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Nephrotic Syndrome Revealing Secondary Syphilis in a 23-year-old Student in Sub-Saharan Africa and Review of the Literature

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Authors' contributions

This work was carried out in collaboration among all authors. Author DA contributed to the patient's treatment and wrote the manuscript. Authors SG and BYJ contributed to the patient's treatment and revised the manuscript. Authors KSA, PM, KKU, KA, OGA, TAHS and CG contributed to the revision of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Glomerulonephritis is one of the renal damages of secondary syphilis.
We report the case of a 23-year-old man, a student with progressive bilateral glaucoma, who consulted nephrology for the oedema to-ascitic syndrome. Clinical and laboratory examination revealed painless generalised edema, syphilitic roseola, nephrotic range proteinuria (10.26 g/24h), severe hypoalbuminemia (16.2 g/l) and hypercholesterolemia. The diagnosis of nephrotic syndrome secondary to syphilis was made and confirmed by positive serology (VDRL and TPHA). After four weeks treatment with anti biotic, significant regression of proteinuria (140mg/24h) and normalization of biological parameters were observed. This case illustrates the importance of early diagnosis and appropriate treatment of nephrotic syndrome secondary to syphilis, enabling rapid and complete recovery.

Keywords: Nephrotic syndrome; secondary syphilis; Subsaharan Africa.

1. INTRODUCTION

Syphilis is a sexually transmitted infection caused by Treponema pallidum [1]. It evolves in three phases: primary (chancre), secondary (treponemal septicemia), and tertiary (neurological and cardiovascular complications). Syphilis has been on the increase in recent years. According to the World Health Organization, there will be 7.1 million new cases of syphilis worldwide in 2020 [2]. In 2022, the United Kingdom recorded a 15.2% increase in syphilis cases compared with 2021, the highest since 1948 [3]. In Africa, its prevalence is around 7.36% among blood donors in Mali [4] and 3.7% among pregnant women in a study in Ethiopia [5]. In Burkina Faso in 2011, a survey carried out in prisons, and another in pregnant women found respective prevalences of 5.7% and 1.7% [6,7]. The clinical manifestation of syphilis is polymorphic, with systemic involvement. Renal involvement is not uncommon in syphilitic infection. Several cases of renal damage have been described in the literature, the most common clinical manifestation being nephrotic syndrome [8-11]. We report a case of nephrotic syndrome in a young adult with secondary syphilis.

2. CASE DESCRIPTION

We report the case of a 23-year-old man, a student with seven years of progressive bilateral glaucoma, protected against viral hepatitis B by the vaccine. He presented to the nephrology department with edematous-ascitic syndrome, plus facial puffiness that had been evolving for about seven days in a non-febrile context.

On initial clinical examination, the patient was found to be in Stage 1 performance status of World Health Organization (WHO) general condition, with coloured anicteric conjunctivae and oedematous-ascitic syndrome, with oedema extending up to the thighs, soft, bucketing, painless and declining, painless, mobile cervical and inguinal adenopathies of varying sizes, the largest of which was 1 cm long, blood pressure 127/78 mm Hg, pulse 80 beats per minute, weight 71 kg, urine dipstick showed albuminuria more than three crosses.

Dermatological examination revealed erythematous, scaly lesions on the palms and soles of the feet, with no endooral lesions, genital ulcerations or nail involvement (Fig. 1).The examination of the rest of the systems was regular.

Laboratory results revealed 24-hour proteinuria was 10.26g/24h, hypercholesterolemia with total cholesterol of 7.75 mmol/l, low density lipoproteins (LDL) cholesterol of 6.33 mmol/l, serum protein electrophoresis showed severe hypoalbuminemia of 16.2 g/l, hypoprotidemia at 44g/l, hyper-alpha 2 microglobulin at 9,7 g/L and hyper-beta 2 and gamma microglobulin, serum creatinine at 105umol/l and Glomerular filtration rate (GFR) was estimated to 99,41 mL/mn according to chronic kidney disease-epidemiology collaboration (CKD-EPI) , C-reactive protein (CRP) at 10.79g/l, hemoglobin 12.8 g/dl, other blood cell lines was normal, normal electrolytes, normal levels of transaminases and prothrombin, urine cytobacteriological examination revealed three albumin crosses and two red cell crosses, and renal ultrasound revealed normal kidney parenchyma and size.

Clinical and paraclinical examinations for etiological and therapeutic purposes revealed the following: otorhinolaryngological and stomatological examinations didn't find any source of infection.

The Venereal Disease Research Laboratory (VDRL) was positive with a title of antibodies to two international units (2 UI), and the Treponema Pallidum Hemagglutination Assay (TPHA) was positive with a title of antibodies to 1280 international units. hepatitis C virus antibodies (anti-HCV) and hepatitis B surface antigen (HBs antigen) were negative, the HIV-serology test was negative by Elisa test, and abdomino-pelvic ultrasound revealed normal-sized, differentiated kidneys with ascites and a small pleural effusion. Immunological tests such as complement tests (C3; C4 and CH50), phospholipase A2 receptor autoantibodies (anti-PLA2R) and antinuclear antibodies could not be performed due to lack of funds. We cannot perform kidney biopsies in our country due to a lack of trained pathologists. We primarily retained the diagnosis of nephrotic syndrome related to secondary syphilis, and we started treatment as described below.

Our initial management was:

- *Benzathine benzylpenicillin* 2.4 MIU intramuscular injection once a week for three weeks
- *Rivaroxaban 10 mg* 1 tablet daily
- *Ramipril 2.5 mg* 1 tablet daily for its antiproteinuric role
- *Spironolactone 50 mg* one tablet daily
- *Atorvastatin 20 mg* 1 tablet daily.

Two weeks after starting treatment, the patient weighed 58 kg (-13 kg) without oedema, with 24-hour proteinuria at 460mg/24h (0.29g/l), serum albumin at 29.1g/l, and total protein at 62g/l.

At four weeks, we still had regression of proteinuria to 290mg/24h, and no oedema or syphilitic roseola. All treatment was stopped in the fourth week, and we began the monitoring phase.

After two months of monitoring, the patient's clinical evaluation was normal, and the biology revealed 24-hour proteinuria at 140mg/24h (0.09g/l), serum albumin at 40.1g/l, total proteins at 70g/l, and creatinine levels were still normal. The evolution of proteinuria and syphilis antibody monitoring are shown in Table 1 and Fig. 2.

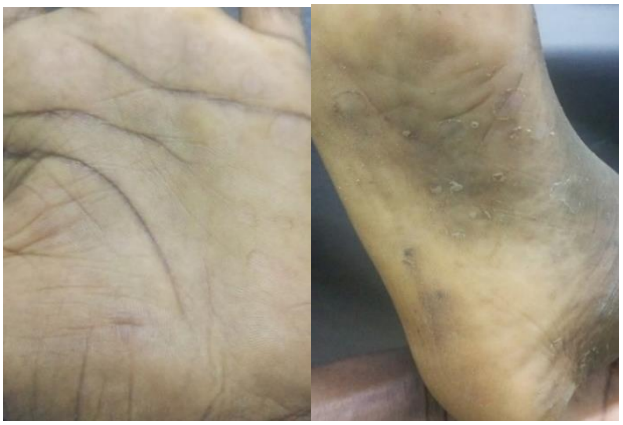

Fig. 1. Syphilitic roseola on palmar and plantar areas

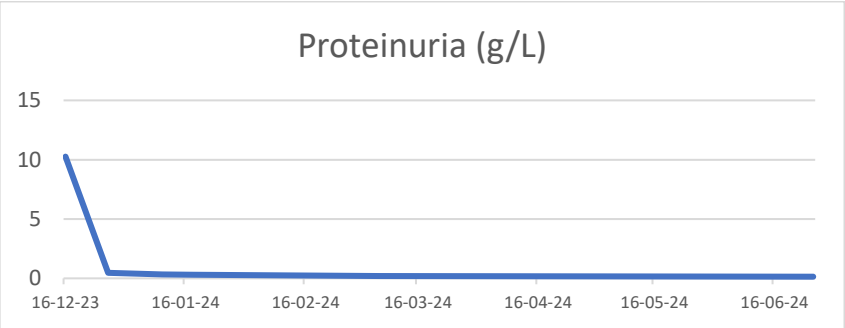

Fig. 2. Evolution of proteinuria over time

Table 1. Summary of biological parameters

Dates	Proteinuria (g/L)	Creatininemia (µmol/L)	Albuminemia (g/L)	serum protein (g/L)	hemoglobin (g/L)	Thrombocytes (platelets per microliter of blood)	Leukocytes (white blood cells per microliter of blood)	TPHA (UI/L)	VDRL (UI/L)
16/12/2023	10,26	113	16,2	44	12,8	353000	5250	1280	2
27/12/2023	0,46	88	NR	62	NR	NR	NR	NR	NR
10/01/2024	0,32	NR	29	NR	NR	NR	NR	NR	NR
18/01/2024	0,29	NR	NR	NR	NR	NR	NR	2560	4
07/02/2024	NR	NR	NR	NR	NR	NR	NR	2560	2
06/03/2024	0,2	NR	NR	NR	NR	NR	NR	2560	2
26/06/2024	0,14	NR	NR	NR	NR	NR	NR	2560	2
03/07/2024	NR	NR	NR	NR	NR	NR	NR	640	NR

g/l : grams per liter ; µmol/L: micromole per liter ; UI/L : international unit per liter ; NR : not realized

3. DISCUSSION

Syphilis is caused by Treponema pallidum, and this germ can lead to a variety of renal manifestations, the most widely described of which is nephrotic syndrome. The pathophysiological mechanisms most often involved are the formation and deposition of immune complexes in the glomeruli, activating inflammation and causing glomerular damage. Histological studies have shown lesions of complex immune related membranoproliferative glomerulonephritis (MPGN) and membranous nephritis, rarely extracapillary glomerulonephritis and tubulointerstitial damage linked to Treponema pallidum infection [8-12]. In our case, histology could not be performed due to insufficient technical resources in Burkina Faso. In our context, we were unable to carry out an immunological work-up on our patient due to a lack of financial resources and the absence of a technical platform to rule out other causes unrelated to the treponemal infection. However, on the basis of a number of clinical and biological arguments, we were able to link this nephrotic syndrome to syphilitic infection in Burkina Faso.

Positive diagnosis of treponemal infection is a public health priority in our context, as it would enable efficient management with satisfactory responses. The non-specific clinical presentation of nephrotic syndrome can lead to delays in diagnosis. Studies have shown that late diagnosis of syphilis can lead to severe renal complications, hence the need to insist on screening for syphilis in nephrotic syndrome, even in children, as we are faced with early sexuality and an upsurge in venereal pathologies [13,14]. Our case proves this, following the diagnosis of syphilis in a 23-year-old boy.

The diagnosis of nephrotic syndrome in the context of a treponemal infection is not uncommon. A positive diagnosis relies on the identification of the pathogen and histological confirmation. In our case, histological diagnosis was not possible due to the lack of technical resources for performing the procedure and the difficulties associated with interpreting histological results. We were also unable to conduct an immunological assessment of glomerular involvement, including the detection of anti-PLA2R antibodies, serum complements (C4, C3, and CH50), and antinuclear autoantibodies. In some cases of primary anti-PLA2R-positive membranous nephropathy and lupus membranous nephropathy, spontaneous remissions have been reported [15,16]. All these factors present limitations in establishing a definitive diagnosis in our case. However, we made the diagnosis based on the clinical and biological evidence available and accessible in our context.

Syphilis is treated with beta-lactam antibiotics, namely penicillin G by injection, which eradicates treponema, which is less resistant to this class of antibiotics [10,17,18]. Treatment of nephrotic syndrome should be symptomatic, as etiological treatment can improve the various renal manifestations. The literature has shown that the majority of cases had complete remission of proteinuria and improvement of other clinical and biological symptoms with well-managed treatment. The two international venereal disease research laboratory (VDRL) and Treponema Pallidum hemagglutination test (TPHA) can remain positive for more than a year after well-managed treatment with absence of clinical symptoms (Table 1) [19].

This case study reminds us that, despite the rarity of nephrotic syndrome secondary to syphilis, infection should always be suspected, especially in at-risk populations. Early diagnosis and management are essential to avoid renal complications. This approach must include systematic diagnosis of sexually transmitted infections in cases of renal damage, particularly nephrotic syndrome. In the current context of declining HIV/AIDS prevalence, a concerning resurgence of sexually transmitted infections, particularly syphilis, has been observed. This trend raises significant public health concerns. It is imperative to intensify efforts in education and prevention, particularly targeting sexually active young populations, o curb this trend and prevent long-term public health consequences.

4. CONCLUSION

Nephrotic syndrome is a renal pathology with a variety of etiologies. Infectious causes are not uncommon. Syphilis is one of the least described causes in the literature. This case of nephrotic syndrome (NS) secondary to treponemal infection is highly instructive, highlighting a number of practical nephrological aspects. In the event of a sudden onset of nephrotic syndrome in an adolescent or young person, we must always consider a venereal infection, such as syphilis, which is increasingly prevalent, especially in Africa.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

CONSENT

We have obtained the patient's written consent for the use of the data collected.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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