

# Hypopituitarism in Men with History of Hypovolemic Shock

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**Abstract** Hypopituitarism is the partial or complete insufficiency of pituitary hormone secretion. It has a diverse etiology, and some causes are of vascular origin. Vascular causes of hypopituitarism are classified as hemorrhagic/ischemic or obstructive/compressive. We report the case of a patient with chronic hypopituitarism found 15 years after the occurrence of hypovolemic shock during surgery performed to remove nasal polyps. We believe that hypopituitarism in this case is very similar to that described by Sheehan, resulting from blood loss and coagulation disorders. Observation of pituitary function in patients with a history of hypovolemic shock may be necessary, as it is mandatory in patients with a history of postpartum bleeding.

**Keywords:** hypopituitarism, pituitary hormone secretion, hemorrhagic

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## 1. Introduction

Hypopituitarism is a medical condition related to high morbidity and mortality if not treated properly. The diagnosis of this condition is not always clear and is sometimes characterized as idiopathic. Hypopituitarism can have many causes including compression by pituitary tumors and genetic defects. Among the causes, postpartum hemorrhage with loss of pituitary function was described by Sheehan in 1938. Among these possible vascular etiologies, include vascular ischaemia after snake bite and hypopituitarism after hemorrhagic fever and hantaviruses.

Vascular causes of hypopituitarism are classified as hemorrhagic/ischemic or obstructive/compressive. Hypopituitarism of obstructive/compressive vascular origin has been associated with carotid artery aneurysms [1], in which vascular injury leads to compression of pituitary tissue associated with hormone deficiency. Among hemorrhagic/ischemic causes, coagulative necrosis in Sheehan's syndrome is well described, although its pathogenesis has yet to be elucidated. Infarction secondary to arrest of blood flow to the anterior lobe of the pituitary gland is the basic process. It remains unclear whether this process results from vasospasm, thrombosis, or vascular compression [2]. We report the case of a patient with chronic hypopituitarism found 15 years after the occurrence of hypovolemic shock during surgery performed to remove nasal polyps. The cause of hypopituitarism in this patient appears to be ischemic due to the occurrence of pituitary deficits and partially empty sella. The patient had a favorable outcome after hormone

replacement and is currently in perfect health, thus preventing histopathological investigation. However, we believe that hypopituitarism in this case is very similar to that described by Sheehan, resulting from blood loss and coagulation disorders. Observation of pituitary function in patients with a history of hypovolemic shock may be necessary, as it is mandatory in patients with a history of postpartum bleeding.

## 2. Case Report

An 83-year-old male patient, with complaints of daily intermittent dizziness and symptomatic postural hypotension for about 4 years. The patient has a history of sinusitis, and complaints have been associated with this diagnosis without improvement. About 15 years ago, the patient developed hypovolemic shock after severe hemorrhage following surgery to remove nasal polyps. In that episode, he had blood pressure levels of 0 x 0 mmHg, the patient developed circulatory shock, with cardio respiratory arrest and was managed with cardiovascular resuscitation was treated with volume expansion and showed a good response to treatment. After some time, the patient began to experience dizziness and malaise, being diagnosed and treated as having sinusitis. Later, during routine examination, hyponatremia was detected, with serum sodium = 120 mEq/l. Given the clinical suspicion of adrenal insufficiency, the patient underwent laboratory tests, which revealed hypothyroidism, hypogonadism, low GH and IGF-1 levels, and reduced cortisol levels (Table 1). The patient underwent cosyntropin stimulation test (250 mg IV), which revealed partial corticotropin deficiency (Table 1). Magnetic resonance imaging (MRI) of sella

turcica showed partially empty sella. The patient started replacement of levothyroxine, hydrocortisone acetate, and testosterone and maintains hormone levels appropriate for age.

**Table 1. Anterior pituitary hormonal evaluation**

Test,	Results	Reference range
Free T4	0.54	0.7 – 1.8 ng/dL
TSH	3.91	0.4 – 4.0 IU/mL
„Cortisol (0' cosyntropin test) *	5.2	4.2 – 28.4 mcg/dL
Cortisol 30 min after cosyntropin **	12.4	
Cortisol 60 min after cosyntropin **	15.2	
ACTH	18.2	7.2 – 63.6 ng/mL
IGF-1	< 25	94 – 252 ng/mL
FSH	2.7	2.8 – 11.3 IU/mL
LH	1.4	1.1 – 11.6 IU/mL
Prolactin	16	4.9 – 29 ng/mL
Testosterone	32.1	181 – 758 ng/mL

\*Basal cortisol level was collected at 9 am. \*\*the cosyntropin test was performed using 250 mg cosyntropin EV.

### 3. Discussion

Sheehan's syndrome occurs as a result of ischemic pituitary necrosis due to severe postpartum hemorrhage. It may be rarely seen without massive bleeding or after normal delivery. Improvement in obstetric care and availability of rapid blood transfusion coincided with a remarkable reduction in the frequency of Sheehan's syndrome particularly in western society. But it has recently been reported more often from well-developed countries. It is one of the most common causes of hypopituitarism in underdeveloped or developing countries. Enlargement of pituitary gland, small sella size, disseminated intravascular coagulation and autoimmunity have been suggested to play a role in the pathogenesis of Sheehan's syndrome in women who suffer from severe postpartum hemorrhage. The patients may seek medical advice because of various presentations ranging from non-specific symptoms to coma and the clinical manifestation may change from one patient to another. Failure of postpartum lactation and failure to resume menses after delivery are the most common presenting symptoms. Although a small percentage of patients with Sheehan's syndrome may cause abrupt onset severe hypopituitarism immediately after delivery, most patients have a mild disease and go undiagnosed and untreated for a long time. It may result in partial or panhypopituitarism and most patients has empty sella on CT or MRI [3,4].

Sheehan observed excessive fibrin on blood vessel of patients and named it *in situ* thrombosis [5]. Although an enlarged pituitary gland during pregnancy may become more susceptible to ischemia, primary thrombosis appears to be a possible explanation for pituitary ischemia in these patients [3]. The placenta is a rich source of thromboplastin, an activator of prothrombin responsible for defibrination which may result in hypofibrinogenemia and risk of abruptio placentae. In late pregnancy, disseminated intravascular coagulation (DIC) may also be triggered by leakage of amniotic fluid or syncytiotrophoblastic

microparticles containing functional tissue factor into the mother's bloodstream [4]. As a consequence, fibrin may be deposited on blood vessel walls, which explains the anatomical changes observed by Sheehan in the classical description of hypopituitarism after postpartum bleeding [5].

Snake bites may cause hypopituitarism by procoagulant enzymes in venom causing coagulative necrosis of the anterior pituitary. The first case of snake bite causing hypopituitarism was described in 1958 in Brazil [6]. Later, in 1976, hypopituitarism following Russell's viper bite [7], a common type of snake in South and Southeast Asian countries, was described. Since then, 50 cases of hypopituitarism following Russell's viper bite (*Daboia russelii* and *Daboia siamensis*) have been reported. Russell's viper venom is known to contain several toxins and some biologically active procoagulant enzymes activating factors V and X, resulting in fibrin formation, which may be associated with DIC [8]. Russell's viper venom also contains "hemorrhagin", a metalloproteinase that damages vascular endothelium. Thus, venom may lead to thromboses and hemorrhages. Focal hemorrhage and microvascular fibrin deposition in the pituitary gland may be responsible for the pathological finding of infarction of the anterior pituitary [3].

Hypopituitarism associated with hemorrhagic fever with renal syndrome has been described [9]. This viral infection is caused by hantaviruses, and its clinical course is characterized by fever, circulatory collapse with hypotension, hemorrhages, and renal failure [10]. There is capillary leakage, suggesting that vascular endothelium is the main target of this infection. Autopsy reports show that in fatal cases there was slight enlargement of the pituitary gland, with signs of hemorrhage and necrotic foci in 75.5% of cases. Cases of survivors developing hypopituitarism revealed pituitary atrophy and empty sella. In these cases, there is shock, vascular collapse, and subsequent hypopituitarism [8].

Based on different etiologies, we have observed that pituitary necrosis, whether in patients with Sheehan's syndrome, in patients envenomed by Russell's viper or in patients with hemorrhagic fever with renal syndrome, presents circulatory abnormalities, often with aggravating factors such as prolonged circulatory collapse, DIC, hyperhydration, and coagulation disorders. Therefore, severe circulatory abnormalities appear to be suggestive of situations of risk for the occurrence of hypopituitarism, even in the long term. The hypopituitarism after ventricular arrhythmia has been demonstrated in a pilot study that included 44 patients which was observed GH deficiency in 27.2% of long-term patients, supporting the hypothesis that blood reduced blood flow can relate to late hypopituitarism [11].

In cases of GH deficiency suspicion, this diagnosis should be done by hypoglycemia test after insulin. However, this test is contraindicated in elderly patients and / or patients with heart disease and in those with epilepsy. The GH replacement in adults is possible, but the cost / benefit ratio is not well established. For this reason we do not do this test in our patient, despite the low level of IGF-1 [12].

An empty sella is defined as a sella which, regardless of its size, is completely or partly filled with cerebrospinal

fluid (CSF). Empty sella is occasionally found as a normal anatomical variation, which is referred to as primary empty sella. On the other hand, empty sella is also seen after surgery, irradiation or medical treatment of pituitary adenoma, which is called secondary empty sella. Magnetic resonance imaging (MRI) is useful in diagnosing empty sella. Primary empty sella is usually free from clinical symptoms but sometimes associated with headache, obesity, visual disturbance, non-traumatic CSF rhinorrhea and pituitary insufficiency. These associated findings constitute the empty sella syndrome. Non-symptomatic cases require no treatment but periodical follow up is necessary [13,14].

In terms of differential diagnosis, lymphocytic hypophysitis should be kept in mind. However, this etiology predominantly affects women between the third and fourth decades of life, and often occurs after pregnancy [15]. Another possibility is a occurrence of Empty Sella Syndrome. At this condition, infarction clinically silent pituitary mass may result in the development of a partial or completely empty sella. The pituitary function often remains intact, because the surrounding tissue is fully functional. The hypopituitarism, however, may develop insidiously. Further, the increased pressure can promote intracranial herniation arachnoid membrane into the pituitary fossa [16].

Although elderly patients may have a history of falls and fractures more frequently, this was not reported by the patient or by relatives. Hypopituitarism cases after trauma are common, but relate the severity of trauma and is usually not observed empty sella in these patients [17]. We believe that, in this patient, the etiology of hypopituitarism was due to circulatory shock, similar to hypopituitarism described by Sheehan. However, systematic studies are needed so that we can establish a causal relationship between hypovolemic shock and hypopituitarism. The establishment of this relationship increases the diagnostic possibilities of vascular origin of hypopituitarism.

## 4. Conclusion

This case shows the detection of chronic hypopituitarism with a deficiency of the thyrotropic, gonadotropic and somatotrophic axes, in addition to partial deficit of the corticotropin axis in an elderly patient with a history of bleeding with progression to hypovolemic shock. We believe that in this case hypopituitarism was caused by pituitary ischemia, similar to cases of hypopituitarism syndrome after postpartum bleeding, as characterized by Sheehan. It may be important to monitor pituitary function in patients with a history or symptoms of hypovolemic shock, even after the acute phase of shock.

## Declaration of Interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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