ORIGINAL RESEARCH

Inflammatory Factor Levels and Clinical Characteristics of Mental Disorders in Patients with Sheehan Syndrome

Yi Lu, MSc; Ran Wei, MSc; Surong Li, MSc; Li Peng, BS; Zhenfeng Shi, BS

ABSTRACT

Background • Sheehan's syndrome often occurs in women aged 20 to 40 years. Bleeding is the main cause of the disease. This syndrome is rarely reported in the literature either in China or abroad, and it is rare in psychiatric clinic.

Objective • To investigate the inflammatory factors levels and clinical characteristics of mental disorders in patients with Sheehan's syndrome in order to improve rational clinical diagnosis and treatment and reduce the occurrence of mental disorders.

Design • This was a retrospective study.

Setting • This study was performed in the Department of Endocrinology of Xingtai People' s Hospital in China.

Participants • A total of 100 patients with Sheehan's syndrome admitted to Xingtai People's Hospital, China, from 2016 to 2021 were included in the study. According to the occurrence of mental disorders during treatment, they were divided into the psychological disorder group (PS group), psychological disorder during treatment group (TPS group) and non-psychological disorder group (NPS group).

Methods • The clinical data of the 3 groups were retrospectively analyzed to explore the levels of inflammatory factors and clinical characteristics of mental disorders in patients with Sheehan's syndrome.

Results • In the PS group, compared with the other 2 groups, onset to diagnosis time was longer ($P < .05$). There was a statistical difference in systolic blood pressure (SBP) among the 3 groups. The SBP in the PS group was the lowest, and that in the TPS group was higher than in the PS group and lower than in the NPS group ($P < .05$). Compared with TPS group, in the PS group the diastolic blood pressure (DBP), blood sodium, blood glucose, free triiodothyronine (FT3), free thyroxine (FT4), tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) levels were not significantly different, but were lower than in the NPS group ($P < .05$). There was no significant difference in age, disease course, body mass index (BMI), thyroid-stimulating hormone (TSH), cortisol, adrenocorticotropic hormone (ACTH), growth hormone (GH), Prolactin (PRL), follicle-stimulating hormone(FSH), luteinizing hormone (LH) and estradiol (E2) in the 3 groups. In the treatment process, the amount of hydrocortisone administered on the first, second day, and third day and the first 3 days in the TPS group were significantly higher than in the NPS group, and the increased rate of serum sodium on the first day in the TPS group was significantly higher than in the NPS ($P < .05$).

Conclusion • Mental health illnesss are more likely to occur in patients with Sheehan's syndrome who are not diagnosed in time for various reasons, in patients with obvious anterior pituitary dysfunction, and in patients with high levels of inflammatory factors, large doses of glucocorticoid at the early stage of the disease and rapid increase of serum sodium at the first day of treatment. (*Altern Ther Health Med.* 2023;29(2):218-223)

Yi Lu, MSc, Associate Chief Physician, **Ran Wei,** MSc, Laboratorian in Charge; **Li Peng,** BS, Nurse in Charge; **Zhenfeng Shi,** BS, chief physician; Department of Endocrinology, Xingtai People's Hospital, Xingtai, Hebei, China. **Surong Li,** MSc, Associate Chief Physician, Department of Pain Treatment, Xingtai People's Hospital, Xingtai, Hebei, China.

Corresponding author: Yi Lu, MSc
E-mail: chinaxtnfmluyi@163.com

INTRODUCTION

Sheehan's syndrome is a clinical syndrome of partial or complete hypopituitarism caused by pituitary ischemic necrosis during delivery or postpartum hemorrhage in women.[1-2] Clinical manifestations of Sheehan's syndrome are complex and diverse, depending on the type, extent and speed of development of the pituitary hormone deficiency.[3] Some patients with Sheehan's syndrome were treated for a mental disorder as the first symptom, and some developed mental disorders during the treatment process. The study found that the incidence of mental disorders in patients with

Sheehan's syndrome was approximately 25% to 40%.[4] Stress factors such as infection can aggravate a patient's condition, even induce pituitary crisis, which further increases the occurrence of mental disorders. Therefore, it is of great importance to explore and analyze the levels of inflammatory factors present and the clinical characteristics of patients with Sheehan's syndrome complicated by mental disorders, so as to improve its rational clinical diagnosis and treatment and reduce the occurrence of mental disorders.

The severity of Sheehan's syndrome varies, and its clinical manifestations are diverse. In addition, grassroots physicians do not have a good understanding of the disease, which results in in a high rate of missed diagnosis and misdiagnosis, delayed diagnosis and treatment and a significantly increased incidence of concomitant mental disorders. There have been few studies on the inflammatory factors and clinical characteristics of mental disorders in patients with Sheehan's syndrome. Our study retrospectively analyzed patients with Sheehan's syndrome in order to deepen the understanding of the disease in clinical work, so as to result in early diagnosis and reduce the occurrence of mental disorders.

MATERIALS AND METHODS

General Information

With the approval of the Medical Ethics Committee of our hospital, data from 100 patients with Sheehan's syndrome diagnosed in the department of endocrinology of Xingtai People's Hospital, China, from 2016 to 2021 were collected through the medical record query system.

Inclusion criteria. Patients were included in the study if: (1) they had a clear history of intrapartum or postpartum hemorrhage; (2) they had postpartum agalactia, amenorrhea, pubic hair loss, fatigue, fear of cold, loss of appetite and other hypopituitarism symptoms; (3) laboratory examination showed that pituitary hormone secretion was insufficient, and adrenocorticotropic hormone (ACTH), prolactin (PRL), growth hormone (GH), luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were partially or completely deficient.

Exclusion criteria. Patients were excluded from the study if they had: (1) other causes of anterior pituitary dysfunction, such as lymphocytic hyphositis, primary vacuole sella, head tumor surgery or radiotherapy history or head trauma; (2) a history of mental illness or a family history of mental illness; (3) a history of other heart, lung, brain or kidney diseases. Judgment criteria for mental disorders[5] included brain dysfunction; there are varying degrees of behavioral, cognitive, emotional, will and other mental disorders, such as delusions, hallucinations, emotional disorders, mania, depression and strange behavior, hypobulia.

Methods

Venous blood was collected from patients. Serum ACTH, cortisol, PRL, LH, FSH, free triiodothyronine (FT3), free thyroxine (FT4) and thyroid stimulating hormone (TSH) were detected by a Chemiluminescence Immunoassay kit (Suzhou Boyuan Medical Technology Co., Ltd, China) in the laboratory of Xingtai People' s Hospital. Blood glucose and sodium were detected by automatic biochemical analyzer (Roche Cobas 601, Diamond Diagnostics Inc, Holliston, Massachusetts USA). TNF-α and IL-6 were detected by ELISA kit（Zhuhai Aikang Company, China）flow cytometry.

Stastical Analyses

IBM, SPSS 21.0 statistical software was used for analysis. Normal distribution of measurement data was represented by ($\bar{\chi} \pm s$). For between-group comparison, the enumeration data of homogeneity of variance were analyzed by one-way analysis of variance (LSD minimum significant difference method). The enumeration data that did not conform to homogeneity of variance were analyzed by nonparametric test Tamhane' s T2. The data of skew distribution were represented by median (range), and rank sum test was used for comparison between groups. $P < .05$ indicated a statistically significant difference.

RESULTS

Patient General Information and Clinical Characteristics

The average age of the study patients was 57.60 ± 8.75 years, the average disease course was 29.74 ± 8.15 years at the time of treatment, and the average period of bleeding from delivery or postpartum to the diagnosis of Sheehan's syndrome was 14.24 ± 8.18 years. Of the patients, 94 (94%) were from rural or mountainous areas, 6 cases (6%) were from an urban area, 54 (54%) were uneducated, 33 (33%) has a primary education, 12% had a junior high school education, and 1 (1%) had a high school senior and above education level.

Comparison of Inflammatory Factor Levels and Clinical Data in the 3 Groups

Of the 100 patients, 7 (7%) had mental disorders, which were diagnosed as Sheehan's syndrome for the first time. The specific manifestations of mental illness are shown in Table 1. The PS group, TPS group and NPS group inflammatory factor levels and clinical characteristics/differences are shown in Table 2. There was no significant difference in age, disease course, BMI, TSH, cortisol, ACTH, GH, PRL, FSH, LH or estradiol (E2) between the 3 groups. The time from onset to diagnosis in the PS group was significantly longer than in the TPS and NPS groups ($P < .05$), while there was no significant difference between the TPS and NPS groups. Blood pressure was compared in the 3 groups, and a statistical difference was noted. The systolic blood pressure (SBP) in the PS group was significantly lower than in the TPS and NPS groups, while the SBP in the TPS group was lower than in the NPS group ($P < .05$). The diastolic blood pressure (DBP) in the PS and TPS groups showed no significant difference, while DBP in the PS and TPS groups was lower than in the NPS group ($P < .05$). The serum sodium level was compared in the PS and TPS

Table 1. Specific Manifestations of Mental Disorders in PS Group

Type	Performance	Number of patients	Occurrence ratio	Total (%)	*t*	*P* value
Behavioral disorder	Refusing to eat	2	28.57%	8 (80)	7.200	.007
	Talking nonsense	3	42.86%			
	Murmuring to oneself	2	28.57%			
	Inconstancy of crying and laughing	1	14.29%			
	Limb waving	1	14.29%			
	Swearing	2	28.57%			
Thinking disorder	Victim delusion	3	42.86%	2 (20)		
	Auditory hallucination	1	14.29%			
	Illusion	1	14.29%			

Abbreviations: PS, Psychological disorder in Sheehan's syndrome.

Table 2. Comparison of inflammatory factor levels and clinical data in the 3 Groups ($x \pm s$ or median [Range])

Group	PS group	TPS group	NPS group	t/u	*P* value
Age	63.29 ± 4.39	55.83 ± 8.35	57.49 ± 8.99	$t_{1,2}$=1.928 $t_{1,3}$=1.681 $t_{2,3}$=0.283	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
Disease Course	33.71 ± 4.68	29.89 ± 6.68	29.33 ± 8.67	$t_{1,2}$=1.317 $t_{1,3}$=1.314 $t_{2,3}$=0.256	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
Time of diagnosis	33.71 ± 4.68	11.83 ± 6.86	13.00 ± 6.18	$t_{1,2}$=7.719 $t_{1,3}$=8.618 $t_{2,3}$=0.706	$P_{1,2}$<.05 $P_{1,3}$<.05 $P_{2,3}$>.05
BMI	23.63 ± 4.21	21.98 ± 1.86	22.14 ± 1.73	$t_{1,2}$=1.382 $t_{1,3}$=1.862 $t_{2,3}$=0.347	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
Systolic pressure	98.71 ± 7.34	106.33 ± 10.10	117.43 ± 7.44	$t_{1,2}$=2.046 $t_{1,3}$=6.713 $t_{2,3}$=5.284	$P_{1,2}$<.05 $P_{1,3}$<.05 $P_{2,3}$<.05
Diastolic pressure	64.00 ± 7.66	62.78 ± 7.17	71.51 ± 9.95	$t_{1,2}$=0.375 $t_{1,3}$=2.017 $t_{2,3}$=3.504	$P_{1,2}$>.05 $P_{1,3}$<.05 $P_{2,3}$<.05
Blood sodium before treatment	112.23 ± 4.94	115.02 ± 5.55	126.68 ± 3.58	$t_{1,2}$=1.160 $t_{1,3}$=9.884 $t_{2,3}$=11.045	$P_{1,2}$>.05 $P_{1,3}$<.05 $P_{2,3}$<.05
Blood glucose before treatment	4.35 ± 0.43	4.29 ± 0.41	5.97 ± 1.06	$t_{1,2}$=0.324 $t_{1,3}$=3.994 $t_{2,3}$=6.584	$P_{1,2}$>.05 $P_{1,3}$<.05 $P_{2,3}$<.05
FT3	2.23 (1.25~4.01)	2.66 (1.69~4.07)	3.62 (1.15~4.99)	$u_{1,2}$=0.801 $u_{1,3}$=3.109 $u_{2,3}$=2.171	$P_{1,2}$>.05 $P_{1,3}$<.05 $P_{2,3}$<.05
FT4	6.90 (4.98~11.13)	7.24 (5.12~12.70)	11.62 (9.15~12.99)	$u_{1,2}$=0.867 $u_{1,3}$=9.646 $u_{2,3}$=6.102	$P_{1,2}$>.05 $P_{1,3}$<.05 $P_{2,3}$<.05

Group	PS group	TPS group	NPS group	t/u	*P* value
TSH	1.63 (0.27~4.55)	1.60 (0.35~4.94)	2.09 (0.26~5.09)	$u_{1,2}$=0.248 $u_{1,3}$=1.673 $u_{2,3}$=1.163	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
Cortisol	34.19 ± 5.51	36.79 ± 5.39	38.98 ± 2.89	$t_{1,2}$=0.166 $t_{1,3}$=0.792 $t_{2,3}$=1.515	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
ACTH	3.72 ± 1.15	3.96 ± 2.05	4.94 ± 0.91	$t_{1,2}$=0.196 $t_{1,3}$=1.415 $t_{2,3}$=0.883	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
GH	1.11 (0.45-1.81)	1.21 (0.47-2.97)	1.29 (0.52-3.26)	$u_{1,2}$=1.104 $u_{1,3}$=0.400 $u_{2,3}$=1.301	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
PRL	1.69 (1.13-2.01)	1.85 (1.02-14.45)	2.08 (0.36~20.03)	$u_{1,2}$=0.684 $u_{1,3}$=0.571 $u_{2,3}$=1.226	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
FSH	3.64 (0.51-11.66)	3.98 (0.53-13.03)	4.12 (0.59-16.27)	$u_{1,2}$=0.752 $u_{1,3}$=0.694 $u_{2,3}$=0.954	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
LH	1.66 (0.82-4.54)	1.74 (0.22-8.36)	2.06 (0.24-16.35)	$u_{1,2}$=0.801 $u_{1,3}$=0.811 $u_{2,3}$=1.417	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
E2	6.49 (1.19-20.00)	7.82 (1.19-30.72)	8.81 (1.03-34.74)	$u_{1,2}$=0.801 $u_{1,3}$=1.537 $u_{2,3}$=1.502	$P_{1,2}$>.05 $P_{1,3}$>.05 $P_{2,3}$>.05
TNF-α	6.73 ± 0.60	6.71 ± 0.49	4.38 ± 1.04	$t_{1,2}$=0.086 $t_{1,3}$=5.866 $t_{2,3}$=9.233	$P_{1,2}$>0.05 $P_{1,3}$<.05 $P_{2,3}$<.05
IL-6	27.01 ± 4.39	24.36 ± 4.64	16.70 ± 2.72	$t_{1,2}$=1.300 $t_{1,3}$=5.886 $t_{2,3}$=9.211	$P_{1,2}$>.05 $P_{1,3}$<.05 $P_{2,3}$<.05

Abbreviations: ACTH, adrenocorticotropic hormone; E2, estradiol; FSH, follicle-stimulating hormone; FT3, free triiodothyronine; FT4, free thyroxine; GH, growth hormone; IL-6, interleukin 6; PRL, prolactin; NPS, non-mental disorders group; PS, Psychological disorder in Sheehan's syndrome; TNF-α, tumor necrosis factor alpha; TSH, thyroid stimulating hormone.

groups before treatment, with no significant difference, but was lower than in the NPS group ($P < .05$). Blood glucose in the PS and TPS groups was compared before treatment, with no significant difference, but was lower than in the NPS group ($P < .05$). There was no significant difference in FT3 and FT4 levels in the PS and TPS groups, but they were lower than in the NPS group ($P < .05$). The TNF-α and IL-6 levels were compared between PS group and TPS group, with no significant difference, but they were significantly higher than in NPS group.

Comparison of Glucocorticoid Dose in the First 3 Days and Increased Rate of Serum Sodium on the First Day in the TPS and NPS Groups During Treatment

There were 18 patients diagnosed with mental disorders during the treatment of 93 patients with Sheehan's syndrome without mental disorders; the incidence of mental disorders was 19.35%. Compared with the NPS group, the dosage of glucocorticoid at the first, second, and third days and the first 3 days were larger in the TPS group, and the blood sodium

Table 3. Comparison of Glucocorticoid Dose and Blood Sodium Increase Between the TPS and NPs Groups During Treatment (median [range])

Group	Hydrocortisone dose on the first day (mg)	Hydrocortisone dose the next day (mg)	Hydrocortisone dose on the third day (mg)	Total hydrocortisone in the first 3 days (mg)	Increase in blood sodium on the first day (mmol/L)
TPS	150 (60-200)	100 (40-160)	60 (30-110)	310 (130-460)	7.18 (5.95-8.00)
NTPS	60 (30-110)	30 (30~60)	30 (20-60)	120 (80-230)	4.78 (4.01~7.11)
u	17.300	24.198	6.581	14.821	5.021
P value	<.05	<.05	<.05	<.05	<.05

Abbreviations: NTPS, non-psychological disorder in Sheehan's syndrome; TPS, psychological disorder during treatment in Sheehan's syndrome.

increased faster at the first day in the TPS group ($P < .05$). The specific performance is shown in Table 3.

DISCUSSION

Sheehan's syndrome is the main cause of pituitary dysfunction in third world and developing countries, and women who live in rural areas are the primary patient population in China, which is consistent with results of our statistical analysis.[6] This is related to poor economic conditions, relatively outdated medical treatments, patients' low educational level, poor awareness of medical treatment and other factors. Clinical manifestations of Sheehan's syndrome depend on the degree, type and speed of pituitary hormone deficiency and atrophy of corresponding target organs. Non-specific and delayed symptoms are different, and the severity of the disease varies. Therefore, patients with Sheehan's syndrome often have a delayed diagnosis.[7-8] Our study also showed that there were different degrees of delayed diagnosis in patients with Sheehan's syndrome. The onset to diagnosis time in all 100 patients was 4.24 ± 8.18 years, while in 7 patients in the PS group it was 33.71 ± 4.68 years. Therefore, delayed diagnosis due to various causes may be one of the risk factors for mental disorders in patients with Sheehan's syndrome.

Mental disorders in patients with Sheehan's syndrome are not uncommon. Some patients see a doctor with mental disorders as the first manifestation, which can increase the difficulty of treatment during the process of diagnosis and treatment, and even be misdiagnosed due to mental disorders.[9] Psychiatric disorders in patients with Sheehan's syndrome are associated with hypopituitarism, hyposecretion of target gland hormones, direct or indirect brain injury and neurochemical dysfunction.[10] Specific analysis is as follows:

1. **Hyponatremia.** There are different degrees of hyponatremia in patients with Sheehan's syndrome, which is related to the low levels of adrenal cortical hormone and thyroid hormone. Hyponatremia can cause brain cell edema and increased intracranial pressure.[11] Our study found that the lower the serum sodium level of a patient with Sheehan's syndrome was, the higher the risk for mental illness.
2. **Hypoglycemia.** Hypoglycemia can cause central nervous system (CNS) damage such as to the cerebral cortex, white matter and hippocampus.[12-13]
3. **Hypotension**. Hypotension leads to insufficient perfusion of brain tissue, leading to hypoxic encephalopathy.[14-15] At the same time, hypotension can lead to increased expression of intracranial C-fos gene, thereby causing nerve cell information conduction disorder.[16]
4. **Secondary hypothyroidism** in Sheehan's syndrome can lead to a decrease in blood flow to some areas of the brain and result in hypoxic encephalopathy,[17] inducing mental symptoms.
5. **Low gonadal hormone levels**. Normal levels of estrogen and progesterone have protective effects on the nervous system. Low gonadal hormone levels can induce depression, anxiety and even visual and auditory hallucinations and fear.[18]

In our study, we found that patients with Sheehan's syndrome with mental disorders showed different degrees of hypotension, hyponatremia, hypoglycemia and pituitary hormone and target gland hormone deficiency. The PS group had the lowest SBP; in the TPS group it was higher than the PS group and lower than the NPS group ($P < .05$). There was no significant difference in the PS group compared with the TPS group in DBP, blood sodium, blood glucose, FT3, FT4, TNF-α or IL-6 levels, but they were lower than in the NPS group ($P < .05$).

Patients with more obvious anterior pituitary dysfunction were more prone to mental disorders. Therefore, we should pay attention to tracing the perinatal history of patients with suspected Sheehan's syndrome, pay attention to physical examination, make a timely diagnosis of the nonspecific symptoms of patients with Sheehan's syndrome, and consider a possible diagnosis of Sheehan's syndrome for unexplained mental disorders, hypoglycemia, hypotension and hyponatremia.

The symptoms of patients with Sheehan's syndrome are often aggravated by stress factors such as infection, and even induce pituitary crisis, which further increases the probability of mental illness. TNF-α is a cytokine produced by activated mononuclear-macrophages, which can directly kill tumor

cells but has no obvious toxic effect on normal cells. It has a variety of biological effects, can directly act on immune cells and induce an inflammatory response. IL-6 is a kind of interleukin that is involved in the occurrence and development of various inflammatory diseases. Our study found that there was no significant difference between the PS and TPS groups in TNF-α or IL-6 levels, but these were significantly higher than in the NPS group ($P < .05$). Inflammation, infection, tissue damage and other stressors can cause the body to produce a variety of inflammatory factors, including TNF-α, IL-6, etc.[19] The elevated levels of inflammatory factors in patients with mental disorders suggest that the inflammatory response of the body is more severe due to stress factors such as infection in patients with mental disorders. In the process of clinical diagnosis and treatment, attention should be paid to the identification of infection incentives, timely detection of hidden infection factors, and reasonable diagnosis and treatment in order to reduce the occurrence of mental disorders.

The treatment principle for Sheehan's syndrome is to replace the lack of a targeted hormone; glucocorticoid is the most important hormone and the first choice for supplementation and replacement. With stress it is necessary to increase the dose of glucocorticoid moderately. The 2016 Endocrine Society Clinical Practice Guideline for Hormone Replacement Therapy for Adult Hypopituitarism[20] clearly states that hydrocortisone is the preferred hormone replacement therapy in patients with hypopituitarism. Hydrocortisone drug instructions clearly state that the drug can cause patients to feel happy, excited, restless, delirious, have orientation disorder and other mental symptoms. The study found an increased risk for compromised mental health in patients taking a daily dose of prednisone >40 mg.[21] Patients with hypopituitarism may develop mental illness even if they are treated with low-dose glucocorticoids. Some studies[22-23] have reported that 2.5 mg of prednisone induced psychiatric disorders. The possible reason is that patients with Sheehan's syndrome have a low cortisol level over an extended period of time and when the glucocorticoid receptor function is upregulated the individual sensitivity of patients to glucocorticoid is significantly increased.[24] When increasing the glucocorticoid dose under stress, the application of high-dose glucocorticoids causes apoptosis of the hippocampal pyramidal and striatum nerve cells and induces mental health illness.[25] The hypercorticosteroid state induces neuronal cell membrane hyperpolarization, selectively inhibits spontaneous electrical activity, enhances B-hydroxylase and phenylethanolamine-*N*-transmethylase activity, increases noradrenaline synthesis, inhibits tryptophan hydroxylase activity, reduces 5-hydroxytryptamine concentration in the CNS and leads to a neurotransmitter imbalance, which induces psychiatric disorders.[26] Our study found that compared with the NPS group, the first, second and third day and the first 3 days of glucocorticoid dose were larger in the TPS group ($P < .05$). Therefore, it is necessary to pay attention to the rational application of glucocorticoids in the treatment process, select effective physiological doses, avoid excessive drug use under stress, and avoid glucocorticoid-related mental disorders.

In our study, 100 patients had varying degrees of hyponatremia. The treatment process was initiated, and the increase of serum sodium in the TPS group was more significant than in the NPS group on the first day ($P < .05$). After hormone replacement therapy, serum sodium levels increased faster in patients with Sheehan's syndrome than in patients with hyponatremia caused by other causes. Therefore, attention should be paid to avoid demyelinating disease of the CNS caused by excessive elevation of blood sodium levels.[27] But in our study, all patients with the first day of blood sodium elevation were in line with the guidelines,[28-29] and mental illness caused by demyelination of the CNS caused by excessive sodium supplementation could be excluded. Patients with more rapid blood sodium elevation are more likely to develop mental illness, which may be associated with more rapid changes in the brain osmotic pressure gradient. Therefore, sodium supplementation treatment in patients with Sheehan's syndrome should be more prudent, and the rate of increase in blood sodium should be more gradual.

Study Limitations

Our study sample size was relatively small, so the next step is to more comprehensively and carefully analyze patient situations, so as to provide more accurate and real suggestions for the diagnosis and treatment of Sheehan syndrome.

SUMMARY

In summary, with the improvement of perinatal healthcare in China, the incidence of Sheehan's syndrome decreased significantly, and the clinical diagnosis and treatment experience became relatively insufficient. Clinicians should pay attention to nonspecific clinical manifestations in patients with Sheehan's syndrome, screen, diagnose and treat suspected patients in time, shorten the time of diagnosis and avoid delay in diagnosis and treatment. Treatment should include reasonable hormone replacement therapy, meet the patient's physiological needs and avoid the use of excessive or insufficient drugs. At the same time, it is necessary to identify aggravating factors such as infection in time and eliminate the causes. Under stress, the glucocorticoid dose should be increased in a reasonable manner, adverse events associated with glucocorticoid should be reduced and sodium supplementation should be reasonable in order to reduce the occurrence of mental disorders in patients with Sheehan's syndrome.

HEBEI MEDICAL SCIENCE RESEARCH PROJECT PLAN

Study on the level of inflammatory factors and risk factors of mental disorders in patiens with Sheehan syndrome (#20191693)

REFERENCES

1. Kilicli F, Dokmetas HS, Acibucu F. Sheehan's syndrome. *Gynecol Endocrinol*. 2013;29(4):292-295. doi:10.3109/09513590.2012.752454
2. Diri H, Tanriverdi F, Karaca Z, et a1. Extensive investigation of 114 patients with Sheehan's syndrome: A continuing disorder. *Eur J Endocrinol*. 2014;171(3):311-318. doi:10.1530/EJE-14-0244
3. Lemieux AT, Kopecky K, Sovic W, et al. Sheehan syndrome leading to acute systolic and diastolic heart failure: A case report. *J Heart Lung Transplant*. 2021;40(4):476-477. doi:10.1016/j.healun.2021.01.1970
4. Silva N, Galhenage J, Dayabandara M, et al. Sheehan syndrome presenting with psychotic manifestations mimicking schizophrenia in a young female: A case report and review of the literature. *Case Rep Endocrinol*. 2020;2020(5):1-6. doi:10.1155/2020/8840938
5. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). Washington DC:American Psychiatric Pub. 2013.
6. Viswanath S, Laway BA. Unmasking of hypoparathyroidism by zoledronic acid infusion in a patient with Sheehan syndrome. *Indian J Endocrinol Metab.* 2020;24(3):291-292. doi:10.4103/ijem.IJEM25320
7. Ramiandrasoa C, Castinetti F, Raingeard I, et al. Delayed diagnosis of Sheehan syndrome in a developed country:a retrospective cohort study. *Eur J Endocrinol*. 2013;169(4):431-438. doi:10.1530/EJE-13-0279
8. Kelestimur F. Sheehan syndrome. *Pituitary*. 2003;6(1):181-188. doi:10.1023/B:PITU.0000023425.20854.8e
9. Sethuram R, Guilfoil DS, Amori R, et al. Sheehan syndrome: An unusual presentation without inciting factors. *Women's Health Rep*. 2020;1(1):287-292. doi:10.1089/whr.2019.0028
10. Chang YC, Tsai JC, Tseng FY. Neuropsychiatric disturbances and hypopituitarism after traumatic brain injury in an elderly man. *J Formos Med Assoc*. 2006;105(2):172-176.
11. Spasovski G, Vanholder R, Allolio B, et a1. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Nephrol Dial Transplant*. 2014;29(Suppl 2):il-i39. doi:10.1093/ndt/gfu040
12. Kirchhoff BA, Lugar HM,Smith SE, et al.Hypoglycaemia-induced changes in regional brain volume and memory function. *Diabet Med*. 2013;30(4):e151-156. doi:10.1111/dme.1213.
13. Auer RN. Hypoglyemic brain damage. *Forensic Sci Int*. 2004;146(2-3):105-110. doi:10.1016/j.forsciint.2004.08.001
14. Chaparro RE, Quiroga C, Bosco G, et a1.Hippocampal cellular loss after brief hypotension. *Springerplus*. 2013:2(1):23. doi:10.1186/2193-1801-2-23
15. Su D H, Liao K, Chen H W, et al. Hypopituitarism: a sequela of severe hypoxic encephalopathy. *J Formos Med Assoc*. 2006;105(7):536-541. doi:10.1016/S0929-6646(09)60147-9
16. Kim M S, Hyo Kim J, Kry D, et al. Effects of acute hypotension on expression of cFos-like protein in the vestibular nuclei of rats. *Brain Res*. 2003,962(1-2):111-121. doi:10.1016/s0006-8993(02)03977-x
17. Bauer M, Goetz T, Glenn T, et a1. The thyroid-brain interaction in thyroid disorders and mood disorders. *J Neuroendocrinol*. 2008;20(10):1101-1114. doi:10.1111/j.1365-2826.2008.01774.x
18. Hasjim BJ, Fujitani RM, Kuo IJ, et al. Unique case of recurrent pelvic congestion syndrome treated with median sacral vein embolization. *Ann Vasc Surg*. 2020;68(8):569-569. doi:10.1016/j.avsg.2020.04.008
19. Arora G , Sahni N. Anesthetic management of a patient with Sheehan's syndrome and twin pregnancy while undergoing a cesarean section. *J Postgrad Med*. 2020;66(1):51-53. doi:10.4103/jpgm.JPGM_47319
20. Fleseriu M, Hashim IA, Karavitaki N, et al. Hormonal replacement in hypopituitarism in adults: An endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2016;101(11):3888-3921. doi:10.1210/jc.2016-2118
21. Ciriaco M, Ventrice P, Russo G, et al. Corticosteroid-related central nervous system side effects. *J Pharmacol Pharmacother*. 2013;4(Suppl 1);S94-S98. doi:10.4103/0976-500X.120975
22. Chatterjee SS, Mitra S, Mallik N, et al. Even very low dose hydrocortisone might precipitate psychosis in Sheehan's syndrome: A need for caution. *J Neurosci Rural Pract*. 2016;7(2):333-334. doi:10.4103/0976-3147.176189
23. Hong SI, Cho DH, Kang HC, et al. Acute onset of steroid psychosis with very low dose of prednisolone in Sheehan's syndrome. *Endocr J*. 2006,53(2):255-258. doi:10.1507/endocrj.53.255
24. Ross DA, Cetas JS. Steroid psychosis: A review for neurosurgeons. *J Neurooncol*. 2012;109(3):439-447. doi:10.1007/s11060-012-0919-z
25. Mondelli V, Pariante CM, Navari S, et a1.Higher cortisol levels are associated with smaller left hippocampal volume in first-episode psychosis. *Schizophr Res*. 2010;119:75-78. doi:10.1016/j.schres.2009.12.021
26. Mandal S, Mukhopadhyay P, Ghosh S. Sexual dysfunctions in Sheehan's syndrome. *Endocrine Practice*. 2021;27(12):1212-1215. doi:10.1016/j.eprac.2021.07.013
27. Schneider P, Nejtek VA, Hurd CL. A case of mistaken identity: Alcohol withdrawal, schizophrenia, or central pontine myelinolysis? *Neuropsychiatr Dis Treat*. 2012;8:49-54. doi:10.2147/NDT.S27634
28. Singh H, Afroze M, Shafi N, et al. Prevalence of coronary calcium deposits in Sheehan's syndrome patients on long term replacement treatment. *Pituitary*. 2022;25(1):92-99.
29. Spasovski G, Vanholder1 R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Eur J Endocrinol*. 2014;170:G1-G47. doi:10.1530/EJE-13-1020