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CASE REPORT

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Coexistence of thrombotic thrombocytopenic purpura and adult-onset Still's disease

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Abstract

The association of Thrombotic thrombocytopenic purpura (TTP) and adult-onset Still's disease (AOSD) is very uncommon. Hereby, we present a case of TTP occurring in patient with a known AOSD and the successful outcome after plasma exchanges.

KEYWORDS

adult Still's disease, microangiopathy, thrombotic thrombocytopenic purpura

1 | INTRODUCTION

Thrombotic thrombocytopenic purpura (TTP) was first described in 1925 as an uncommon and rare hematologic disorder.[1] It is defined by the classic pentad including fever, neurologic signs and renal function abnormalities, thrombocytopenia, microangiopathic hemolytic anemia.[2] It is caused by a major deficiency of a disintegrin and metalloprotease with thrombospondin type I repeats-13(ADAMTS13) activity. In rare cases, this deficiency begins in the childhood with inherited forms but most of the time, it occurs during adulthood due to anti-ADAMTS13 autoimmune etiology.[2,3] This thrombotic microangiopathy is a potentially lethal disease with a high mortality rate once undiagnosed and untreated.[4]

Most conditions associated with TTP include infections, various drugs and autoimmune illnesses, such as the antiphospholipid syndrome and systemic lupus erythematosus.[5-7]

Adult-onset Still's disease (AOSD) is an uncommon multisystemic autoimmune inflammatory illness characterized by three classic signs: fever, joint pain, and salmon colored skin lesions. It is considered as a diagnosis of exclusion and it has been reported less frequently in association with TTP.[8-10]

Hereby, we present a case of TTP occurring in patient with a known AOSD and the successful outcome after the initiation of a treatment based on plasma exchanges.

2 | CASE REPORT

A 24 year-old Tunisian woman was referred to our department for the first time in February 2006. She had a chronic polyarthralgia accompanied by a spiking fever. Clinically, she also had episodes of arthritis, evanescent maculopapular cutaneous eruption and cervical lymphadenopathy. She didn't present any sign for a current

infection or neoplasia. Laboratory tests showed a biological inflammatory syndrome with elevated levels of the Erythrocyte Sedimentation Rate (ESR) and the C - reactive protein (CRP), hyperferritinaemia at 345 μg/L (normal <300 μg/L), an increased white cell count at 14×10^9/L (normal 4–10 × 109/L) and a normal platlet count at 280×10^9/L (normal 140–440 × 109/L). All the investigations excluded infections, auto-immune illnesses and malignancy. The diagnosis of AOSD was established and the patient was treated first with high doses of corticosteroids and all her symptoms resolved. The evolution was marked by multiple relapses of her disease in its chronic articular form (Figure 1) and other treatments were tested such as methotrexate and hydroxychloroquine.

At the age of 35 year-old, she was admitted again after 1 month of intense arthralgias involving her shoulders, elbows and wrists. She had also recurrent nosebleed episodes.

The physical examination was remarkable for multiple ecchymosis on the lowers extremities. She had afever. Her joints were painful with movement and her left wrist was swollen. There were neither lymphadenopathies nor splenomegaly. Her neurologic examination was normal.

Initial laboratory data were: ferritin 1335 μg/L, CRP and ERS levels were elevated at 49 mg/L (normal <6 mg/L) and 102 mm/h (normal 3–23 mm/h), respectively. Blood smear showed frequent schistocytes (10%) (Figure 2) and increased reticulocytes rate 286×10^9/L in addition to hemogram disorders: low circulating platelet count 6×10^9/L, anemia 7.4 g/dl (normal 12–18 g/dl). Electrolytes, kidney function test, liver enzymes and antinuclear antibodies were within normal range.

The funduscopic examination revealed diffuse retinal hemorrhage involving peripapillary and peripheral retina. There was no evidence of an evolutive infection or neoplasia: a computed tomography scan of the brain, thorax, abdomen, and a bone marrow aspiration didn't show any significant abnormality.

It was suspected that she had TTP based on microangiopathic hemolytic anemia and thrombocytopenia that cannot be explained otherwise. Of note, blood tests for ADAMTS13 activity and inhibitor were not available in the hospital.

To reduce bleeding frequency, the patient received platelets transfusion and high-dose corticosteroid therapy. Then, intravenous immunoglobulin treatment was added but with no significant improvement. The platelet count did not exceed 15×10^9/L. Finally, within the application of plasmapheresis regimen, her symptoms began to resolve: there have been no further arthralgias or hemorrhage signs. Her ferritin decreased, LDH level was within normal limits, her platelet count stabilized at 334×10^9/L and the hemoglobin remained at 9.4 g/dl.

The patient was discharged on prednisone therapy with plans for extended taper.

Actually, she is going fine with a follow-up of 15 months.

3 | DISCUSSION

Still's disease is a multisystemic inflammatory disorder that affects young adults. It is an uncommon rheumatic illness where the diagnosis is based on clinical findings, laboratory data as well as the exclusion of infections, malignancies and the other autoimmune arthritis.[8] Our patient had AOSD according to the criteria proposed by Yamaguchi and the ASD Research Committee[8] and the exhaustive workup reasonably ruled out others diagnosis, giving a very high probability of an AOSD in its chronic arthritis form with several relapsing febrile polyarthritis.

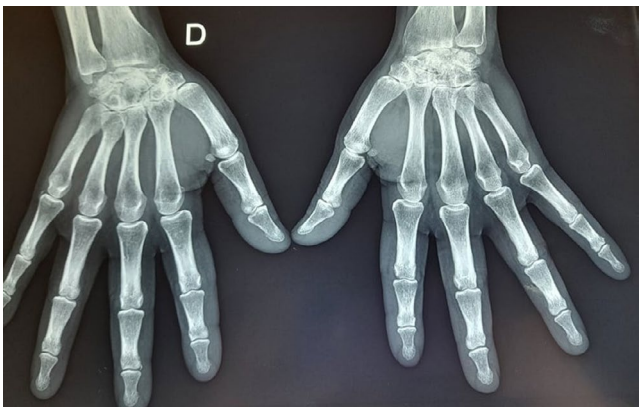

FIGURE 1 Frontal radiograph of the hands shows severe osteopenia severe narrowing of the radiocarpal joint with carpal ankylosis and destruction of the intercarapl articulation

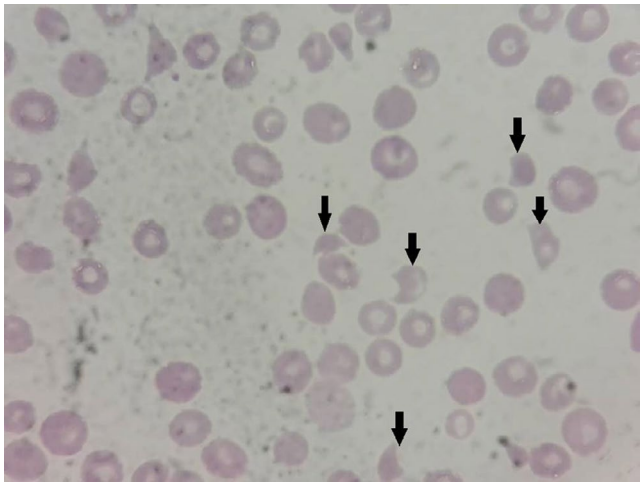

FIGURE 2 Blood smear showed frequent schistocytes

TABLE 1 Main characteristics of patients with Thrombotic thrombocytopenic purpura and adult onset Still's disease

	Masson et al.[10]	Boki et al.[14]	Boki et al.[14]	Portoles et al.[15]	Perez and Rodwig[16]	Hirata et al.[17]	Robert et al.[18]	Okwuosa et al.[19]	This case
Gender	F	F	F	M	F	F	F	M	F
Age (years)	45	33	28	31	45	23	17	27	35
Fever	+	+	+	+	+	+	+	+	+
Arthralgia and/or arthritis	+	+	+	+	+	+	+	+	+
Sore throat	+	NA	NA	+	+	NA	NA	+	−
Adenopathies	−	NA	−	−	NA	NA	NA	−	−
Rash	+	+	+	+	+	NA	+	+	−
Hypertrans-aminasemia	−	NA	NA	+	−	−	+	+	−
Time from ASD to TTP	17 years	3 years	8 years	19 days	3 days	4 years	3 months	4 weeks	11 years
Anticardiolipinantibodies	NA	−	−	−	−	NA	NA	−	−
Serumcreatinine(μmol/l)	660	123	187	565	HD	97	396	132	64
Diminished ADAMTS-13 activity	ND	NA	NA	ND	ND	+	−	ND	ND
Kidneybiopsy	Renal TMA (postmortem)	ND	ND	Arteriolar and glomerularTMA	ND	ND	ND	ND	ND
Treatment	CS	PP, PI, CS, Aspirin	PI, CS	PP, PI, CS, HD	CS, PP, HD,splen-ectomy, AZA,	CS, AZA, PP	PP, CS, HD	PP, CS, Cy, vincristine	CS, IV Ig, PP
Outcome	Death	CR	CR	PR visualimpairment	CR	CR	CR	PR visualimpairment	CR

Abbreviations: ASD, adult Still's disease; AZA, azathioprine; CR, complete remission; CS, corticosteroids; Cy, cyclophosphamide; HD, hemodyalisis; IV Ig, intravenous immunoglobulins; NA, not available; ND, not done; PI, plasmainfusion; PP, plasmapheresis; PR: partial remission; TMA, thrombotic microangiopathy; TTP, Thromboticthrombocytopenicpurpura.

As a clinical situation, Thrombotic Micro-Angiopathies (MAT) must be diagnosed in an urgent manner in order to initiate adequate intervention. Pathologically, they are marked by the development of platelet microthrombi that occlude small arterioles which lead to hemolytic anemia and thrombocytopenia. PTT is a part of MAT, it is a rare disease with an incidence of one new case per million people per year.[11] His clinical picture includes fever, neurologic abnormalities, acute renal insufficiency, hemolytic anemia and thrombocytopenia with no other apparent cause. This classic pentad occurs in a minority of patients, as low as 2%[12] and only 44% of the patients had renal failure.[11] In this case, there was not a neurologic deterioration or a renal dysfunction.

The dosage of ADAMTS13 protease is important for understanding the pathogenesis of the congenital and acquired causes of TTP. It is used to confirm secondary character of this disorder.[13] But, these assays were not always available in our laboratory.

The association between TTP and AOSD is not common. At least to our knowledge, this is the ninth case reported in the literature.[4] The main characteristics of the patients having AOSD and TTP are summarized in Table 1.[10,14-19]

In these cases, the male/female ratio was 2/7 and the timefrom the diagnosis of AOSD to PTT ranged from 3 days to 17 years. The mean age of TTP onset is 31.55 years (17–45). TTP occurredwithinthefirst 6 months of diagnosing AOSD in 4 cases. Arthralgias and fever were constantly found in the physical examination of all the patients and only 2 of them had normal levels of serum creatinine.

Diminished ADAMTS13 activity was reported in one of these cases. Almost all patients (8/9) were treated with plasmapheresis in addition to corticosteroids, and among them 6 (75%) had complete remission, whereas a permanent visual impairment was noted in 2 cases. The patient who recieved only glucocorticoid therapy died and the kidney biopsie showed thrombotic microangiopathy. Other drugs were testedin these cases such as vincristine, intravenous immune globulin,cyclophosphamide, azathioprine and splenectomy was performed once.

The outcome of TTP in AOSD mainly depends on the early application of the treatments. For adults, plasmapheresis regimen is the only treatment for which there are firm data on its effectiveness.[20] Once not previously employed, corticosteroids, intravenous immunoglobulin, rituximab and immunosuppressive drugs such as cyclosporine, azathioprine, and cyclophosphamide can be used in refractory TTP cases.[21,22] Rare therapeutic trials suggested lower rates of relapse after splenectomy.[12-23]

In Conclusion, the dual diagnosis of TTP and AOSD has interested scientists and physicians since it was first discovered. Whether their association was coincidental or the two described disorders have similar pathogenic mechanisms, the purpose of this paper is to insist on the importance of searching for a TTP once clinical evocative symptoms are reported by a patient with AOSD.

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We thank the patient for allowing us to report this case. A written consent of the patient was obtained.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

R Ben Salah and Y Bouattour: collected data and information and were the major writers of the present work. C Turki: performed, described, and analyzed data; Z Bahloul, F Frikha: contributed to data analysis and manuscript writing.

ETHICAL APPROVAL

The patient has consented to publication the case and all data.

STATEMENT ABOUT DIGITAL PHOTOGRAPHS

There are no digital photograph in this manuscript.

CONSENT

Informed written consent was obtained from the patient.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

1. El Garf A, Gaber W, Elbaz T, El Garf K. Thrombotic thrombocytopenic purpura associated with chronic HCV infection. *The Egyptian Rheumatologist*. 2012;34(3):107-110.
2. Amorosi E, Ultmann J. Thrombotic thrombocytopenic purpura: report of 16 cases and review of the literature. *Medicine*. 1966;45:139-159.
3. George JN. Clinical practice. Thrombotic thrombocytopenic purpura. *N Engl J Med*. 2006;354(18):1927-1935.
4. Gopal M, Cohn CD, McEntire MR, Alperin JB. Thrombotic thrombocytopenic purpura and adult onset Still's disease. *Am J Med Sci*. 2009;337(5):373-376.
5. Bamidele OF, Akintayo RO, Bojuwoye MO, Alabi TO, Akintayo FC, Bamidele OV. Thrombotic thrombocytopenic purpura as the first presentation in systemic lupus erythematosus. *Reumatologia*. 2018;56(4):268-270.

6. Dolin HH, Dziuba M, Pappada SM, Papadimos TJ. Presumed antiphospholipid syndrome and thrombotic thrombocytopenic purpura: an infrequent association. *Clin Case Rep*. 2019;7(10):1984-1988.
7. Kotzen ES, Roy S, Jain K. Antiphospholipid syndrome nephropathy and other thrombotic Microangiopathies Among patients with systemic lupus erythematosus. *Adv Chronic Kidney Dis*. 2019;26(5):376-386.
8. Yamaguchi M, Ohta A, Tsunematsu T, et al. Preliminary criteria for classification of adult Still's disease. *J Rheumatol*. 1992;19:424-431.
9. Shrestha B, Li YQ, Fu P. Leprosy mimics adult onset Still's disease in a Chinese patient. *Egypt Rheumatol*. 2018;40(3):217-220.
10. Masson C, Myhal D, Menard H, Lussier A. Purpura thrombotique thrombopenique fatal chez une patiente atteinte d'une maladie de Still de l'adulte. *Rev Rhum Mal Osteoartric*. 1986;53:389-391.
11. Conlon PJ, Howell DN, Macik G, KovaliK EC, Smith SR. The renal manifestations and outcome of thrombotic thrombocytopenic purpura/hemolytic uremic syndrome in adults. *Nephrol Dial Transplant*. 1995;10:1189-1193.
12. Vesely SK, George JN, Lämmle B, et al. ADAMTS13 activity in thrombotic thrombocytopenic purpura-hemolytic uremic syndrome: relation to presenting features and clinical outcomes in a prospective cohort of 142 patients. *Blood*. 2003;102:60-68.
13. Robert V, Eszto P, Perrotez JL, Galzin M, Poussel JF. Prise en charge par échanges plasmatiques d'un purpura thrombotique thrombocytopénique au cours d'une maladie de Still : à propos d'un cas. *Ann Fr AnesthReanim*. 2006;25(5):532-534.
14. Boki KA, Tsirantonaki MJ, Markakis K, Moutsopoulos HM. Thrombotic thrombocytopenic purpura in adult Still's disease. *J Rheumatol*. 1996;23:385-387.
15. Portoles J, de Tomas E, Espinosa A, Gallego E, Nieva GS, Blanco J. Thrombotic thrombocytopenic purpura and acute renal failure in adult Still's disease. *Nephrol Dial Transplant*. 1997;12:1471-1473.
16. Perez MG, Rodwig FR Jr. Chronic relapsing thrombotic thrombocytopenic purpura in adult onset Still's disease. *South Med J*. 2003;96:46-49.
17. Hirata S, Okamoto H, Ohta S, et al. Deficient activity of von Willebrand factor-cleaving protease in thrombotic thrombocytopenic purpura in the setting of adult-onset Still's disease. *Rheumatology (Oxford)*. 2006;45:1046-1047.
18. Robert V, Eszto P, Perrotez J-L, Galzin M, Poussel J-F. Treatment by plasmapheresis of a thrombotic thrombocytopenic purpura associated to a Still's disease: a case report. *Ann Fr AnesthReanim*. 2006;25(5):532-534.
19. Okwuosa TM, Lee EW, Starosta M, et al. Purtscher-like retinopathy in a patient with adult-onset Still's disease and concurrent thrombotic thrombocytopenic purpura. *Arthritis Rheum*. 2007;57:182-185.
20. Rock GA, Shumak KH, Buskard NA, et al. Comparison of plasma exchange with plasma infusion in the treatment of thrombotic thrombocytopenic purpura. *N Eng J Med*. 1991;325(6):393-397.
21. Aliford SL, Hunt BJ, Rose P, Machin SJ. Guidelines on the diagnosis and management of the thrombotic microangiopathic hemolytic anemias. *Br J Haematol*. 2003;120:556.
22. George JN, Woodson RD, Kiss JE, Kojouri K, Vesely SK. Rituksimabth (Espace_réservé1)erapy for thrombotic thrombocytopenic purpura: a proposed study of the Transfusion medicine/Hemostasis clinical Trials network with a systematic review of rituximab therapy for immune.mediated disorders. *J Clin Apher*. 2006;21:49-56.
23. Crowther MA, Heddle N, Hayward CPM, Warkentin T, Kelton JG. Splenectomy done during hematologic remission to prevent relapse in patients with thrombotic thrombocytopenic purpura. *Ann Intern Med*. 1996;125:294-296.

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