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Acute Parvovirus Infection Unmasking a Craniopharyngioma Causing Hypopituitarism

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Abstract We present the case of a young male patient who arrived at the emergency room due to headache, constitutional and gastrointestinal symptoms. Upon presentation and during hospitalization, a complex clinical and chemical picture unfolded, and several diagnoses were considered. Eventually, it was concluded that panhypopituitarism secondary to craniopharyngioma was the cause of his symptoms. This long-standing condition was unmasked by an acute infection with Parvovirus. Treatment with hormone replacement therapy brought prompt improvement in both laboratory values and clinical condition.

Keywords: *parvovirus, craniopharyngioma, hypopituitarism*

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1. Case Presentation

A 25-year-old male presented to the emergency department complaining of vomiting, weakness, headache and shortness of breath. His past medical history was notable for familial congenital stationary night blindness (CSNB) which has caused him to have impaired vision.

Upon further questioning, it was revealed that several months prior to his presentation he started suffering from night sweats, joint pain, recurrent abdominal pain, vomiting and weight loss. During evaluation by his general practitioner, he was referred for upper and lower gastrointestinal endoscopies which were reported as normal. One week prior to he started suffering from retro-orbital headaches and photophobia, accompanied by severe weakness. He had no polyuria or polydipsia. One day prior to the presentation he vomited several times and started feeling unwell.

Upon assessment, his temperature was 36.4°c, blood pressure 101/56 mmHg, heart rate 64 beats per minute, and oxygen saturation 99% on room air. His physical examination was notable for spontaneous horizontal gaze nystagmus, a known finding attributed to his underlying retinopathy. Small, soft, nontender lymph nodes were palpated in the left cervical and left groin areas. Oral mucosa was moist, skin turgor was normal, and no peripheral edema was noted. Secondary sex characteristics were normal for an adult male. The rest of the examination was unremarkable.

Blood test showed anemia, hyponatremia, hypocalcemia and alkalemia (Table 1). Serum osmolality was 265 mOSM/kgH_2O. Urine was positive for ketones with fractional excretion of sodium (FENa) of 1.4% and osmolality of 535 mOsm/kgH_2O. Chest X-ray and electrocardiogram were normal. He was treated in the emergency room with intravenous 0.9% NaCl with no change in serum sodium and was admitted to the medical ward for further evaluation.

Upon admission, cytopenias were the predominant feature of his blood count (Table 1); He developed leukopenia and hypoproliferative (reticulocytes 0.2%) anemia. Vitamin B12 and folic acid levels were within normal limits. Notably, complement levels were low with C3 34.2 mg/dL and C4 8.55 mg/dL. Anti-nuclear antibodies and rheumatoid factor were negative. Immunoglobulin levels were within normal limits. Whole-body computed tomography (CT) with intravenous contrast material showed no lymphadenopathy but was significant for an enhancing suprasellar lesion, measuring 14*13*15 millimeters. The hypophysis was demonstrated undamaged and no mass effect was observed. A non-contrast head CT showed no calcifications within the mass. This lesion was further assessed by magnetic resonance imaging (MRI) of the brain showing a suprasellar lesion measuring 18*15 mm with peripheral cystic parts and central enhancement (Figure 1). The lesion was limited

by a capsule, pushing the optical chiasma upwards, inseparable from the hypophyseal stalk but without invading the hypophyseal gland. Radiologically, the main differential diagnosis was craniopharyngioma, germinoma, meningioma and lymphoma. Visual fields tests were compatible with bitemporal hemianopsia. Optical coherence tomography scan showed thinning of the nasal, superior and inferior retinal nerve fiber layer (RNFL), in both eyes.

Concurrently with imaging, further evaluation was continued. A bone marrow biopsy demonstrated relative myeloid hyperplasia with maturation and relatively few erythroid cells (increased M:E ratio); Megakaryocytes were normal in number and appearance. Immunohistochemical staining revealed no concerning features (Figure 2) and molecular analysis did not show B-cell gene rearrangement. Marrow cultures for mycobacteria and plain marrow cultures were negative after prolonged incubation.

Further studies were conducted and were negative for human immunodeficiency virus, Hepatitis B and C viruses. Blood and urine cultures were negative. Cytomegalovirus and Epstein-Barr virus serologies were positive for IgG and negative for IgM. Toxoplasma serologies were both negative. Parvovirus serologies revealed a strongly positive IgM and positive IgG. Thyroid-stimulating hormone (TSH) level was 0.65 mU/L, free T4 and T3 levels were 9.77 and 2.3 pmol/L, respectively. 8 AM cortisol levels in two consecutive days were 323 and 221 nmol/L. Adrenocorticotropic hormone (ACTH) stimulation test showed cortisol levels of 315 nmol/L at baseline and 307 and 824 nmol/L, 30 and 60 minutes after low dose ACTH injection. Testosterone levels were very low, 0.68 nmol/L, with luteinizing hormone (LH) 0.61 U/L, follicle-stimulating hormone (FSH) 1.63 U/L and prolactin 343.5 mU/L. (Table 1).

As the patient's clinical and laboratory picture was considered indicative of panhypopituitarism, he was treated with levothyroxine, hydrocortisone and water intake restriction. This brought about a resolution of the vomiting and shortness of breath. During his hospital stay, blood counts gradually improved (Table 1) and on the 12th day, his blood count had nearly normalized. Sodium levels also normalized, and ferritin levels dropped. He was discharged in a good condition. One month later, he underwent elective craniotomy and excision of the supra-sellar tumor. Pathology evaluation of the lesion confirmed the diagnosis of craniopharyngioma.

During a follow up two weeks after surgery, the patient felt tired, with decreased libido, but with improved appetite and satisfactory weight gain. Sodium levels were normal. LH, FSH, testosterone, TSH and insulin growth factor-1 levels were still low. He was continued on levothyroxine, hydrocortisone and testosterone. On follow up one month later, the patient felt better and gained further weight. Brain MRI showed no residual disease.

Table 1. Laboratory results throughout the hospitalization. ACTH, adrenocorticotropic hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; TSH, thyroid-stimulating hormone

Laboratory Test	Reference Range	Day 1	Day 2	Day 5	Day 12
Hemoglobin (g%)	13.9 - 17.7	9.6	8.8	9.5	8.8
Mean corpuscular volume (fL)	80.1 - 95.3	89.3	91.1	90.5	98.2
Platelets (10^9/L)	166 - 389	138	130	235	617
White blood cells (10^9/L)	3.79 - 10.33	4.1	1.7	4.7	9.4
Neutrophils (10^9/L)	1.78 - 7	3.2	0.8	2.1	5.9
Sodium (mmol/L)	136 - 145	126	133	131	138
Potassium (mmol/L)	3.5 - 5.1	3.5	4.1	4.3	3.5
Calcium (mmol/L)	2.08 - 2.6	1.89	2.05	2.15	2.18
Phosphate (mmol/L)	0.8 - 1.7	0.7	1	1.1	1.2
Creatinine (micromol/L)	62 - 115	76	58	82	74
Albumin (g/L)	32 - 48	40	42	40	39
Lactate Dehydrogenase (U/L)	120 - 246	193	230	188	
C-reactive protein (mg/dL)	0 - 0.5	1.75	1.77	0.42	
Lactic acid (mmol/L)	0.5 - 2.2	0.7			
pH	7.38 - 7.42	7.55	7.4	7.4	7.392
HCO^-_3 (mmol/L)		16.5	23.5	22.8	23.5
pCO_2(mmHg)		19.1	38.7	37.5	39.5
Ferritin (ng/mL)	22 - 322	3782		1211	266
Vitamin B12 (pg/mL)	211 - 911	332			
Folic acid (ng/mL)	>5.4	5.6			
TSH (mU/L)	0.55 - 4.78		0.65		
Free T4 (pmol/L)	10 - 20		9.77		
Free T3 (pmol/L)	3.5 - 6.5			2.3	
Growth hormone (ng/mL)	2.76 - 230			0.75	
Prolactin (mU/L)	44 - 375			343	
Cortisol (nmol/L)	145 - 620		323	221	
ACTH (pmol/L)	1.9 - 10.2			3.82	
Testosterone (nmol/L)	8.4 - 28.7			0.68	
FSH (U/L)	1.4 - 18.1			1.63	
LH (U/L)	1.5 - 9.3			0.61	
C3 (mg/dL)	90 - 180		34.2	38.7	
C4 (mg/dL)	10 - 40		8.55	12.5	

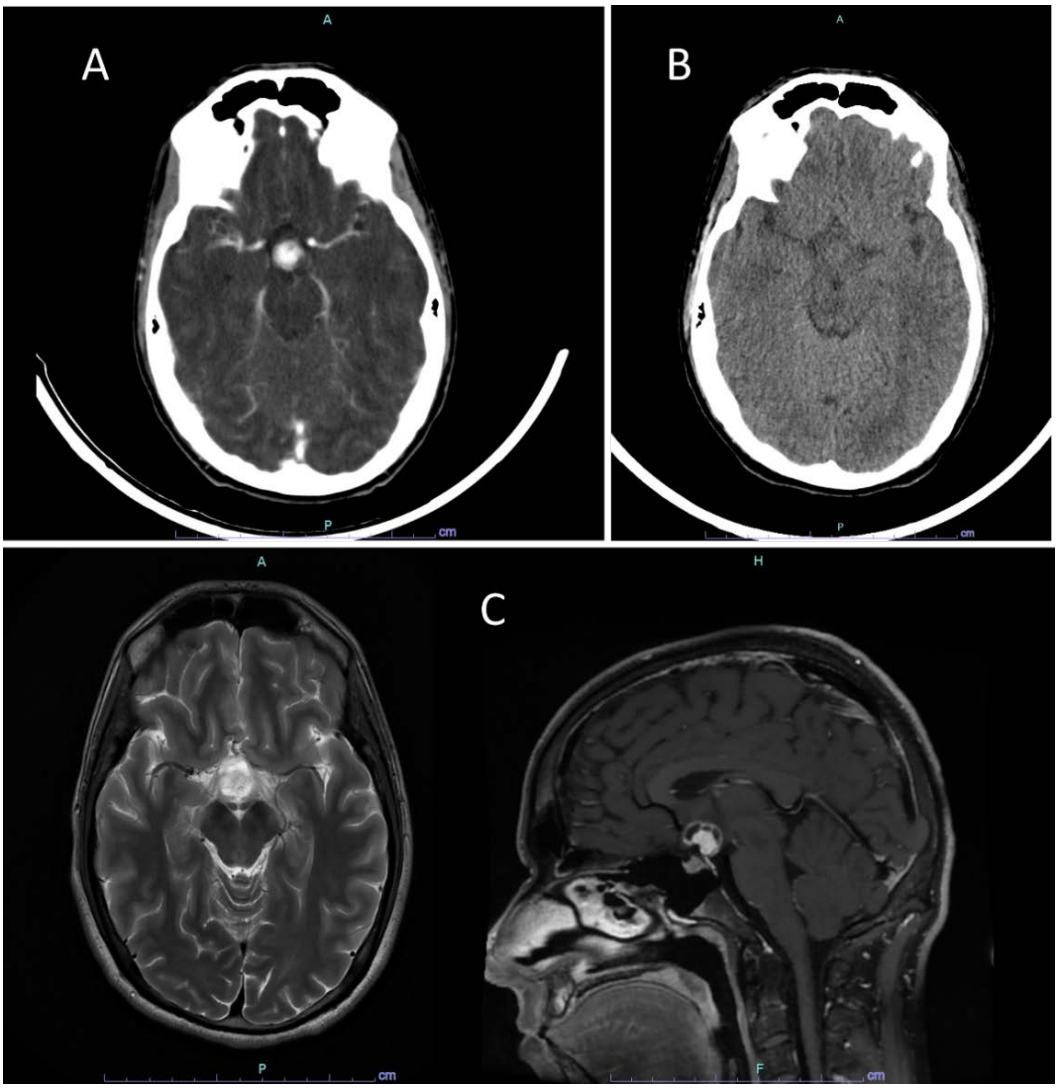

Figure 1. Brain Imaging. A, head CT with intravenous contrast - suprasellar lesion measuring 14*13*15 mm with enhancement. B, head CT without contrast - no calcifications are noted in the suprasellar mass. C, brain MRI - suprasellar lesion measuring 18*15 mm with peripheral cystic part and central enhancement

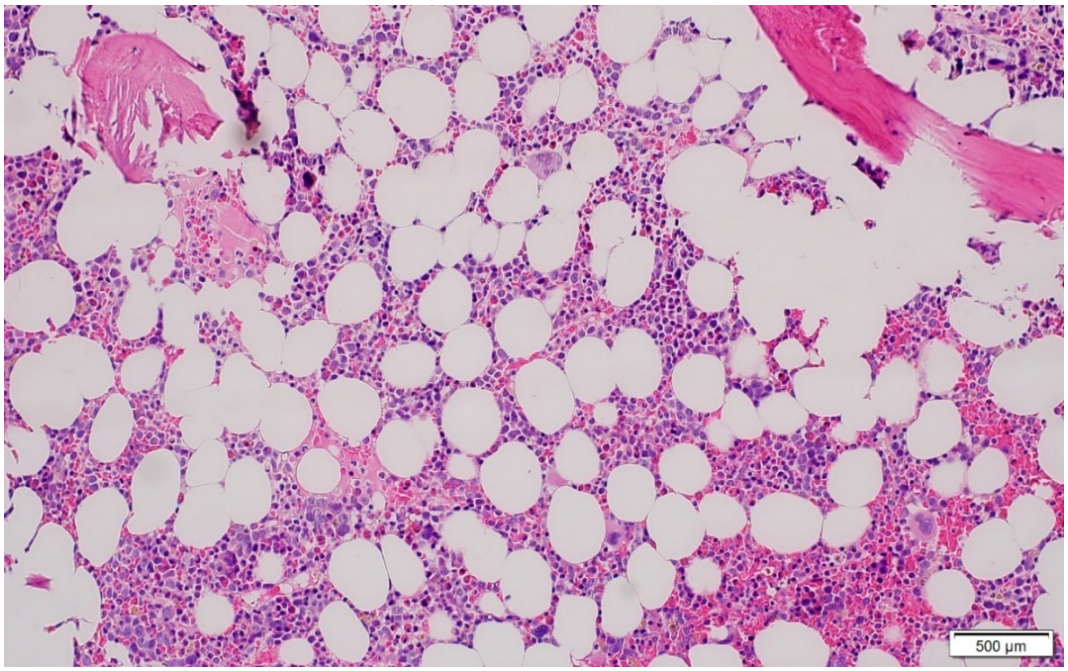

Figure 2. Bone marrow pathology. Normocellular trilineage bone marrow with relative hyperplasia of the myeloid series with maturation, and relatively few erythroid cells (increased myeloid: erythroid ratio). The megakaryocytes are normal in number and appearance

2. Discussion

This case presents an unusual scenario of a young patient hospitalized for anemia, hyponatremia and constitutional symptoms. An initial finding on head CT was significant but incompletely explained his symptoms, although panhypopituitarism was confirmed by hormone tests. Further workup of his reduced blood counts and elevated inflammatory markers revealed serologies typical for acute parvovirus 19 infection.

Craniopharyngioma is a non-glial intracranial suprasellar/parasellar tumor derived from embryonic tissue. Incidence is 0.5-2.0 cases per million persons per year, and 30-50% of cases are diagnosed during childhood and adolescence. Initial symptoms usually include manifestations of intracranial pressure such as headache and nausea. In adults, endocrine deficits are more common presenting symptoms. They are caused by a disturbance to the hypothalamic-pituitary axes that affect the secretion of growth hormone (75%), gonadotrophins (40%), ACTH (25%) and TSH (25%). Preoperative diabetes insipidus (DI) may also be present (17%) [1,2]. Standard imaging includes magnetic resonance imaging in addition to non-contrast computed tomography aimed at detecting typical calcifications [3]. Although calcifications are one of the predominant radiologic features of craniopharyngioma, it has been suggested that their absence in computed tomography, as in our case, may reduce the probability of recurrence [4]. Treatment options include surgery and radiation, but complete resection is the preferred treatment in order to preserve visual and hypothalamic function [1,5]. Transient postsurgical DI occurs in 80-100% of all cases, while 40-93% of patients suffer from permanent DI1. Long term prevalence rate of total anterior pituitary insufficiency is 89% [6]. In adults, overall survival rates are 89-94% at 5-years, 85-90% at 10-years and 62-76% at 20-years follow up [7].

Human Parvovirus B19 is a single-strand DNA virus. Following infection and viremia, the virus displays bone marrow tropism, targeting erythroblasts and halting erythroid development. Hemoglobin levels may fall, especially in patients with short red blood cell life span caused by other factors, sometimes causing transient aplastic crisis [8,9]. Thrombocytopenia and leukopenia have also been reported. Less common, but more severe, conditions are associated with Parvovirus infection and include pancytopenia, aplastic anemia, bone marrow necrosis, myelodysplastic syndrome, hemophagocytic lymphohistiocytosis and acute leukemia [10]. Hypocomplementemia, as in our case, was rarely described, sometimes with an association to arthropathy [11], lupus-like presentation [12], or self-limited glomerulonephritis [13].

This patient's disease may be broadly divided into electrolyte and hormonal issues stemming from hypophyseal dysfunction, constitutional symptoms probably stemming from both Parvovirus infection and the intracranial neoplasm, and the hematological manifestation which was likely triggered by Parvovirus infection and possibly exacerbated by panhypopituitarism. Hormone deficiencies such as hypothyroidism and hypogonadism can affect hematopoiesis [14], but pancytopenia secondary solely to panhypopituitarism is rare and mainly described as part of Sheehan's syndrome [14,15]. To our relief, bone marrow evaluation was incompatible with malignancy or hemophagocytic lymphohistiocytosis, diagnoses that were proposed due to the high ferritin and pancytopenia. Negative antinuclear antibodies and rheumatoid factor, along with normal renal function, diminished the possibility of autoimmune disease. The rapid improvement in blood cell counts should likely be attributed to the resolution of the viral infection, but the initiation of hormone replacement therapy may have played a part. Of note, the striking reticulocytopenia, reduced complement levels and elevated ferritin, along with some of the unexplained constitutional symptoms, have brought us to consider Parvovirus, an oft-neglected culprit with which these findings are nonetheless consistent [11].

The hyponatremia was attributed to hypothyroidism and relative adrenal insufficiency. The negative standard low dose ACTH test was likely negative due to the acute or sub-acute central hypocortisolism with preserved adrenal function. High urine sodium and osmolality, euvolemic status support this "SIADH like" state, known to be caused by hypocortisolism [16] and quick normalization of serum sodium levels after water restriction, thyroid and glucocorticoid replacement therapy support this diagnosis [17].

3. Conclusion

This patient presented with a complex clinical and chemical picture, where despite the internist's love for Occam's razor, we were forced to consider several diagnoses, each explaining part of his presentation and synergistically explaining all of it. Along the way, we were taught and reminded of several truths regarding Parvovirus infection, pituitary function and electrolyte abnormalities, lessons we herein share with you.

Conflicts of Interest

The authors have no conflicts of interest to disclose.

Patient Consent Statement

The patient gave his consent to publish this data.

Abbreviations

ACTH, adrenocorticotropic hormone; CT, computed tomography; DI, diabetes insipidus; FSH, follicle-stimulating hormone; LH, luteinizing hormone; MRI, magnetic resonance imaging; TSH, thyroid-stimulating hormone

References

[1] Müller HL. Craniopharyngioma. *Endocr Rev*. Jun 2014; 35(3): 513-43.

[2] Müller HL. Childhood craniopharyngioma--current concepts in diagnosis, therapy and follow-up. *Nat Rev Endocrinol*. Nov 2010; 6(11): 609-18.

[3] Warmuth-Metz M, Gnekow AK, Müller H, Solymosi L. Differential diagnosis of suprasellar tumors in children. *Klin Padiatr*. 2004 Nov-Dec 2004; 216(6): 323-30.

[4] Eldevik OP, Blaivas M, Gabrielsen TO, Hald JK, Chandler WF. Craniopharyngioma: radiologic and histologic findings and recurrence. *AJNR Am J Neuroradiol*. Sep 1996; 17(8): 1427-39.

[5] Flitsch J, Müller HL, Burkhardt T. Surgical strategies in childhood craniopharyngioma. *Front Endocrinol (Lausanne)*. 2011; 2: 96.

[6] Pereira AM, Schmid EM, Schutte PJ, et al. High prevalence of long-term cardiovascular, neurological and psychosocial morbidity after treatment for craniopharyngioma. *Clin Endocrinol (Oxf)*. Feb 2005; 62(2): 197-204.

[7] Erfurth EM, Holmer H, Fjalldal SB. Mortality and morbidity in adult craniopharyngioma. *Pituitary*. Mar 2013; 16(1): 46-55.

[8] Potter CG, Potter AC, Hatton CS, et al. Variation of erythroid and myeloid precursors in the marrow and peripheral blood of volunteer subjects infected with human parvovirus (B19). *J Clin Invest*. May 1987; 79(5): 1486-92.

[9] Anderson MJ, Higgins PG, Davis LR, et al. Experimental parvoviral infection in humans. *J Infect Dis*. Aug 1985; 152(2): 257-65.

[10] Kerr JR. A review of blood diseases and cytopenias associated with human parvovirus B19 infection. *Rev Med Virol*. Jul 2015; 25(4): 224-40.

[11] Nocton JJ, Miller LC, Tucker LB, Schaller JG. Human parvovirus B19-associated arthritis in children. *J Pediatr*. Feb 1993; 122(2): 186-90.

[12] Kalish RA, Knopf AN, Gary GW, Canoso JJ. Lupus-like presentation of human parvovirus B19 infection. *J Rheumatol*. Jan 1992; 19(1): 169-71.

[13] Lilleberg HS, Eide IA, Geitung JT, Svensson MHS. Acute glomerulonephritis triggered by parvovirus B19. *Tidsskr Nor Laegeforen*. 10 2018; 138(17).

[14] Lang D, Mead JS, Sykes DB. Hormones and the bone marrow: panhypopituitarism and pancytopenia in a man with a pituitary adenoma. *J Gen Intern Med*. May 2015; 30(5): 692-6.

[15] Laway BA, Bhat JR, Mir SA, Khan RS, Lone MI, Zargar AH. Sheehan's syndrome with pancytopenia--complete recovery after hormone replacement (case series with review). *Ann Hematol*. Mar 2010; 89(3): 305-8.

[16] Li H, Huang L, Wu G, et al. Be aware of the effects of glucocorticoids on SIADH: A case report. *Medicine (Baltimore)*. Feb 2019; 98(7): e14295.

[17] Adrogué HJ, Madias NE. Hyponatremia. *N Engl J Med*. May 2000; 342(21): 1581-9..