

**Case Report**

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## A case of minimal change disease associated to Rubinstein Taybi syndrome

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### Abstract

**Introduction:** Focal segmental glomerulosclerosis (FSGS) is the main glomerular nephropathy secondary to malformative uropathies. The latter can be included in the poly malformative syndromes in the pediatric population. However, other glomerular impairments may rarely be associated with some polymalformative syndromes as reported in this rare case of a minimal change disease (MCD) associated with Rubinstein Taybi syndrome (RSTS).

**Materials and methods:** We report a case of pure nephrotic syndrome in a young male patient with RSTS.

**Case presentation:** It is about a 27 year old young patient diagnosed since birth with a Rubinstein Taybi. In 1994, he was hospitalized in pediatrics for acute pyelonephritis. Retrograde urethroscopy (RUC) showed bilateral vesicoureteral reflux (VUR) grade 3 with functional renal asymmetry on scintigraphy. The patient was admitted in nephrology department in 2019 for a pure and intense nephrotic syndrome with abrupt onset. The initial diagnosis retained was glomerular nephropathy particularly a FSGS secondary to his malformative uropathy. Subsequently, in view of the persistence of an intense nephrotic syndrome, the absence of VUR at the RUC, as well as the functional renal symmetry at the scintigraphy, it was decided to perform a renal biopsy. The biopsy showed an optically normal kidney with the presence of some meningial C3 deposits. MCD was then retained. The patient received corticosteroid therapy with a favorable clinical and biological response.

**Conclusion:** Even if reflux nephropathy remains the most frequent cause of glomerulopathy secondary to malformative uropathy, we should not hesitate to perform a renal biopsy in front of an intense nephrotic syndrome with no functional renal impact of the VUR.

**Keywords:** Nephrotic syndrome; Minimal change disease; Rubinstein Taybi syndrome.

## Introduction

Minimal change disease (MCD) is one of the most common glomerulonephritis. It is the major cause of nephrotic syndrome (NS) in children (it accounts between 70% and 90% of NS in children under the age of 10 years) [1]. It is a podocytopathy mostly revealed by a nephrotic syndrome mainly pure (without hypertension, hematuria and organic kidney failure). In children, NS is defined by a first morning or 24h protein-creatinine ratio 2 g/g associated to either hypoalbuminemia or edema, according to the recent guidelines of the Kidney Disease: Improving Global Outcomes (KDIGO) [2]. In adults, MCD incidence varies between 10% and 15% of adult idiopathic NS. [1] It is a clinical and biological entity defined by massive selective proteinuria (> 3.5g/day), decreased serum albumin (< 30 g/l) or edema [2].

In the histologic study, the glomeruli appear normal without any lesions visible in light microscopy and without deposits of immunoglobulins or complement in immunofluorescence. In the Electronic microscopy, we find effacement of the podocyte foot process without any electronic deposits [1,2]. The response to corticosteroid treatment makes it possible to distinguish sensitive forms, which have a good prognosis, as opposed to the resistant forms, which may lead to irreversible glomerular damage and chronic renal failure in the absence of response to second-line prescribed treatment mainly the immunosuppressive therapy [2]. Before starting treatment for MCD in adults, a secondary cause of the nephrotic syndrome must be ruled out. Indeed, MCD is always primary in children but can be secondary in adults. In this chapter of secondary MCDs, we find drug induced nephrotic syndrome (non-steroidal anti-inflammatory drugs, interferon ...), hematological causes such as Hodgkin's disease, infections, auto immune diseases and atopic nephrotic syndromes [1]. Even if Focal segmental glomerulosclerosis (FSGS) is the major glomerular nephropathy secondary to malformative uropathies especially the reflux nephropathy [3] that can be included in the poly malformative syndromes, other glomerular impairments such MCD may rarely be associated with some polymalformative syndromes. We report a very rare case of nephrotic syndrome secondary to minimal change disease, proven by kidney biopsy associated to RSTS in a young male patient

## Patient and clinical description

**Patient informations:** It is about a 27 year old young diagnosed since early childhood (since the age of 04 years) with a Rubinstein Taybi syndrome associating dwarfism, growth retardation, spondyloepiphyseal dyschondroplasia and ophthalmological involvement made of strabismus and amblyopia. He doesn't have similar cases of RSTD in his family, it's apparently a sporadic case. However, first-degree parental consanguinity has been reported. In 1994, he was hospitalized in pediatrics for acute pyelonephritis. Retrograde urethrocytostcopy (RUC) showed bilateral vesicoureteral reflux (VUR) grade 3 with functional renal asymmetry on scintigraphy.

The patient was admitted in nephrology department in 2019. He had a pure and intense nephrotic syndrome with an abrupt onset.

**Clinical findings:** The clinical examination showed a conscious and oriented patient. He had no fever. Blood pressure

was 130/80 mmhg. Heart rate was 94 bpm. Cardiopulmonary auscultation was normal. The abdominal exam revealed moderate ascites. He also had renal-like edema of both lower limbs.

**Laboratory and radiologic findings:** On biology, 24-hour proteinuria was 28 g/d. Urine cytology didn't show hematuria. Blood creatinine level was 109 micromoles/l controlled to 60 micromoles after diuretic treatment. At the Serum protein electrophoresis: protidemia was 40 g/l, albuminemia 15.6 gr/l, alpha2 globulinemia 14.9 g/l and gamma globulinemia 3.1 g/l. Serum complement was normal as well as anti-nuclear antibodies and anti-neutrophil cytoplasm antibodies. The thyroid workup was normal. The lipid profile showed a cholesterol level at 16.2 mmol/l, an LDL-C at 12.6 mmol/l, and a triglyceridemia at 3.3 mmol/l. The ascite puncture showed a transudate fluid. Abdominal ultrasound revealed a large intra peritoneal effusion and two well differentiated kidneys of normal size.

**The initial diagnostic approach:** The initial diagnosis retained was glomerular nephropathy particularly a FSGS secondary to his malformative uropathy.

**Therapeutic intervention and follow-up:** He received symptomatic treatment consisting on diuretics for his nephrotic syndrome. Subsequently, in view of the persistence of intense nephrotic syndrome, with recurrent hospitalizations for generalized edema requiring intravenous diuretics and albumin perfusions, we decided to perform a RUC and a renal scintigraphy to verify the reflux and its kidney function impact. Afterwards, in front of the absence of any VUR at the RUC, as well as the functional renal symmetry at the scintigraphy, it was decided to perform a renal biopsy. The biopsy showed an optically normal kidney in the light microscopy and some mesangial complement deposits in the immunofluorescence study.

In view of these findings, the diagnosis of MCD was considered. The patient received corticosteroid therapy during 6 months associated with adjuvant treatments consisting of vitamin D, calcium and gastric protection with low salts and sugar diet. Starting dose of corticosteroids was 1 mg/kg/d received during 4 weeks then we started tapering doses in front of clinical and biological remission. He had a complete remission of his nephrotic syndrome (negative proteinuria and normal serum albumin) after 4 weeks of treatment. His serum creatinine level was normal.

During his follow-up during one year, he has never been hospitalized in nephrology department. The patient noted a clear improvement in his clinical condition, particularly the disappearance of edemas, which allowed him to re integrate into social and professional life, as well as reaching his artistic activities of dance and theater.

## Discussion

Rubinstein Taybi syndrome is genetic disease that was described the first time in 1963 [4]. The mode of transmission is autosomal dominant. However, in almost 99% of cases, RSTS cases are sporadic without other similar cases found in the patient's family. In the literature, a small number of familial cases have been reported [5-7].

In our patient, we didn't find any other cases of RSTS in any member of his family. It's a de novo sporadic case.

This syndrome is very rare. In fact, according to the current literature data, its incidence is between 1/100,000 and 1/125,000 births [8]. Clinically, it's defined by the association of mental retardation, growth retardation, large thumbs, large toes, and facial dysmorphism. Important additional features are described such as microcephaly, enlargement of other fingers, recurrent respiratory infections, feeding problems, keloid formations, hirsutism, clenched teeth, hypotonia, laxity of ligaments, cryptorchidism, and ophthalmological features such as glaucoma [4,9].

In the antenatal period, RSTS diagnosis is almost never made. It's very rarely evoked during pregnancy because the rarity of antenatal signs. The diagnosis is frequently made at birth or in infancy in front of the regular presence of a usual growth retardation, characteristic facial abnormalities, mental disability and large thumbs. Our patient was diagnosed since early childhood by observing a post natal growth retardation, a dwarfism, broad thumbs and a spondyloepiphyseal dyschondroplasia. He didn't have intellectual disabilities. Concerning renal aspects which can be associated to Rubinstein syndrome and, according to the literature, renal or urinary tract anomalies incidence is estimated range from 24 to 66% of patients diagnosed with RSTS. These abnormalities can be renal agenesis, renal or pyloric duplications, hydronephrosis, VURs, or glomerulopathies (nephrotic syndromes) [10-17].

Very rare cases of nephrotic syndrome in patients diagnosed with RSTS were published [17] but frequently the kidney biopsy was not performed. The uniqueness of this case is the fact that it is a histologically proven MCD. The most important message is the importance of the kidney biopsy in front of any unexplained nephrotic syndrome. Even though FSGS secondary to malformative uropathy would be the most frequent etiology of glomerular nephropathy in the presence of a malformative syndrome, we should always keep in mind other causes of nephrotic syndrome and think to perform a renal biopsy in front of any diagnostic doubt. In our patient, in view of the history of vesico ureteral reflux in childhood, we retained a reflux nephropathy as the etiology of his nephrotic syndrome. However, the absence of VUR at the control RUC led us to perform a renal biopsy which showed MCD. The patient presented a rapid improvement of his nephrotic syndrome after starting corticoids. Performing biopsy was mandatory in front of this nephrotic syndrome. Even in this context of reflux nephropathy, NS could be explained in only unique condition which is the presence of functional renal impairment objectified on a renal scintigraphy.

## Conclusion

Rubinstein Taybi syndrome is a poly malformative syndrome secondary to an extremely rare genetic disorder. It can be associated to several renal abnormalities. We reported in this article the first case of minimal change disease histologically proven in a young male patient diagnosed RSTS since early childhood. Even if reflux nephropathy remains the most frequent cause of glomerulopathy secondary to malformative uropathy, we should not hesitate to perform a renal biopsy in front of an intense nephrotic syndrome with no functional renal impact of the VUR proven by scintigraphy. Kidney biopsy remains the gold standard for the diagnosis of different glomerular nephropathies. The clinical interest of histology is threefold, it is as well diagnostic as therapeutic and prognostic.

## Declarations

**Competing interests:** The authors declare no competing interests.

**Authors' contributions:** All authors gave Substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data, participated in drafting the article or revising it critically for intellectual content and gave final approval of the version to be published.

**Consent publication:** The patient gave his consent to publish his anonymous data.

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