Open Access Library Journal
2022, Volume 9, e9486
ISSN Online: 2333-9721
ISSN Print: 2333-9705

# Atypical Shu (PTT) Induced by Chronic Drinking of Cocaine: A Case

**Alpha Boubacar Bah[1*], Flahaut Gauthier[2], Mamadou Saliou Balde[1], Mamadou Cellou Balde[1], Gabriel Choukroun[2]**

[1]Department of Nephrology and Hemodialysis, Intercommunal Hospital Center of Ariège Valleys (CHIVA), Foix, France
[2]Department of Nephrology, Hemodialysis and Renal Transplantation, HUS-PTT and Rare Diseases Competence Center at the CHU Amiens, Amiens, France
Email: *bahalpha427@gmail.com

**How to cite this paper:** Bah, A.B., Gauthier, F., Balde, M.S., Balde, M.C. and Choukroun, G. (2022) Atypical Shu (PTT) Induced by Chronic Drinking of Cocaine: A Case. *Open Access Library Journal*, **9**: e9486.
https://doi.org/10.4236/oalib.1109486

**Received:** October 25, 2022
**Accepted:** November 14, 2022
**Published:** November 17, 2022



## Abstract

The thrombocytopenia associated with cocaine consumption has been well documented]. Severe thrombocytopenia usually occurs within 3 weeks of intravenous or inhaled cocaine abuse. Microangiopathic hemolytic anemia (MHA) associated with cocaine is rare. We would like to report a case of cocaine-induced atypical hemolyticus uremic syndrome. **Clinical Observation:** this is a 29-year-old Causasian patient, followed in a psychiatric center under duress for 6 years for behavioral disorders, hallucinations and attacks on others related to schizophrenia. He is known for drug addiction and heroin, cannabis and cocaine. The patient was found on the ground by the firefighters at 10:53 a.m. when he had been out on leave from 4:30 p.m. the day before in a context of hypothermia at 28˚C, unconscious. On arrival in intensive care, the vital parameters were: blood pressure 105/56mmHg, PAM: 70 mmHg, heart rate 60 beats/min, saturation 96%, Weight: 92.7 Kg, Height: 167 cm. Patient sedated, curarized. The initial assessment showed a blood glucose level of 7.16 mmol/l; Urea: 6.6 mmol/l; Creatinine: 130 µmol/l with a peak at 790 µmol/l; Potassium: 6.06 mmol/l; Myoglobin: 316,000 µg/l, LDH: 782 IU/l; CK: 23.086 IU; $HCO_3$: 17.5 mmol/l, Lactate: 4.7 mmol/l (−1.3); Hemoglobin: 17.7 g/dl (12 - 18), Hematocrit: 53.2% (34 - 52); Platelets: 261 G/l 90 - 1.2); Fibrinogen: 3.72 g/l; blood and urine toxin assays were positive for Cocaine, Cannabis, benzodiazepines and opiates. The initial evolution was quickly favorable on the hemodynamic and neurological level with ad integrum recovery after stopping sedation and rapid self-extubation. However, the renal function continues to deteriorate, he becomes anuric, the EER was started continuously by CVVHF in view of the suspicion of acute renal failure by rhabdomyolysis. The appearance of stigmata of TMA with a collapsed haptoglobin at 0.20 g/l (VN: 0.34 - 2), schistocytes at 2.1% (VN: <1%) and moderate

thrombocytopenia at 114,000/mm$^3$ led his transfer to the Nephrology Intensive Care Unit. The secondary evolution was marked on the nephrological plan by an improvement of the renal function after a rise of the creatinine until a peak with 790 µmol/l then constant fall with 372 µmol/l, a resumption of the diuresis allowing the stop of the dialysis sessions. The etiological assessment of TMA came back in favor of a TTP secondary to cocaine consumption with a collapsed ADAMST 13 activity < 10%, the anti-ADAMST 13 were negative. **Conclusion:** We reported a case of atypical HUS (PTT) induced by chronic cocaine use with a collapsed ADAMST 13 activity.

## Subject Areas

Cardiology, Hematology, Pharmacology

## Keywords

Atypical HUS, Cocaine, Platelets, ADAMST 13

## 1. Introduction

Thrombocytopenia associated with cocaine use has been well documented [1] [2]. Severe thrombocytopenia usually occurs within 3 weeks of intravenous or inhaled cocaine abuse [1] [3]. Microangiopathic hemolytic anemia (MAH) associated with cocaine is rare. It occurs in a heterogeneous group of diseases and is characterized by mechanical destruction of red blood cells in the micro vasculature resulting in schistocytes on peripheral blood smear and other laboratory evidence of intravascular hemolysis. AHM in association with thrombocytopenia is seen in thrombotic microangiopathies, including thrombotic thrombocytopenic purpura (TTP). The PTT was originally described by Moschowitz in 1924 [4] and named by Singer *et al.* in 1947 [5]. Initially defined by the classic AHM pentad, thrombocytopenia, fever, central nervous system abnormalities, and renal dysfunction. The new diagnosis of TTP requires only two AHM elements and thrombocytopenia in the absence of any other clinically apparent etiology [6]. Our understanding of the pathogenesis of TTP has improved over the past decades. Patients with TTP have an increase in abnormally high circulating von Willebrand factor (ULVWF) multimers in their plasma [7] and microthrombi from these patients are platelet rich with abundant von Willebrand factor (vWF) [8]. vWF is stored in Weibel-Palade bodies in endothelial cells and circulated as ULVWF, which have high affinity for glycoprotein Ib-IX which is able to spontaneously induce agglutination of circulating platelets by the absence of simple stress [9]. Simple stress facilitates the disentangling of ULVWF released by endothelial cells. Circulation of ADAMTS13 is responsible for cleavage of these ULVWFs immediately after release into smaller vWF multimers that do not induce spontaneous platelet adhesion or agglutination [10] [11]. Studies have demonstrated that idiopathic TTP, the most common form of TTP, is caused by

proteolytic inhibitors or inactivators of ADAMTS13, primarily autoantibodies [7] [8]. This results in a deficit of ADAMTS13 and persistence of ULVWF. Platelets adhere to platelet microthrombi forming the ULVWF. There are several secondary causes of TTP, including autoimmune diseases, pregnancy, and medications [6]. Tests for ADAMTS13 activity and the presence of inhibitors aid in the diagnosis of TTP. In idiopathic TTP ADAMTS13 is usually less than 10% and inhibitor detection tests are positive. However, idiopathic TTP is a clinical diagnosis, and while ADAMTS13 data may be helpful, it is not diagnostic of TTP. Secondary TTP is inconsistently associated with decreased ADAMTS13 levels or the presence of an inhibitor. Cocaine is one of the most commonly abused illicit drugs. Cocaine exposure causes platelet activation, release of granules, and formation of platelet-containing microaggregates. Acute renal failure is an emerging complication in patients with acute cocaine intoxication. Renal biopsies revealed thrombotic microangiopathy with fibrinoid necrosis of arterioles and glomerular tufts. Cocaine-mediated endothelial damage and platelet activation may play important pathogenetic roles in cocaine users who develop acute renal failure and malignant hypertension [1] [2] [12] [13].

Therapeutic plasma exchange is the primary treatment for TTP and the process results in removal of ULVWF and ADAMTS13 inhibitors and replenishes functional ADAMTS13. Other causes of AHM, such as malignant hypertension, can be confused with TTP.

We describe a case of AHM associated with acute cocaine toxicity complicated by renal failure and thrombocytopenia with collapsed ADAMTS 13 activity.

## 2. Case Reported

A 29-year-old Caucasian man, followed in a psychiatric center under duress for 6 years in a context of behavioral disorders, hallucinations and aggression of others. Two days before his hospitalization in intensive care lived in a therapeutic apartment and with permission to go out 3 times a week from 4:30 p.m. to 9:00 a.m. the next day. A history of schizophrenia under SURFARLEM 50 mg/day, PAROXETINE 20 mg/day, QUETIAPINE 800 mg/day, AKINETON 12 mg/day, ATARAX 25 mg/day, OXAZEPAM 10 mg/day RISPERDAL 50 mg every 15 days; consumption of heroin, Cannabis, and Cocaine. The patient was found on the ground by the firefighters at 10:53 a.m. when he had been out on leave from 4:30 p.m. the day before in a context of hypothermia at 28˚C, unconscious. Upon arrival of the SMUR, Glasgow at 7/15 is in non-reactive mydriasis. Orotracheal intubation in front of consciousness disorders, vomiting and respiratory pauses then transfer to intensive care unit. On arrival in intensive care, the vital parameters were: blood pressure 105/56mmHg, PAM: 70 mmHg, heart rate 60 beats/min, saturation 96%, Weight: 92.7 Kg, Height: 167 cm. Patient sedated, curarized. No mottling, no signs of heart failure, no murmur, heart sounds regular. Under Controlled Assisted Ventilation, the vesicular murmurs are bilateral, symmetrical with diffuse rhonchis. The abdomen is supple, pain-

less, hydro-aeric noises are not perceived. The diuresis was preserved. The electrocardiogram registers a regular sinus rhythm, enlarged QRS complexes, Osborn J waves in all leads. The chest X-ray is normal. Transthoracic ultrasound showed TVI under Ao at 9.55 cm/s, no pericardial effusion, contractility disorders secondary to hypothermia, E/A at 1.22, GP IT at 12.5 mmHg, E/Ealat at 8.41 Ealat at 3.14 cm/s.

Biology showed: Blood sugar at 7.16 mmol/l (3.83 - 5.83); "Urea" 6.6 mmol/l (3.2 - 7.1); "Creatinine" 130 µmol/l (64 - 104) with a peak at 790 µmol/l; "Sodium" 133 mmol/l (136 - 145); "Potassium" 6.06 mmol/l (3.50 - 4.50); "Chloremia" 99 mmol/l (98 - 107); "Bicarbonates" 26 mmol/l (22 - 29); "Proteins" 87.2 g/l (63 - 88); "Calcemia" 2.26 mmol/l (2.20 - 2.55); "Corrected serum calcium" 2.07 mmol/l (2.20 - 2.60); "Phosphoremia" 3.12 mmol/l (0.86 - 1.50); "CRP" 12 mg/l (0.1 - 5); "Total bilirubin" 4.5 mmol/l (5 - 20); "Direct bilirubin" 2.2 mmol/l (3 - 6); "Myoglobin" 316,000 µg/l (17 - 105); "Alkaline phosphatases" 84 UI/l (40 - 160); "Gama GT" 31 IU/l (12 - 64); "AST" 290 IU/l (5 - 64); "ALT" 75 IU/l (−55); "LDH" 782 IU/l (100 - 250); "CK" 23.086 IU (20 - 180); "Lipasemia" 15 UI/l (−50); "Ph blood" 7.29 (7.35 - 7.45); "$PCO_2$" 33 mEq (35 - 48); "$PO_2$" 106 mEq (63 - 108); "$HCO_3$" 17.5 mmol/l (19 - 29 mmol/l); "Lactate" 4.7 mmol/l (−1.3); Alcoholemia < 0.1 g. "White blood cells" 14.6 G/l (4 - 11) with 88% PNN predominance; "Hemoglobin" 17.7 g/dl (12 - 18), "Hematocrit" 53.2% (34 - 52); "Platelets" 261 G/l (150 - 500); "MCV" 89.1 (90 - 100), "MCHC" 33.3 (32 - 35); "PT" 100% (70 - 100); "TCA ratio" 1.19 (0.90 - 1.2); Fibrinogen: 3.72 g/l (2 - 4); blood and urine toxin assays were positive for Cocaine, Cannabis, benzodiazepines and opiates. The tenuous conduct was the installation of a coolgard for progressive internal reheating of approximately 1 degree/H, effective reheating without ventricular arrhythmia at 30˚C, sedation by Hypnovel and Sufentanil. Realization of EEG at 30˚C with a BIS of 80, which seems high compared to hypothermia, decision totreat a possible epileptic condition with Gardenal 15 mg/kg in Bolus then 400 mg/24H. The initial evolution was quickly favorable on the hemodynamic and neurological level with ad integrum recovery after stopping sedation and rapid self-extubation. However, the renal function continues to deteriorate with a creatinine at 432 µmol/and becomes auric, an EER was started continuously by CVVHF on a right femoral catheter in view of the suspicion of acute renal failure by rhabdomyolysis. The occurrence of stigmata of TMA with a collapsed haptoglobin at 0.20 g/l (VN: 0.34 - 2), the presence of schistocytes at 2.1% (VN: <1%) and moderate thrombocytopenia at "114.000/$mm^3$" led to his transfer to the Nephrology Intensive Care Unit. The secondary evolution was marked on the nephrological plan by an improvement of the renal function after a rise of the creatinine until a peak with 790 µmol/then constant fall with 372 µmol/l, a resumption of the diuresis allowing the stop of the dialysis sessions. On the hematological level, mechanical hemolytic anemia requires red blood cell transfusions for anemia at 6.6 g/dl. The etiological assessment of TMA returned in favor of a TTP secondary to cocaine consumption characterized by hemolytic

anemia with collapsed haptoglobin, the presence of schistocytes, thrombocytopenia and a collapsed ADAMST 13 activity < 10%, anti ADAMST AC 13 were negative. AntiPF4 antibodies were also negative, Anti-Nuclear Abs negative, Vitamin B12 deficiency, explored by performing an esogastroduodenal fibroscopy ruling out the diagnosis of Biermer's disease. No specific treatment of thrombotic microangiopathy (MAT) has been carried out, however we observed a spontaneous disappearance of the stigmata of MAT, an improvement in ADAMST activity from 13% to 36%.

## 3. Discussion

We speculate that thrombocytopenia is due to peripheral consumption mediated by a non-immune mechanism. Tumlin *et al.* reported a case of acute renal failure due to thrombotic microangiopathy accompanied by microangiopathic hemolysis [3]. Several authors have published that vasoconstriction induced by cocaine causes diffuse vascular endothelial lesions and therefore promotes microangiopathic hemolysis and acute renal failure. These vascular endothelial lesions, as in malignant hypertension, pre-eclampsia, burns, etc. cause thrombocytopenia.

In our patient, we excluded a coagulation disorder induced by heparin with antiPF4 Ac which came back negative. Megaloblastic anemia due to cocaine-induced vitamin B12 deficiency which can cause profound anemia and an increase in red blood cells manifesting as an increase in serum bilirubin and LDH and a decrease in haptoglobin has been also excluded. We finally retained a PTT linked to the consumption of cocaine. Additionally, Saez *et al.* Recently found increased levels of several markers of endothelial damage such as circulating endothelial cells (CECs) and plasma levels of stromal cell-derived factor-1 (SDF-1), monocyte chemotactic protein 1 (MCP-1), d soluble intracellular adhesion (sICAM), high sensitivity protein C reagent (hsCRP) and endothelin-1 (ET-1) in chronic cocaine users [14]. CEC and MCP-1 counts remained elevated even after cocaine withdrawal. Cocaine also appears to cause platelet activation and aggregation. Although in vitro studies havebeen contradictory, several of the in vivo studies demonstrated platelet activation after acute cocaine administration and chronic cocaine use [13] [15]. This platelet activation could be primary or represent a secondary phenomenon to an endothelial lesion.

Renal biopsy was not performed in view of the risk benefit in our patient and the recovery of his constant renal function after stopping dialysis. The stigmata of TMA disappeared during the patient's stay in hospital without recourse to specific treatment. One study reported a case of TTP with an ADAMTS13 level < 3% and had a positive urine cocaine screen. The patient was unresponsive to plasma exchange (PE) and steroids and died of sepsis 15 days after central line insertion. No other relevant information was provided by the authors who also did not specify the potential for cocaine-induced TMA [16]. Two studies conducted by George and Howard *et al.* [3] [6] [17] found that approximately 26% of patients treated with EP have major complications. Identifying patients who

do not need PE would reduce unnecessary risks, as well as healthcare costs. However, the high mortality associated with idiopathic TTP in the absence of PE leads to the slightest doubt of performing PE.

## 4. Conclusion

In our case, we reported an observation of a 29-year-old Caucasian male patient who presented an atypical HUS (PTT) picture induced by chronic cocaine consumption with a collapsed ADAMST 13 activity. Faced with severe renal insufficiency and associated metabolic disorders, hemofiltration sessions were performed. The evolution was favorably marked by the disappearance of the biological stigmata of thrombotic microangiopathy, the constant recovery of renal function allowing the cessation of hemofiltration and the normalization of ADAMST 13 activity without recourse to specific treatment.

## Conflicts of Interest

The authors declare no conflicts of interest.

## References

[1] Lessinger, C.A. (1990) Severe Thrombocytopenia Associated with Cocaine Use. *Annals of Internal Medicine*, **112**, 708-710. https://doi.org/10.7326/0003-4819-112-9-708

[2] Orser, B. (1991) Thrombocytopenia and Cocaine Abuse. *Anesthesiology*, **74**, 195-196. https://doi.org/10.1097/00000542-199101000-00033

[3] Koury, M.J. (1990) Thrombocytopenic Purpura in HIV-Seronegative Users of Intravenous Cocaine. *American Journal of Hematology*, **35**, 134-135. https://doi.org/10.1002/ajh.2830350216

[4] Moschcowitz, E. (1925) An Acute Febrile Pleiochromic Anemia with Hyaline Thrombosis of the Terminal Arterioles and Capillaries: An Undescribed Disease. *Archives of Internal Medicine*, **36**, 89-93. https://doi.org/10.1001/archinte.1925.00120130092009

[5] Singer, K., Bornstein, F.P. and Wile, S.A. (1947) Thrombotic Thrombocytopenic Purpura: Hemorrhagic Diathesis with Generalized Platelet Thrombosis. *Blood*, **2**, 542-554. https://doi.org/10.1182/blood.V2.6.542.542

[6] George, J.N. (2006) Thrombotic Thrombocytopenic Purpura. *The New England Journal of Medicine*, **354**, 1927-1935. https://doi.org/10.1056/NEJMcp053024

[7] Moake, J.L. and McPherson, P.D. (1989) Abnormalities of von Willebrand Factor Multimers in Thrombotic Thrombocytopenic Purpura and the Hemolytic-Uremic Syndrome. *The American Journal of Medicine*, **87**, 9N-15N.

[8] Asada, Y., Sumiyoshi, A., Hayashi, T., Suzumiya, J. and Katetani, K. (1985) Immunohistochemistry of Vascular Lesion in Thrombotic Thrombocytopenic Purpura, with Special Reference to Factor VIII Related Antigen. *Thrombosis Research*, **38**, 469-479. https://doi.org/10.1016/0049-3848(85)90180-X

[9] Arya, M., Anvari, B., Romo, G.M., Cruz, M.A., Dong, J.F., McIntire, L.V., Moake, J.L. and Lopez, J.A. (2002) Ultralarge Multimers of von Willebrand Factor Form Spontaneous High-Strength Bonds with the Platelet Glycoprotein Ib-IX Complex: Studies Using Optical Tweezers. *Blood*, **99**, 3971-3977.

https://doi.org/10.1182/blood-2001-11-0060

[10] Furlan, M., Robles, R., Galbusera, M., Remuzzi, G., Kyrle, P.A., Brenner, B., Krause, M., Scharrer, I., Aumann, V., Mittler, U., Solenthaler, M. and Lammle, B. (1998) von Willebrand Factor-Cleaving Protease in Thrombotic Thrombocytopenic Purpura and the Hemolytic-Uremic Syndrome. *The New England Journal of Medicine*, **339**, 1578-1584. https://doi.org/10.1056/NEJM199811263392202

[11] Tsai, H.M. and Lian, E.C.Y. (1998) Antibodies to von Willebrand Factor Cleaving Protease in Acute Thrombotic Thrombocytopenic Purpura. *The New England Journal of Medicine*, **339**, 1585-1594. https://doi.org/10.1056/NEJM199811263392203

[12] Gu, X. and Herrera, G.A. (2007) Thrombotic Microaniopathy in Cocaineabuse-Associated Malignant Hypertension. *Archives of Pathology & Laboratory Medicine*, **131**, 1817-1820. https://doi.org/10.5858/2007-131-1817-TMICAM

[13] Heesch, C.M., Wilhelm, C.R., Ristich, J., Adnane, J., Bontempo, F.A. and Wagner, W.R. (2000) Cocaine Activates Platelets and Increases the Formation of Circulating Platelet Containing Microaggregates in Humans. *Heart*, **83**, 688-695. https://doi.org/10.1136/heart.83.6.688

[14] Saez, C.G., Olivares, P., Pallavicini, J., Panes, O., Moreno, N., Massardo, T., Mezzano, D. and Pereira, J. (2011) Increased Number of Circulating Endothelial Cells and Plasma Markers of Endothelial Damage in Chronic Cocaine Users. *Thrombosis Research*, **128**, e18-e23. https://doi.org/10.1016/j.thromres.2011.04.019

[15] Pereira, J., Saez, C.G., Pallavicini, J., Panes, O., Pereira-Flores, K., Cabreras, M.J., Massardo, T. and Mezzano, D. (2011) Platelet Activation in Chronic Cocaine Users: Effect of Short Term Abstinence. *Platelets*, **22**, 596-601. https://doi.org/10.3109/09537104.2011.578181

[16] Balaguer, F., Fernandez, J., Lozano, M., Miquel, R. and Mas, A. (2005) Cocaine-Induced Acute Hepatitis and Thrombotic Microangiopathy. *JAMA*, **293**, 797-798. https://doi.org/10.1001/jama.293.7.797

[17] Howard, M.A., Williams, L.A., Terrell, D.R., Duvall, D., Vesely, S.K. and George, J.N. (2006) Complications of Plasma Exchange in Patients Treated for Clinically Suspected TTP-HUS. *Transfusion*, **46**, 154-156. https://doi.org/10.1111/j.1537-2995.2006.00687.x