mix of any of the signs or symptoms listed below.[8]

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Sheehan's syndrome's most common initial symptoms are difficulties with or total absence of lactation (agalactorrhea).[6] Another common sign is infrequent menstrual cycles (oligomenorrhea) or absent menstrual cycles (amenorrhea) following delivery.[8] In addition to menstrual irregularities other signs of sex hormone deficiency are hot flashes, decreased libido, and breast involution.[5] Symptoms and signs of thyroid disorder are tiredness, intolerance to cold, constipation, weight gain, hair loss, slowed thinking, as well as a slowed heart rate and low blood pressure.[9] Adrenal gland malfunction can present acutely or chronically. In a more chronic case, it is similar to Addison's disease with symptoms including fatigue, weight loss, hypoglycemia (low blood sugar levels), low hemoglobin levels (anemia) and hyponatremia (low sodium levels) that develop over several months or years.[10] Acute adrenal insufficiency is referred to as an adrenal crisis, which can be life-threatening, and occurs very shortly after the inciting event i.e. significant blood loss post-partum in the context of Sheehan's syndrome.[11] Adrenal crisis signs and symptoms include hypoglycemia, hypotension, weakness, fatigue, and seizures from severe hyponatremia.[11]

Growth hormone deficiency is one of the most common hormone deficiencies of hypopituitarism seen in Sheehan's syndrome.[9] Low levels of growth hormone may present with low energy, body aches, or subtle wrinkling of the skin around the eyes or mouth.[5][7] The symptoms of anti-diuretic hormone deficiency are increased thirst, excessive urination, headache, and fatigue.[12] Hematological changes might be seen as well such as anemia or low platelets (thrombocytopenia).[9] Hyponatremia is seen in many cases of Sheehan's syndrome because it can result from multiple etiologies. Drops in thyroid hormones and glucocorticoid/adrenal hormones can indirectly lead to hyponatremia through water retention, while blood loss can trigger hyponatremia through ADH secretion.[7] The development of Syndrome of Inappropriate Anti-Diuretic Hormone in patients with Sheehan's syndrome has been documented in the literature, although the mechanism is not well understood.[7]

As stated, Sheehan's syndrome is caused by damage to the pituitary, thereby causing a decrease in one or more of the hormones it normally secretes. Sheehan's syndrome typically occurs because of excessive blood loss after delivery (post-partum hemorrhage), although there are several risk factors that may contribute to its development.[8] This syndrome does not appear to be exclusively linked to childbirth, as Sheehan's syndrome has been reported in pregnant patients that experienced massive hemorrhage from non-obstetrical causes.[8] The pituitary gland grows and has a higher metabolic demand during pregnancy because the pituitary needs to rev up the production of certain hormones associated with pregnancy.[8][4] This higher metabolic demand, in turn, leads to higher demand for blood flow.[4]

Thus, if the body enters a state of shock from excessive blood loss in post-partum delivery, the pituitary gland is more susceptible to injury.[4] Although the vast majority of cases of Sheehan's syndrome occur in the setting of massive blood loss, cases have been documented of acute Sheehan's syndrome occurring with blood loss volumes that are not considered "massive".[13][4] Some possible predisposing factors to Sheehan's syndrome may include: disseminated blood coagulation (DIC), hypotension, small sella turcica size, and blood clots from a pre-existing hypercoagulable disorder.[8] Atony of the uterus is a leading cause of post-partum hemorrhage, therefore uterine atony could induce Sheehan's syndrome.[14]

This syndrome seems to arise when certain factors compound each other to cause pituitary injury. The physiologic enlargement of the pituitary gland in conjunction with an interference in its blood supply ultimately result in pituitary ischemia and necrosis.[8] One cause of pituitary growth associated with the risk of Sheehan's syndrome is the hyperplasia of lactotrophs which produce prolactin, the hormone responsible for milk production.[4] Other hormone-secreting cells of the pituitary undergo rapid growth in pregnant women as well, which contribute to the gland's enlargement.[9]

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The anterior pituitary is supplied by a low pressure portal venous system.[14] The anterior pituitary is more commonly affected in Sheehan's syndrome because of the structure of the portal venous system. Posterior pituitary involvement leading to central diabetes insipidus is much rarer, and typically reflects more extensive damage to the organ and more severe disease.[12] It has been suggested that the arrangement of the pituitary's blood supply contribute to its susceptibility for injury. "The highly vascularized pituitary tissue involves one of the most rapid blood flow in the human body and probably, therefore, has a tendency to infarction because even small degrees of change in the pituitary intravascular pressure cause an arrest of blood flow".[8] Ischemia may occur as a result of vasospasm from shock, hypotension, thrombosis, or direct vascular compression of the hypophyseal artery from the enlarged pituitary gland itself.[8][4][14] The presence of disseminated intravascular coagulation (i.e., in amniotic fluid embolism or HELLP syndrome) also appears to be a factor in its development.[8]

Typically an important clue that leads to a diagnosis of Sheehan's syndrome is identifying a deficiency in one or more of the hormones produced directly, or indirectly, by the pituitary gland. The extent of hormone deficiency, and which hormones are affected depends on the extent of the damage to the pituitary. Hormonal assays measure the levels of these hormones which include but are not limited to T4, TSH, estrogen, gonadotropin, cortisol, and ACTH.[7] It might be difficult to detect damage to these hormone pathways if hormone levels are at the borderline of the abnormal range. In this case, stimulation tests will be done to determine if the pituitary is responsive to hypothalamic hormones.[14]

MRI is useful in diagnosing Sheehan's syndrome since it examines the structure of the pituitary and may identify any anatomical damage.[4] MRI findings will vary based on how early or late in the disease process the test is being conducted. If an MRI is conducted early enough in the disease process the pituitary may appear larger than normal, and show changes that are consistent with damage from lack of blood supply.[15] Later in the disease process of this syndrome the damage imposed on the pituitary gland will cause it to shrink, and leave a partially empty or totally empty sella turcica on MRI.[7] At present, the part that autoimmunity plays in the development of Sheehan's syndrome is uncertain. Several case reports have identified anti-pituitary antibodies in patients diagnosed with Sheehan's.[4] Some patients also tested positive for anti-hypothalamus antibodies.[20] Given that many patients that have developed Sheehan's syndrome do not have detectable levels of these antibodies, it is unclear whether these antibodies cause this syndrome or result from it.[8]

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