

Fragmented Realities: Dapsone, Schistocytes, and thrombotic microangiopathy

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Introduction: Dapsone, owing to its anti-inflammatory and antibacterial properties, has several indications in medicine, including immune thrombocytopenic purpura. Hemolysis is a well-documented adverse effect of dapsone - particularly, though not exclusively, in patients with glucose-6-phosphate dehydrogenase deficiency - via an oxidative mechanism. By contrast, no case series relating the onset of schistocytosis during dapsone treatment has currently been published. Observing schistocytosis in several patients treated with dapsone - suggesting thrombotic microangiopathy (TMA) in thrombocytopenic patients - prompted us to conduct the present study to describe the clinical and biological association between dapsone and schistocytosis, and its clinical consequences.

Patients and methods: We conducted a single-centre retrospective study to describe the characteristics of patients treated with dapsone in whom schistocytosis was detected.

Results: During the 2005–2021 period, 19 adult patients received dapsone in our institution. Among them, 10 patients (52.6%) had detectable schistocytes, ranging from 2 to 44/1000 erythrocytes (Table 1). As compared to other patients treated with dapsone without schistocytosis, those with schistocytes had more profound hemolytic anemia (decrease in hemoglobin, – 2.7 g/dL versus –1.6 g/dL), with more frequent low haptoglobin and higher methemoglobinemia (5.2% versus 1.9%). No organ failure or thrombotic histological damage was reported. Posology was decreased or dapsone interrupted in all patients. Schistocytosis regressed on discontinuation of treatment (Figure 1).

Discussion: Schistocytosis was frequent in patients treated with dapsone. Despite the absence of TMA-target organ damage observed in this series, clinical TMA cannot be ruled out owing to the discontinuation of dapsone in most patients.

Conclusion: Dapsone is associated with schistocytes in over of patients, with anemia and low haptoglobin, suggesting mechanical intravascular hemolytic anemia, i.e., thrombotic microangiopathy. Putative target organ damage remains to be investigated in larger cohorts.

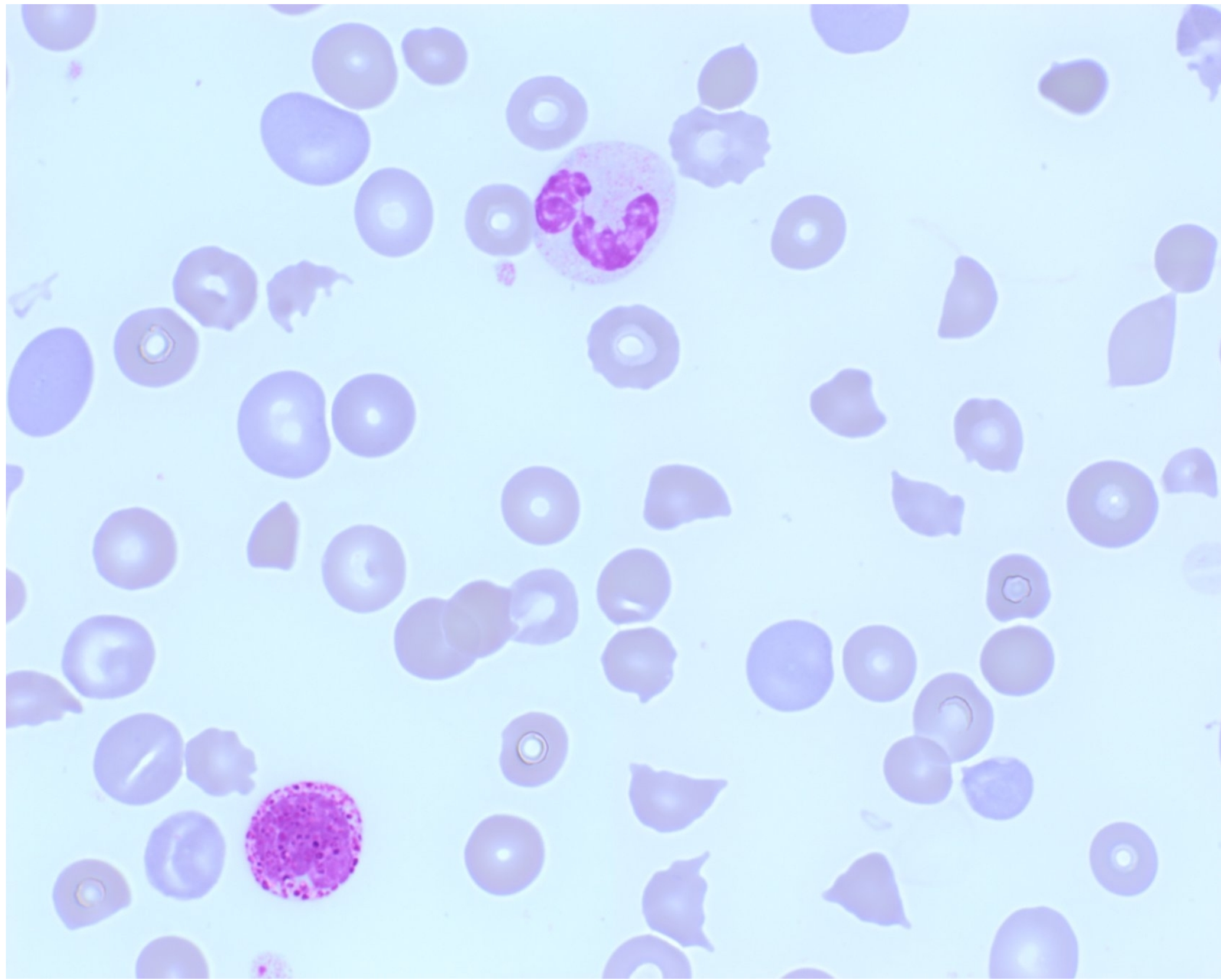


Table 1 : Laboratory findings

	Group A: schistocytes (n = 10)	Group B: no schistocytes (n = 9)	Pvalue
Schistocytes level, %	1.3 (0.2-4.4)	0	/
Hemoglobin, g/dL	10.6 (7.8-12.6)	12.7 (6.9-14.1)	0.065
Hemoglobin diff, g/dL	-2.7 (-0.4; -5.4)	-1.6 (-0.4; -7.4)	0.14
MCV, fL	98.8 (87.9-110.5)	93.3 (85.1-97.5)	0.018
Reticulocyte count, G/L	189 (66-306) ¹	126 (35-300) ²	0.17
Platelet count, G/L	134 (7-330)	133 (29-304)	1.0
Platelet count diff, G/L	+20 (-70; +325)	-17 (-46; +110)	1.0
Creatinine, µmol/L	81 (55-166) ¹	75 (57-84) ³	0.91
Creatinine diff, µmol/L	+2.5 (-30; +13) ²	-4.0 (-24; +18) ⁴	0.71
Estimated GFR, mL/min.1,73m ²	85 (37-137) ¹	88 (58-122) ³	0.95
GFR diff, mL/min.1,73m ²	-5.0 (-18; +48) ²	+4 (-32; +30) ⁴	0.51
Lactate dehydrogenase, U/L	557 (239-671) ¹	273 (208-507) ⁵	0.076
Unconjugated bilirubin, µmol/L	11 (8-18) ²	9 (1-26) ⁴	0.56
Haptoglobin < 0,3 g/L, no	8/9 (88.9%) ¹	3/5 (60%) ⁴	/
Methemoglobin level, %	5.2 (1.3-15.6) ²	1.9 (1.4-2.4) ⁶	0.38
Vitamin B9 deficiency, no	1 ³	2 ⁵	/
Vitamin B12 deficiency, no	0 ³	0 ⁵	/
Iron deficiency, no	0 ³	0 ⁶	/
Prothrombin time < 70%, no	1 ²	2 ⁵	/
Activated partial thromboplastin time ratio > 1,20, no	1 ³	1 ⁵	/
Fibrinogen, g/L	3.2 (2.3-5.9) ³	5.3 (4.4-6.2) ⁷	0.22
Hemoglobin > 1 month after discontinuing treatment diff ⁺ , g/dL	+2.4 (+1.4; +3.5) ²	/	/
GFR > 1 month after discontinuing treatment diff ⁺ , mL/min.1,73m ²	+10 (-10; +18) ²	/	/

data are presented as number or median (range).

n¹²³⁴⁵⁶⁷: 1,2,3,4,5, 6 or 7 missing data.

MCV: mean corpuscular volume; CRP: C-reactive protein.

diff: difference between blood smear value and pre-treatment value.

diff⁺: difference between value > 1 month and blood smear value.

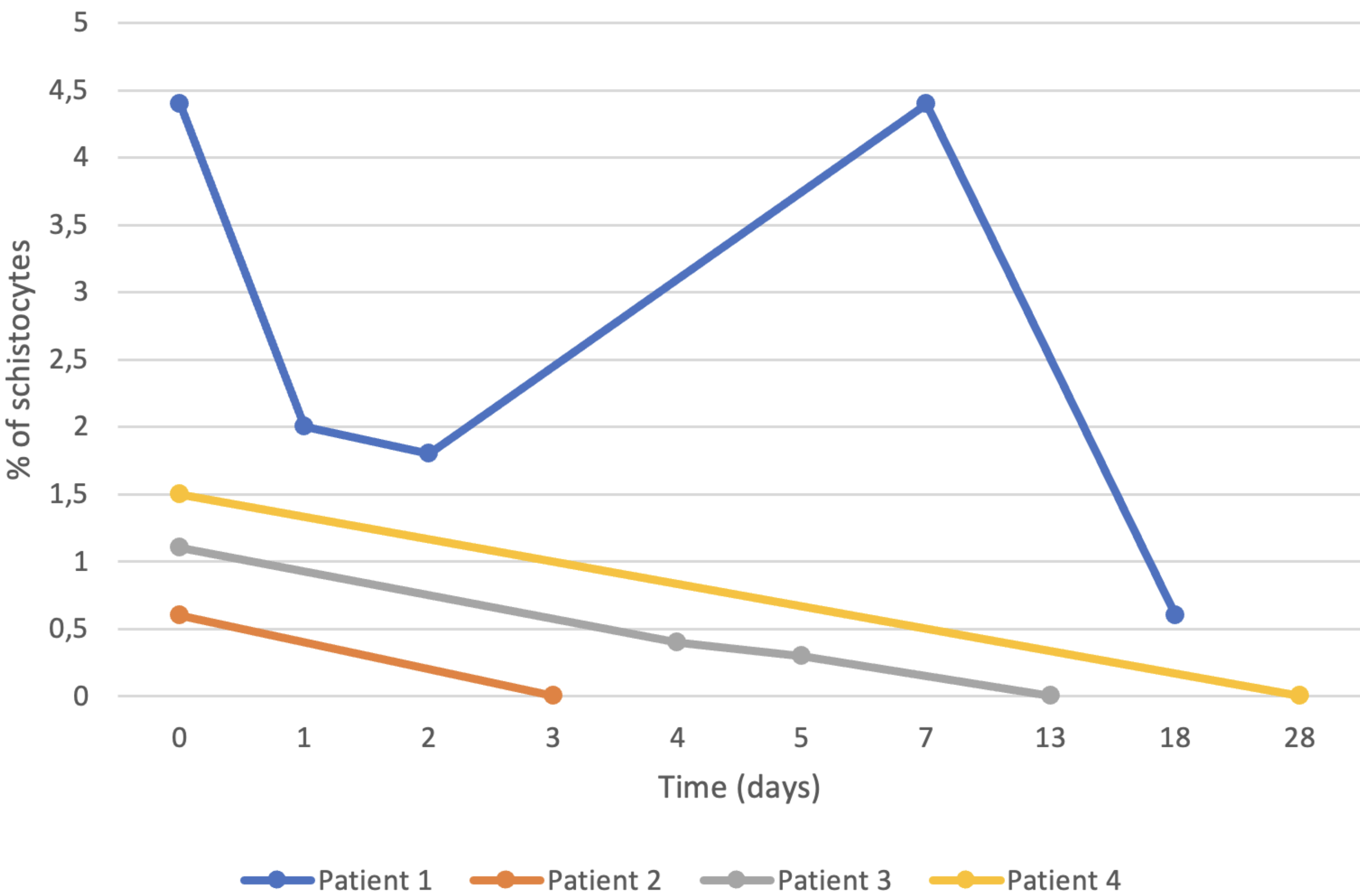


Figure 1 : Evolution of the schistocytes after discontinuation of Dapsone

