# Nephritic syndrome associated to skin infection, hepatitis A, and pneumonia: a case report

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## SUMMARY

***Introduction:*** Glomerulonephritis is the most common cause of acute and chronic renal disease. The prototype of acute glomerulonephritis is acute post-infectious glomerulonephritis. Recently, increased cases of glomerulopathy have been associated with bacterial, viral, and other infections. Acute nephritic syndrome is part of glomerulonephritis with an acute beginning, characterized by hematuria, hypertension, edema, and oliguria due to the reduction of glomerular filtration reflected in an increase of nitrogen compounds.

***Development:*** This paper shows a male infant at 2 years and 7 months of age with nephritic syndrome associated to a skin infection, pneumonia, and hepatitis A virus infection.

***Conclusion:*** Acute glomerulonephritis may be associated to streptococcus or another coincidental infection. Children with skin infection, hepatitis A, or pneumonia who reveal abnormal urinalysis, hypertension, azotemia, or oliguria should be evaluated for concomitant glomerulonephritis.

***Keywords:*** *Glomerulonephritis; Hepatitis A; Edema; Hypertension; Jaundice.*

***Síndrome nefrítico asociado con infección cutánea, hepatitis A y neumonía: informe de un caso***

## RESUMEN

***Introducción:*** La glomerulonefritis es la causa más frecuente de enfermedad renal aguda y crónica. El prototipo de la glomerulonefritis aguda es la glomerulonefritis aguda post-infecciosa. Recientemente, se ha asociado un aumento en la cantidad de glomerulopatías con infecciones bacterianas, virales y otras. El síndrome nefrítico agudo hace parte de las glomerulonefritis de comienzo agudo, caracterizado por hematuria, hipertensión arterial, edema, oliguria y disminución de la filtración glomerular con la retención de productos azoados.

***Desarrollo:*** Se presenta un niño de 2 años y 7 meses de edad con síndrome nefrítico asociado con infección cutánea, neumonía e infección por virus de la hepatitis A.

***Conclusión:*** La glomerulonefritis aguda puede estar asociada con estreptococo solamente o con otra infección coincidental. Los niños con infección cutánea, hepatitis viral o neumonía, que hayan presentando anormalidades en el uro análisis, hipertensión, azohemia u oliguria, se deben evaluar para glomerulonefritis asociada.

***Palabras clave****: Glomerulonefritis; Hepatitis A; Edema; Hipertensión; Ictericia.*

Acute nephritic syndrome (ANS) or acute glomerulonephritis (AGN) consists of the sudden appearance of hematuria, hypertension, oliguria, edemas, and deterioration of the renal function in varying degrees. Not all these symptoms will be present in all cases of acute glomerulonephritis[1]. ANS is the most frequent form of Post-infectious Acute Glomerulonephritis (PIAGN); hence, the terms ANS, AGN, and PIAGN are frequently indiscriminately used.

This is the most common of childhood renal syndromes, predominating during pre-school and grade school age, with a maximum frequency between 6 and 7 years of age[2]. Clinical manifestations are rare in children under 3 years of age, but cases have been

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described during breastfeeding stages, adolescence, and adulthood[2,3]. It is more frequent in boys than in girls at a ratio of 2:1.

The true incidence of nephritic syndrome is unknown, because -currently- there are many sub-clinical or asymptomatic cases, manifested only with micro-hematuria, hypocomplementemia, and/or proteinuria without symptomatology. Fifteen percent of the siblings of hospitalized index cases evidence glomerulonephritic commitment, but, of these, 70% correspond to sub-clinical forms[1]. In developing nations, the incidence remains high because of the following factors: overcrowding, poor hygienic conditions, low socio-economic levels, relative inaccessibility to treatment.

## CLINICAL CASE

Male patient at 2 years and 7 months of age brought to emergency service per clinical evidence of 15-day evolution consisting of hyaline rhynorrhea and non-emetogenic wet cough, accompanied by fever between 39-40°C, for which he was prescribed amoxicillin at a local pharmacy, leading to diminished fever. Four days prior to admission, there is edema of lower limbs and «coca-cola» colored urine, generalized paleness, and icteric sclerae dye, for which care was sought at a local health center where he was remitted to this institution with the following clinical impression: 1. pneumonia 2. hematuria on study, and 3. nephritic syndrome.

***Perinatal antecedents.*** Product of the fourth pregnancy of mother G: 4 P: 3 A: 1 C: 0, institutional vaginal birth without complications. Psychomotor development: normal. Maternal breastfeeding up to one year of age and weaning at 6 months with mashed potatoes and soups. Complete vaccination (with vaccine records). Pathologies: impetigo 2 weeks ago. Family antecedents: asthma (brother). Physical exam upon admission: weight: 14 kg ($60^{th}$ percentile), SC: 0.6, height: 89 cm ($75^{th}$ percentile), Fc: 100/min, Fr: 34/min. BP: 90/60 (systolic blood pressure: $50^{th}$ percentile and diastolic blood pressure: $90^{th}$ percentile). T: 37.2°C. Jaundice in sclerae, non-toxic, good general status, normocephalic, mobile neck without masses. Symmetrical thorax without retractions and with diminished vesicular murmur in the right pulmonary field, absence of crackles, with mobilization of secretions in both pulmonary fields, and with rhythmic cardiac sounds without murmurs. Abdomen: soft, depressible with hepatomegaly at 3 cm from the right costal border, without splenomegaly. Extremities: hypochromic spots, possible stigma of pyodermatitis, first-degree soft edema in lower limbs, pulse present. Neurological: without motor deficit or apparent sensitivity.

***Clinical impression reveals.*** 1. Nephritic syndrome secondary to: A. Pyodermatitis. B. Right side pneumonia. C. Viral hepatitis. The following clinical exams were done: hemoglobin: 7.7 g%; hematocrit: 24%; leucocytes: 8300 x $mm^3$; neutrophils: 39%; lymphocytes: 58%; eosinophils: 3%. Platelets: 452.000/$mm^3$ (N: 150.000-450.000/$mm^3$). TP: 13.4 s. (N: 12 s.). TTP: 27 s. (N: 30 s.). Urinalysis: color: intense amber, aspect: turbid, Ph: 6, density: 1.025 (1.010-1.030), albumin: negative, glucose: negative, bilirubin: +++, urobilinogen: normal, hemoglobin: ++, bacteria: ++, leucocytes: 7-10 xc, erythrocytes: 17-20 xc, WBC casts: 0-2 xc. Urinary red blood cell morphology: eumorphics: 40%, dysmorphics: 60%. ESP: red blood cells: moderate hypochromia, moderate anisocytosis, scarce macrocytes, X microcytes, moderate poikilocytosis, XX anulocytes, white blood cells and platelets: normal in number and morphology. Reticulocytes: 1.8%. Ionogram: sodium: 137 mmol/l (N: 135-145 mmol/l), chloride: 112 mmol/l (N: 95-108 mmol/l), potassium: 4.2 mmol/l (N: 3.6-5.5 mmol/l). Creatinine: 1.46 mg/dl (N: 0.6-1.2 mg/dl). Blood urea nitrogen: 6.7 mg/dl (N: 7-18 mg/dl). GOT: 567.0 U/l (N: 0-40 U/l). GPT: 463.0 U/l (0-40 U/l). Total bilirubin: 4.65 mg/dl (N: <1 mg/dl). Direct bilirubin: 2.7 mg/dl (N: <0.25 mg/dl). Indirect bilirubin: 1.95 mg/dl (N: 1.95 mg/dl). Sicklemia: negative in 24 hours. Complement C3: 78.50 mg/dl (N: 90-180 mg/dl). Complement C4: 76.00 mg/dl (N: 10-40 mg/dl). Hemoglobin electrophoresis: 100% Hb $A_1$. CPK: 7 U/l (N: 24-190 U/l). Thick blood film: negative for malaria. Acs hepatitis A IgM: positive. Total abdominal ultrasound: hepatomegaly and secondary reactive cholecystitis. Thorax posterior-anterior and lateral X-ray: pneumonic infiltrate in right upper lobe.

Low-sodium diet was ordered with restriction of oral liquids (600 ml/$m^2$sc/day); hydric balance was carried out, revealing oliguria at 4 days after admission (diuresis: 0.4 ml/kg/hour), for which furosemide is administered. Antibiotic therapy was ordered (crystalline penicillin) to work on the pneumonia. The patient was hospitalized for 10 days, presenting improvement of the diuresis, non-feverish, normalized laboratory workups: nitrogen compounds, hemogram, transaminases, and bilirubin.

**Table 1**
**Causes of nephritic syndrome**

| Infectious | Not infectious |
|---|---|
| **Bacterial** | **Systemic** |
| Group A ? Hemolytic *Streptococcus* | Henoch-Schöenlein Purpura |
| *Streptococcus viridans* | Systemic Lupus |
| *Streptococcus pneumoniae* | Erythematosus |
| *Streptococcus zooepidemicus* | Membranoproliferative glomerulonephritis |
| *Staphylococcus epidermidis* | IgA nephropathy |
| *Staphylococcus aureus* | Wegener granulomatosis |
| *Brucella meningococcal* | Polyarteritis nodosa |
| *Leptospira corynebacterium* | **Others** |
| *Mycoplasma* | Medications |
| **Viral** | Toxins |
| Varicella | Antivenin |
| Rubella | Vaccines |
| Cytomegalovirus | Endogenous antigens |
| Hepatitis A, B, and C | Thyroglobulin |
| Epstein-Bar Virus | Organo-gold compounds |
| Parvovirus B19 | |
| Measles | |
| Parotitis | |
| Enterovirus | |
| **Parasitic** | |
| *Toxoplasma gondii* | |
| *Rickettsia* | |
| *Plasmodium malariae and falciparum* | |
| *Filaria* | |
| *Trichinella* | |
| **Fungical** | |
| *Coccidiodes immitis* | |

## DISCUSSION

The classical example of acute nephritic syndrome is constituted by acute post-streptococci glomerulo-nephritis. Although there are multiple causes of acute nephritic syndrome (Table 1), among the most common, after post-streptococci there are: systemic infections and Henoch-Schöenlein purpura[2,3].

The main infectious agent is the group A ? -hemolytic streptococcus (*S. pyogenes*). The serotypes keeping a relationship with pharyngeal infection are: 1, 2, 4, 6, 18, 25, and 49; the most isolated serotypes in dermal infection are: 2, 49, 55, 57, and 70. The most commonly isolated serotype in both foci is 49[2,3]. In studies carried out of epidemic outbursts, the incidence was 23.8% for coetaneous infection due to streptococci and 11.4% in pharyngeal infection due to type 12. Among other bacterial causes we may mention: *Streptococcus zooepidemicus*, *S. viridans*, *Staphylococcus aureus*, *Staphylococcus epidermicus*, *Corynebacterium*, *Mycoplasma*, *Brucela*, *Meningococci*, *Leptospira*, and *Streptococcus pneumoniae.*

***Among parasitic causes.*** *Toxoplasma gondii, Trichinella, Rickettsia, Plasmodium malariae* and *falciparum,* filaria. Mycoses: *Coccidiodes immitis.*

***Viral causes.*** The literature has mentioned the virus for varicella, rubella, cytomelovirus, parvovirus B19, Epstein-Barr virus, enterovirus, measles, parotitis, and the virus for hepatitis, as in the clinical case presented previously. Viral hepatitis is a well-recognized cause as a chronic and acute renal disease[3].

The hepatitis B virus has been related with glomerulonephritis, but it has been more associated with membranous and mesangiocapilar nephropathy[4]. The hepatitis C virus causes several forms of glomerulonephritis, including that mediated by cryoglobulinemia. There are reports in literature of the association between glomerulonephritis and virus, but cases reported with hepatitis A virus are few and rare. Acute glomerulonephritis in these patients may be only associated to hepatitis A virus or to another coincidental infection, including streptococcus, as in the patient in our clinical case, who presented prior coetaneous infection with hypochromic spots on the extremities (pyodermatitis stigma), pneumonia, hepatitis A documented with IgM antibodies for hepatitis A virus.

It is possible that the physiopathology of these rare cases of glomerulonephritis associated to hepatitis A virus infection derive immunologically from reactions similar to acute glomerulonephritis. These reactions can occur with other viral infections. The mechanisms involved in the production of the glomerular lesion associated with viral infection are diverse. The viruses may directly infect the glomerular cells and induce a cytopathogenic effect. Patient data published in literature reveal that acute glomerulonephritis may be caused by hepatitis A virus infection, as well as by other viruses. More case reports are needed in the future to determine the exact mechanism of renal disease during this infection.With respect to clinical findings, this clinical case presented: macroscopic hematuria, WBC casts with erythrocyte dysmorphism in urine at 60%, which shows the glomerular origin of the hematuria. Furthermore, oliguria was present with elevated creatinine, which required administration of furosemide; there was no evidence of proteinuria in the urine test. The edema and the oliguria presented by the patient ceased with the use of diuretics. This patient did not reveal blood hypertension, with systolic blood pressure within the 50$^{th}$ Percentile and diastolic blood pressure within the 90$^{th}$ percentile. Among hematologic manifestations, we observed moderate anemia due to possible dilutional hypervolemia. The diminished complement C3 fraction was documented. Aside from antecedents of coetaneous infection and hepatitis A viral infection, the patient reported in this revision also presented pneumonia evidenced via thoracic X-ray. Literature has reported cases of acute glomerulonephritis associated with pneumonia[5-7]. Cases have been reported with positive cultures for *S. pneumoniae*, reinforcing the concept that other microorganisms different to *S. pyogenes* can cause acute glomerulonephritis and these should be kept in mind in the differential diagnosis of any child presenting acute glomerulonephritis and respiratory manifestations.

Because of the high prevalence of pulmonary, coetaneous, and pharyngeal infections in our environment due to streptococcus and hepatitis a viral infection, these have become problematic issues in public health that can lead to a variety of renal diseases. Understanding the mechanisms of why these infectious agents can induce renal damage will permit more effective treatment strategies to revert the renal disease produced by said infections. Due to the aforementioned, studies are needed with a sufficient number of patients to analyze the main renal lesions secondary to these infectious agents and to propose management strategies to avoid the final phase of renal disease.

In conclusion, acute glomerulonephritis may be only associated to streptococcus or to another coincidental infection. Also, children with coetaneous infection, viral hepatitis, or pneumonia, who have revealed abnormalities in the urinalysis, hypertension, azotemia, or oliguria, must be evaluated to discard associated glomerulonephritis.

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