Beyond The Sodium Drop: A Middle-Aged Woman's Hidden Endocrine Crisis

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***Abstract*—Sheehan syndrome also called as post-partum pituitary necrosis refers to the necrosis of cells of the anterior pituitary gland following significant post-partum bleeding, hypovolemia, and shock. Due to Advancement in obstetrical care in developed countries it has reduced the incidence of this condition. However, it is still a significant cause of morbidity and mortality in less developed countries. (1) This case report presents an interesting case of sheehans syndrome with an atypical presentation.**

I. INTRODUCTION

British pathologist Harold Leeming Sheehan first described this disorder in 1937, hence named after the scientist. During pregnancy, the pituitary gland naturally enlarges, making it more susceptible to low blood flow states caused by a major hemorrhage and low blood pressure. As a result, the pituitary gland is more susceptible to experience ischemia and necrosis. Sheehan's syndrome leads to various levels of hypopituitarism, the degree of which can vary, ranging from a complete loss of all pituitary hormones (pan-hypopituitarism) to selective deficiencies of specific hormones. The long-term effects of hypopituitarism depend on the hormone which is missing. (2)

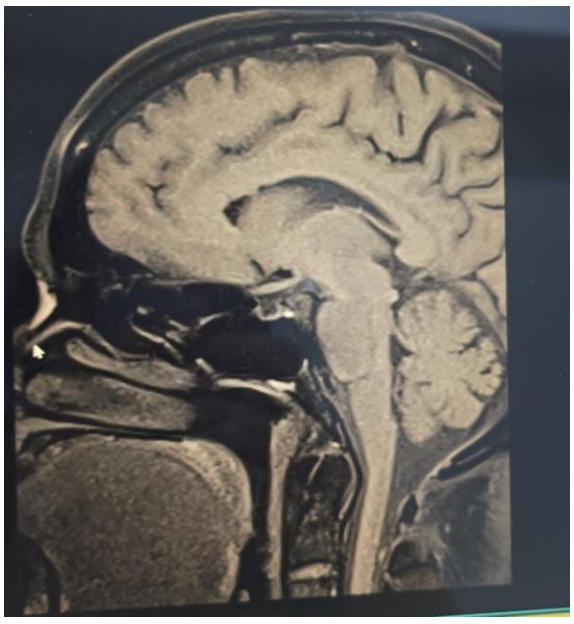
II. CASE REPORT

A 51-year-old female, homemaker by occupation, a Resident of Mandavalli village came to OPD with chief complaints of Swelling and Reddish discoloration of right lower limb for 3 months. Patient was apparently normal 3 months back, later which she developed swelling of right lower limb, started in the foot which is gradually progressive extending upto knee. Not associated with shortness of breath/abdominal distension/decreased urine output. Reddish discoloration of right lower limb for 3 months, associated with pain.Not associated with any local rise of temperature /any trauma.No similar complaints in the past .H/o easy fatigability in the past which severity increased in the last 10 years, for which she was admitted in local govt. hospital 1 year back- documentation not available.

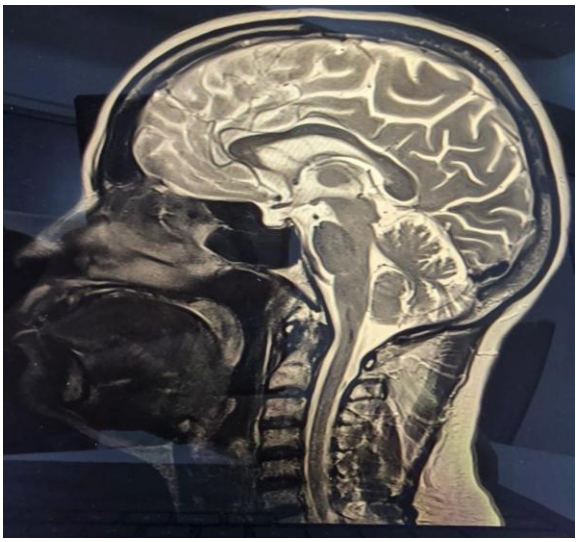
- k/c/o Seizures disorder since the age of 15 years using Tab Phenytoin 100mg 1tab on alternate days. k/c/o Hypertension for 3 years using Tab Amlodipine 5mg once daily Not a known case of Diabetes Mellitus, Chronic kidney disease, Cerebral vascular accident, Coronary artery disease Tuberculosis, Bronchial asthma or Thyroid disorder.
- MENSTRUAL HISTORY: Age of menarche – 13years. Past Menstrual cycles- regular 3-4 days, no pain/clots. Amenorrhoea for 30 years.OBSTETRIC HISTORY- Age at marriage -14 years. P2L1A0D1.Age at 1st child birth – 15 years, spontaneous IUD at home (cause not known) later went to hospital for removal of remaining products of conception. Age at 2nd child birth- 18years, spontaneously conceived, delivered preterm baby at home by normal vaginal delivery No. of living children- 1, No h/o usage of any oral contraceptives
- On examination Patient is conscious, coherent, oriented to time, place, person. She is Moderately built and nourished with height: 156cm, weight: 66kgs, BMI: 27.1kg/m2. Pallor-present, Pedal edema- present in right lower limb, pitting type, extending upto knee. Head to Toe Examination revealed dental carries and Bald tongue with Dry skin, Wrinkling of forehead. Loss of axillary and pubic hair seen along with Breast atrophy. Reddish discoloration of right lower limb present.Systemic

examination was normal. She was started on Antibiotics and Supportive medication.Continued Antihypertensive & Antiepileptics. Baseline investigations were done which revealed total counts of 3870/cumm, anemia with hb of 9.6gm/dl, platelets 1.5lakhs/cumm. LFT were normal except for ALT – 73U/L, AST 383U/L, ALP 85U/L. RFT were normal but revealed HYPONATREMIA with sodium 124meq/l. urine routine examination was normal. Abdominal ultrasonograph showed mild altered echotexture of liver measuring 11cm, cystitis. Arterial and venous Doppler of right lower limb done having cellulitis changes. Her ECG, Chest radiograph and 2Decho were normal.

- We further evaluated anemia with iron studies, stool occult blood, sickling test which all were pointing towards anemia of chronic disease.dermatology referral was taken for reddish discoloration of right lower limb and biopsy performed. Microscopy revealed structure of skin with epidermis lined by keratinised stratified squamous epithelium showing intraepidermal blister formation. Upper dermis shows mild perivascular mononuclear cell infiltrate. No evidence of malignancy-features suggestive of WELL'S SYNDROME. On further evaluation of hyponatremia patient had no history of any usage of diuretics, antipsychotics, antidepressants or carbamazapine all which can cause hyponatremia. Her urine sodium was 79meq/l , tsh 4.188uIU/ml which were normal but her serum cortisol was 2.38ug/dl giving the possible diagnosis of HYPONATREMIA SECONDARY TO ADRENAL INSUFFICIENCY. On probing history, patient revealed: Age at 1st child birth – 15 years, spontaneous IUD at home (cause not known) later went to hospital for removal of remaining products of conception. She even consulted doctor for medication to supress breast milk production She resumed regular menstrual cycles later. Age at 2nd child birth- 18years, spontaneously conceived, delivered preterm baby at home by normal vaginal delivery. Patient was unable to recollect postpartum hemorrhage or prolonged labor. She had lactation failure after 2nd delivery. She had irregular menstrual cycles for 4 years later which she developed amenorrhea. History of fatigue, lack of energy, feeling sleepy throughout the day, Lack of interest in doing household activities.
- During the course of hospital stay, On day 8 patient developed sudden onset abdominal pain, vomitings (3 episodes) Vitals at the time were: Blood pressure-80/60mmhg, Pulse rate – 98bpm, low volume, regular.We suspected ADRENAL CRISIS, and treated her with: Inj HYDROCORTISONE 100mg IV STAT and IVF 500ml NS bolus f/b 1000ml NS @ 100ml/hr. Later, her blood pressure improved to 110/80mmhg. To differentiate between primary and central adrenal insufficiency. As history suggestive of other hormonal deficiencies, we suspected central cause and we have convinced the patient to send S. ACTH sample.the report was a serum ACTH of <1.600. which was below normal for the reference range of 4.7-48.8pg/ml. Along with the given history of patient and evaluted diagnosis of Secondary hypopituitarism it is suggestive of - SHEEHAN'S SYNDROME. Further evaluation of other pituitary hormones showed PANHYPOPITUITARISM with low levels of all pituitary hormones like Luetinizing hormone, follicle stimulating hormone, Prolactin except for TSH.We performed MRI brain to substantiate our diagnosis of sheehans syndrome which showed empty sella with normal posterior pituitary bright spot. the images are attached below.



PATIENT MRI T1 WINDOW SHOWING EMPTY SELLA TURCICA



PATIENT T2 FLAIR WINDOW SHOWING EMPTY SELLA TURCICA WITH CSF SEEPAGE

Our patient was started on prednisolone 35mg in divided doses regimen 15mg-10mg-10mg. Patient responded dramatically Symptomatically- her Appetite improved, Nausea and vomitings subsided, generalized weakness and myalgia improved. Her hyponatremia was improving. There was No recurrence of hypoglycemia/ hypotension episodes afterwards.

III DISCUSSION

Sheehan's syndrome is classically characterized by reduced anterior pituitary hormone secretion following postpartum shock or hemorrhage. In 1963, Sheehan and Whitehead described varying degrees of pathological alterations including atrophy and scarring change in posterior pituitary lobes from postpartum hypopituitary patients examined post mortem. (3) During pregnancy, the pituitary gland enlarges 120% and is therefore highly vulnerable to ischemia in the setting of hypotension and hemorrhage during delivery. Patients can have deficiencies in some or all anterior pituitary hormones and even in posterior pituitary hormones, causing diabetes insipidus. Failure to lactate can result from decreased prolactin levels, and patients can develop amenorrhea from gonadotropin deficiency. Laboratory evaluations should include an ACTH stimulation test, a glucagon stimulation test, insulin-tolerance tests, and free T4 levels. Patients may have anemia, thrombocytopenia, and coagulation disorders, and pituitary imaging is likely to show partial or completely empty sella, as in the present case. Differential diagnoses include pituitary adenoma and lymphocytic hypophysitis (4)

Wells syndrome is characterized by sudden onset of large, inflamed, edematous patches that are often covered with vesicles or bullae; typically, the eruption is preceded by sensations of itching or burning. The lesions may or may not be associated with a low fever, and lesions are preferentially located on the trunk and the extremities. In the days following the initial eruption, the lesions evolve, demonstrating an extension of the patches, which take an annular configuration, with the center healing while the border becomes purple. Inflammatory signs regress within about 10 days while the plaques become indurated and patients typically recover completely and skin appears normal within 4 to 6 weeks. Recurrence is the rule, with variable locations, and the period between recurrences varies from months to several years; however, the prognosis remains good with long-term recovery

Described in 1971, Wells syndrome is a rare dermatosis of unknown etiology. It is characterized by a benign but recurrent evolution. Wells syndrome is mainly observed in adults but can occur at any age. The pathogenesis of Wells syndrome is obscure. Many triggering factors have been reported including insect bites, viral infections (parvovirus B19, herpes simplex virus, varicella-zoster virus, mumps virus), parasitic infections (Ascaris, Toxocara canis, Giardia), bacterial or fungal infections, drugs (antibiotics, non-steroidal anti-inflammatory drugs, thiazide diuretics, anti-TNF, biomedicines) and vaccines. Association of Wells syndrome with other diseases has also been described such as hematologic malignancies (chronic myeloid leukemia, chronic lymphocytic leukemia, polycythemia vera, non-Hodgkin lymphoma), malignant tumors, ulcerative colitis, eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome), hypereosinophilic syndrome (5). Wells syndrome may be prior, revealing, or concomitant to these diseases. The fortuitous nature of some of these situations cannot be ruled out, but one must remain vigilant in case of prolonged evolution beyond 6 months, persistent

eosinophilia, and/or systemic manifestations associated with Wells syndrome. (6) The histological images vary according to the progressive stage of the lesions. Initially, significant edema and a dermal infiltrate of eosinophils are seen. Some of the eosinophils are degranulated. The sub-acute stage is characterized by images called "flame-figures," located in the mid to deep dermis. The flame-figures are composed of a central part consisting of collagen fibers and eosinophilic granules, surrounded by a histiocytic and eosinophilic infiltrate.Subsequently, eosinophils tend to disappear and are replaced by phagocytic granulomas, consisting of histiocytes and sometimes giant cells, around the flame figures. The absence of vasculitis is an important negative sign. n most cases, general corticosteroids (10 to 80 mg daily) allow rapid healing. Tapering the dose over one month is generally well tolerated. Continued low-dose therapy with corticosteroids allows preventing recurrences. Dapsone may be prescribed as first-line treatment in low inflammatory forms. It also seems to give good results in case of corticosteroids resistance (7) IFN-alpha and IFN-beta could represent interesting alternatives. (8) For mild cases, topical corticosteroids may be sufficient. Hypopituitarism followed by decreased blood supply to the anterior pituitary gland may develop, and corticotropic deficiency is the most common finding. Unusual manifestations of adrenal insufficiency include eosinophilia and eosinophilic cellulitis (Well's syndrome), which is characterized by pruritic, erythematous and edematous skin plaques, and may suggest bacterial cellulitis. Antibiotic treatment is not always efficient. This case report highlights that if patients are diagnosed with fever of unknown origin, especially when they have atypical findings as described above, adrenal insufficiency should be considered to avoid the inappropriate use of antibiotics. (9)

IV CONSENT

The consent was taken and signed by respective patient.

V CONFLICTS OF INTEREST

The authors have no conflicts of interest.

VI CONCLUSION

Although sheehans syndrome is a preventable disease in 21st centuary failure to recognize and institute appropriate timely intervention has led to preventable deaths. Hence all physicians should be familiar with this if such cases like this present with an adrenal crisis at a later stage in life and it requires multidisciplinary approach including departments of obstetrics and gynaecology, endocrinology etc.

REFERENCES

[1] Sheehan Syndrome Mark P. Schury; Rotimi Adigun. September 4, 2023.

[2] Sheehan's syndrome unveiled after decade without a diagnosis: A case report Hadi Rabee' [1,2,✉], Tamara Braik [1], Rezeq Alnatour [1], Alaa Shamlawi [1], Ammar Rashed [1]SAGE Open Med Case Rep 2023 Nov

[3] Sheehan's syndrome presenting with panhypopituitarism and central diabetes insipidus: a case reportChin-Fang Chen, Yu-Cheng Liang, Meng-Jie Tsai & Horng-Yih Ou BMC Endocrine Disorders volume 24, Article number: 120 2024

[4] A Case of Sheehan Syndrome 7 Years Postpartum with Transaminitis and HyperlipidemiaSanah Sadiq[1ABCE*], Arnab Chowdhury[1ABCE]DOI: 10.12659/AJCR.930908 Am J Case Rep 2021; 22: e930908

[5] Fujii K, Tanabe H, Kanno Y, Konishi K, Ohgou N. Eosinophilic cellulitis as a cutaneous manifestation of idiopathic hypereosinophilic syndrome. J Am Acad Dermatol. 2003 Dec;49(6):1174-7. [PubMed]

[6] Powell J, Salim A, Muc R, Colloby P, Kaur MR. Persistent hypereosinophilia with Wells syndrome. Clin Exp Dermatol. 2013 Jan;38(1):40-3. [PubMed]

[7] Aberer W, Konrad K, Wolff K. Wells' syndrome is a distinctive disease entity and not a histologic diagnosis. J Am Acad Dermatol. 1988 Jan;18(1 Pt 1):105-14. [PubMed]

[8] Eosinophilia as a marker of adrenal insufficiency in the surgical intensive care unit M Angelis [1], M Yu, D Takanishi, N W Hasaniya, M R Brown PMID: 8957461

[9] A case report of hypopituitarism and Well's syndrome after apoplexy of a silent pituitary gonadotropic adenoma

[10] Hsu, Chia-Chen MD[a]; Lin, Hong-Da MD, PhD[b]; Huang, Chung-Yen MD[a]; Chiang, Yi-Lun MD[a,*]Medicine 101(22):p e29274, June 03, 2022. | DOI: 10.1097/MD.0000000000029274