CASE REPORT

Severe hypoalphalipoproteinaemia in a child with acute post-streptococcal glomerulonephritis (APSGN)

Mohammad B Alayli, Sami A Sanjad

Department of Pediatrics,
American University of Beirut,
Beirut, Lebanon

Correspondence to
Professor Sami A Sanjad,
ss19@aub.edu.lb

SUMMARY

We describe a child with acute post-streptococcal glomerulonephritis (APSGN), who developed a very low plasma high-density lipoprotein cholesterol (α -lipoprotein) in association with transient but massive proteinuria. The hypoalphalipoproteinaemia resolved spontaneously concomitant with the remission in proteinuria and the patient had a complete clinical recovery. Urinary loss of apolipoprotein A1 may have contributed to the hypoalphalipoproteinaemia. To our knowledge, this has not been reported previously in APSGN.

BACKGROUND

Acute post-streptococcal glomerulonephritis (APSGN) is usually a disease of childhood with approximately 400 000 cases occurring annually worldwide, mostly in developing countries.¹ The prognosis is excellent with complete recovery attained in the majority of cases and less than 3% ending with irreversible renal failure or death.²⁻³ Dyslipidemia is uncommon although some patients may have a mild decrease in high-density lipoprotein cholesterol (HDL-C) and elevated total cholesterol and low-density lipoprotein cholesterol (LDL-C).³⁻⁴ We describe a child presenting with APSGN, with transient but massive proteinuria and a very low plasma HDL-C (α -lipoprotein) concentration. Severe hypoalphalipoproteinaemia has not been noted in previously described cases.

CASE PRESENTATION

A 3-year-old boy presented to the hospital with a 3-day history of fever, decreased activity and poor food intake. One day prior to presentation, he developed periorbital swelling and brown urine. There was no history of antecedent sore throat, cough, arthralgias or skin rash. On physical examination he was normotensive with a heart rate of 127 bpm, respiratory rate 24 breaths/min. His weight was 15 kg. He had periorbital and pretibial oedema but no ascites or scrotal swelling. The rest of the examinations including heart, lungs and abdomen were normal.

INVESTIGATIONS

Laboratory studies revealed a mild normocytic anaemia and a normal platelet count. Blood urea nitrogen was 14 mg/dL, creatinine 0.4 mg/dL. Electrolytes and liver function studies were normal. Total serum proteins 62 g/L and albumin 36 g/L. C3 concentration was very low at 0.1 g/L (normal 0.9–1.6). C4 was normal. Total cholesterol 116 mg/dL

(normal <200), LDL-C 57 mg/dL (normal <100), HDL-C 10 mg/dL (normal >40) and triglycerides 270 mg/dL, chol/HDL 10.55. Apolipoprotein (Apo) A1 level 0.63 g/L (normal >1.3 g/L), Apo B 0.82 g/L (normal). ASO titre was 400 units (normal <200 units). Urinalysis showed 2+ protein, numerous red blood cells, white blood cells and granular casts. Urine culture was sterile. Spot urine protein was 2.1 g/L with a protein/creatinine ratio of 7.2 (mg/mg) indicating massive proteinuria (normal <0.2).

DIFFERENTIAL DIAGNOSIS

The clinical presentation with generalised oedema, the subsequent hypertension, the elevated ASO titre and, most significantly, the very low C3 concentration which returned to normal value after 4 weeks (from 0.1 to 1.2 g/L) is characteristic, if not diagnostic of APSGN.

OUTCOME AND FOLLOW-UP

The hospital course was complicated by hypertension of 140/110 mm Hg which responded to a low sodium diet and a thiazide diuretic with a resulting weight loss of 1.4 kg and a blood pressure of 117/60 mm Hg. One week following hospital discharge, urinalysis was negative for protein; microscopic haematuria and granular casts were persistent. Spot urine protein/creatinine, 0.25 (mg/mg). Total serum proteins 75 g/L, albumin 44 g/L, LDL-C 181 mg/dL, HDL-C 57 mg/dL, total cholesterol 264 mg/dL and triglycerides 128 mg/dL. Four weeks later total cholesterol was 130 mg/dL, LDL-C 70 mg/dL and HDL-C 43 mg/dL. C3 rose to a normal value of 1.2 g/dL.

DISCUSSION

APSGN is typically preceded by group A, B-haemolytic streptococcal pharyngeal or skin infections but as many 30–40% of patients may have no antecedent history of an antecedent streptococcal infection³ as was the case with our patient. The disease is characterised by the abrupt onset of gross haematuria, oedema and hypertension within 7–28 days from the original infection.¹⁻² In addition to those symptoms, our patient had significant dyslipidemia characterised by marked reduction in HDL-C concentration, increased triglyceride with normal total cholesterol and LDL-C at presentation. These findings were coincident with transient, but massive proteinuria. Nephrotic range proteinuria may be seen in adults but is unusual in children with APSGN. Abnormal lipid metabolism is common in patients with heavy

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proteinuria and typically comprises increased triglycerides, total cholesterol and LDL-C with normal or slightly decreased HDL-C concentrations.⁴ The hyperlipidaemia is due to increased hepatic synthesis and decreased catabolism^{5 6} and is caused, at least in part, by the decrease in plasma oncotic pressure associated with hypoproteinaemia. This could not be the explanation in our patient since his serum albumin remained in the normal range. The very low concentration of HDL-C was probably secondary to urinary losses, which may have triggered the subsequent rise in cholesterol and LDL-C. This has been demonstrated in experimental models of nephrotic syndrome where high-density lipoproteinuria has been implicated in the pathogenesis of dyslipidemia.⁷ The preferential loss of Apo A1 in the urine might be explained by its relatively low molecular mass of 28 kDa compared to that of albumin which is 67 kDa.⁸ Our patient had a low Apo A1 of 0.63 g/L. The latter is the major structural component of HDL-C contributing to about 65% of its protein composition and plays an important role in lecithin cholesterol acyltransferase activation and the mobilisation of lipids from peripheral tissues.

In most patients with proteinuric renal diseases the lipid abnormalities resolve with spontaneous or steroid induced remission. However, the hyperlipidaemia may become persistent in refractory cases and medical intervention may be needed. In such children statins have been found to be safe and effective in and lowered plasma total cholesterol and LDL-C levels by 44%.⁹ The very low HDL-C as well as the low Apo A1 in our patient raised the possibility of primary disorders associated with hypoalphalipoproteinaemia such as familial hypoalphalipoproteinaemia, and, less likely, Tangier disease, both associated with deficiency in ATP binding cassette A, a cell membrane protein that mediates the transfer of cholesterol and phospholipids from cells to the Apos of lipid-poor HDL-C.¹⁰ Lecithin cholesterol acyltransferase deficiency should also be considered in the differential diagnosis of hypoalphalipoproteinaemia. However, since 2 weeks from presentation the patient's HDL-C had returned to normal levels, all these possibilities were ruled out.

Summing up, our patient presented an atypical clinical picture for APSGN characterised by massive, but transient, proteinuria in association with severe hypoalphalipoproteinaemia which returned to normal subsequently. Since a lipid profile is not obtained routinely in children with APSGN, it is important to

be aware of this unusual and interesting finding, particularly in patients manifesting heavy proteinuria.

Learning points

- ▶ Acute post-streptococcal glomerulonephritis (APSGN) may occur without the classical antecedent streptococcal pharyngeal or skin infection.
- ▶ Massive proteinuria, though rare, may occur in some patients with APSGN.
- ▶ Severe hypoalphalipoproteinaemia in APSGN may be secondary to the urinary losses but if persistent, primary causes need to be ruled out.

Contributors MBA was directly involved in the care of the patient presented. He wrote the first draft of the manuscript which was subsequently edited by the corresponding author SAS.

Competing interests None.

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