



## Diagnostic dilemma in a 3-year-old girl with acute nephritic syndrome and hematologic abnormalities: Questions

Samantha Innocenti<sup>1,2</sup> · Silvia Bernardi<sup>1,3</sup> · Maud Prévot<sup>1</sup> · Antonin Saldmann<sup>4</sup> · Maud Tusseau<sup>5</sup> · Alexandre Belot<sup>6,7</sup> · Jean-Paul Duong Van Huyen<sup>8</sup> · Olivia Boyer<sup>1</sup>

Received: 12 August 2022 / Revised: 26 August 2022 / Accepted: 26 August 2022 / Published online: 17 October 2022  
© The Author(s) 2022

**Keywords** Macrohematuria · Proteinuria · Hypocomplementemia · Anemia · Thrombocytopenia · Childhood

### Case

A 3-year-old girl presented to the Emergency Department with the chief complaint of brown macrohematuria for 2 weeks. Her past medical history revealed scarlet fever and mild upper respiratory tract infections 2 months earlier, and no recent trauma or travel was reported. She had no familiarity for rheumatological disease, and her parents were unrelated. The first clinical examination was unremarkable, including the absence of fever, arthralgia, or skin rash. The patient presented with normal growth and development and up-to-date vaccinations. Abdominal ultrasound reported bilateral kidney hyperechogenicity with a preserved corticomedullary differentiation, and chest radiography was normal. Initial blood and urinary tests are summarized in Table 1 and mainly revealed a non-hemolytic anemia associated with

thrombocytopenia, positive direct Coombs test, hypergammaglobulinemia, and high ESR:CRP ratio. Kidney function was normal, and urinalysis revealed hematuria associated with proteinuria. Furthermore, a persistent activation of the classical complement pathway was noticed in association with a low CH50 and the presence of anti-C1q and anti-C3b antibodies.

After 3 days, the patient presented malar rash, palatal petechiae, and peripheral edema associated with a rapid worsening of anemia and thrombocytopenia.

Autoimmune screen revealed high titer of ANA, anti-dsDNA, ENA, and p-ANCA with anti-platelet, anti-beta2GPI, and anti-phosphatidylserine antibodies associated with LAC positivity but no anti-complement factor B (CFB) and anti-complement factor H (CFH) autoantibodies.

The answers to these questions can be found at <http://dx.doi.org/10.1007/s00467-022-05752-6>.

✉ Samantha Innocenti  
samantha.innocenti@unifi.it

<sup>1</sup> Néphrologie Pédiatrique, Centre de Référence MARHEA, Hôpital Necker-Enfants Malades, APHP, Institut Imagine, Inserm U1163, Université Paris Cité, Paris, France

<sup>2</sup> Nephrology and Dialysis Unit, Meyer Children's Hospital, Florence, Italy

<sup>3</sup> School of Nephrology, Università Degli Studi Di Milano, ASST Papa Giovanni XXIII, Bergamo, Italy

<sup>4</sup> Immunology Department, Hopital Européen Georges Pompidou, APHP, Paris Cité University, Paris, France

<sup>5</sup> Centre International de Recherche en Infectiologie, Univ Lyon, Inserm, U1111, Université Claude Bernard, Lyon 1, Centre National de La Recherche Scientifique, UMR5308, ENS de Lyon, Lyon, France

<sup>6</sup> Pediatric Nephrology, Rheumatology, Dermatology Department, Hôpital Femme Mère Enfant, CRMR RAISE, Hospices Civils de Lyon, Bron, France

<sup>7</sup> The International Center of Research in Infectiology, Lyon University, INSERM U1111, CNRS UMR 5308, ENS, UCBL, Lyon, France

<sup>8</sup> Department of Pathology, Necker-Enfants Malades Hospital, APHP, Paris Cité University, Paris, France

**Table 1** Laboratory tests at referral

	<i>At referral</i>	<i>Normal values</i>
Hemoglobin (g/dL)	8.8	11.5–14
Leukocytes ( $\times 10^9$ /L)	6.44	5.5–15
Platelets ( $\times 10^9$ /L)	62	150–450
Reticulocytes ( $\times 10^9$ /L)	141.0	20–100
Haptoglobin (g/L)	3.4	0.3–2
Total bilirubin ( $\mu$ mol/L)	3	0.8–6.8
ESR (mm)	71	< 10
Schistocytes (%)	< 1	< 1
LDH (UI/L)	322	192–321
Albumin (g/L)	13.2	34–50
Proteins (g/L)	57	64–82
Ferritin (mcg/L)	449	12–224
Triglycerides (mmol/L)	3.94	0.5–2,23
BUN (mmol/L)	4.8	2.5– 6.4
Creatinine ( $\mu$ mol/L)	29	15–34
eGFR (beside Schwartz formula, mL/min/1.73 m <sup>2</sup> )	101	> 90
Proteinuria (g/L)	2.87	0–0.1
Urine creatinine (mmol/L)	1.8	1–5
Urinary P/C ratio (g/mmol)	1.6	
D-dimer (ng/mL)	79,131	< 500
Activated fibrinogen (g/L)	1	2–4
aPTT (s)	45	25–38
Prothrombin ratio (%)	76	70–150
INR	1.14	0.9–1.2
Antithrombin III (%)	75	80–120
Direct Coombs test	Positive	Negative
C3 (mg/L)	239	660–1250
C4 (mg/L)	68	93–380
CH50 (%)	19	70–130
sC5b9 (ng/mL)	> 1820	< 300
Anti-C1q (UA)	204	< 30
Anti C3b antibodies IgG	Positive (598 UA)	Negative
Anti-CFH antibodies	Negative	Negative
Anti-CFB antibodies	Negative	Negative
ANA	> 1:800	< 1:80
Anti-dsDNA antibodies (U/mL)	163	Negative
ENA	Anti-Sm +, anti-RNP +, antiSSA (Ro) +	Negative
Anti-platelet antibodies	Positive	Negative
Anti-beta2GPI antibodies IgG (U/mL)	64	< 20
Anti-cardiolipin antibodies IgG	Negative	Negative
Lupus anticoagulant	Positive	Negative
Anti-phosphatidylserine/thrombin antibodies IgG (U)	> 150	< 30
Anti-phosphatidylserine/thrombin antibodies IgM (U)	> 150	< 30

## Questions

1. Which major diagnoses must be considered in this context?
2. What further investigations would you perform for the work-up of your main hypothesis?
3. If the main hypothesis is confirmed, which treatment regimen could you consider?

**Acknowledgements** We would like to express our gratitude to the patient and her family for participating in this project.

**Funding** Open access funding provided by Università degli Studi di Firenze within the CRUI-CARE Agreement.

## Declarations

**Conflict of interest** The authors declare no competing interests.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>.

**Publisher's note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.