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ORIGINAL ARTICLE

Acute post-streptococcal glomerulonephritis in children of French Polynesia: a 3-year retrospective study

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Abstract The aim of this study was to define the current demographic, clinical and prognostic characteristics of acute post-streptococcal glomerulonephritis (APSGN) in French Polynesia and to compare these features with those of other populations. Fifty children, all of whom were <15 years old and had been admitted to the Territorial Hospital of Papeete for APSGN between January 2005 and December 2007, were retrospectively enrolled in the study. Diagnostic criteria were microscopic or macroscopic haematuria, decreased C3 fraction of the complement and evidence of recent streptococcal infection. The annual incidence was 18 cases per 100,000 children <15 years of age in 2007. Most of the children (98%) enrolled in the study were of Polynesian ethnic origin, 27 were male (54%), and the average age at presentation was 6.7 years. Signs of previous respiratory infections were clearly evident in 40% of the children. Most of the patients presented during the rainy season, correlating with the relatively high incidence of skin infections at this time. The majority of patients had proteinuria (98%), with 25% having proteinuria in the nephrotic range (proteinuria/urinary creatinine >3 g/g). The presentation was severe in 22% of the children (congestive cardiac failure, severe hypertension and/or encephalopathy), and renal failure was an initial presenting symptom in 43.7%. The C3 fraction was lower in severe presentations, but the type of haematuria, level of proteinuria and inflammatory syndrome were not correlated with immediate severe forms or with initial renal failure. Haematuria resolved in a mean of 7.7 months and proteinuria in a mean of 3.9 months. None of the children had hypocomplementemia for more than 8 weeks. Acute post-streptococcal glomerulonephritis is endemic among French Polynesians, and they can be considered to be a high-risk population. Despite a high incidence of skin infections, however, the predominance of respiratory infections potentially indicates that French Polynesia is on the way to become a low-incidence area. Systematic detection and treatment of group A *Streptococcus* should be intensified.

Keywords Group A beta-haemolytic Streptococcus · Streptococcal infection

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Introduction

Group A beta-haemolytic *Streptococcus* (GAS) is the most common infectious agent responsible for acute glomerulonephritis in children, but other infectious agents and other *Streptococci* can be involved, such as *Streptococcus pneumoniae* [1] and Lancefield group G and C *Streptococci* (*S. zooepidermicus*) [2]. Over 470,000 cases of acute post-streptococcal glomerulonephritis (APSGN) occur annually, leading to approximately 5000 deaths; 97% of these cases occur in less well-developed countries [3]. As in numerous tropical areas, APSGN is endemic in French Polynesia. The aim of the study reported here was to evaluate epidemio-

logical, clinical, biological and evolutive features of this disease in French Polynesia and to compare these features with other endemic or low-incidence populations.

Patients and methods

Hospital records of children <15 years of age who had been admitted for APSGN to Territorial Papeete's Hospital in French Polynesia between January 2005 and December 2007 were reviewed. Diagnostic criteria for APSGN were microscopic or macroscopic haematuria (with or without proteinuria), decreased C3 fraction of the complement and evidence of recent streptococcal infection. Recent streptococcal infection was established by the presence of elevated anti-streptococcal antibody titres [anti-streptolysin O (ASO), antideoxyribonuclease B (ADNaseB)] relative to the limits established by the local laboratories. ADNaseB levels were considered to be abnormal when the values were >120 UI/ml in pre-school children and >340 UI/ml in school-aged children. Anti-streptolysin O was considered to be elevated at levels >200 UI/ml. Epidemiological data, clinical features, investigations, treatment and outcome were recorded at the onset of the hospitalization period, at the end or at the seventh day of hospitalization and at the latest medical follow-up consultation.

Quantitative values were expressed as means and standard deviations (SD) and qualitative values as percentages. The non-parametric Mann–Whitney and Fisher exact tests were used to assess significance. P values <0.05 were considered to be statistically significant.

Results

During the 3-year period covered by the study, 50 children presented APSGN in accordance to the inclusion criteria: 22 cases in 2005, 16 cases in 2006 and 12 cases in 2007. The demographic data on this patient cohort are presented in Table 1. There were slightly more males than females (54 vs. 46%), and the mean ages of the children was 6.7± 2.9 years. Most children were between 4 and 6 years old (52%). The majority of children came from Tahiti (70%); the others came from Pacific Islands administratively dependent on Papeete, with the exception of one patient who was not of Polynesian ethnicity, but Caucasian. Most of the patients (60%) were diagnosed during the rainy season (from November to May). To evaluate the importance of overcrowding at home in the dissemination of streptococcal infections, we reviewed the number of persons living in the same house of an ill child. Based on the 18 patients (32%) for whom this information was available, the number of people per house was 6.6±2.5.

Table 1 Demographic data of children with acute post-streptococcal glomerulonephritis

Demographics	*n*	Percentage of patient cohort
Sex		
Male	27	54
Female	23	46
Ethnicity		
Polynesian	49	98
Caucasian	1	2
Island		
Tahiti	35	70
Moorea	2	4
Iles Sous le Vent	4	8
Tuamotu	2	4
Australes	7	14
Season		
Rainy	30	60
Dry	20	40
Mean age, years (mean ± SD)	6.7±2.9	
Persons in the same house (18 available values), *n* (mean ± SD)	6.6±2.5	

SD, Standard deviation

Of the 50 patients, two had presented with APSGN 1 and 2 years previously, respectively, one of whom had been dialysed for 10 days at the time. A summary of the data on the clinical presentations of the patient cohort is given in Table 2. Of the 50 children, 37 (74%) had a known recent history of streptococcal infection: ten (20%) skin infections (excoriations, impetigo, erysipelas or pyoderma), 15 (30%) upper respiratory tract infections, five (10%) pulmonary infections and seven (14%) associations of the upper respiratory tract and skin infections concurrently. The delay between the streptococcal infection and the first symptoms of APSGN was 9.2±8.4 days for the respiratory infections and 9.5±4.2 days for the skin infections. The most common reason for consultation was fever (30/50, 60%), but abdominal symptoms (such as abdominal pain, nausea, vomiting) were not rare (10/50, 20%). Only 14% (7/50) of patients showed direct signs of APSGN (such as macroscopic haematuria, oedema, hypertension and oliguria). Arterial hypertension was observed in 32/50 (64%) children, with severe hypertension (arterial pressure over the 97.5th percentile plus 30 mmHg) present in four of these [4]. Eleven patients (22%) had severe presenting symptoms (congestive cardiac failure, severe hypertension and/or encephalopathy) at admission. Mild renal failure [glomerular filtration rate (GFR) <80 ml/min per 1.73 m^2, determined with the Schwartz Formula] was present at

Table 2 Clinical features of patients at presentation

Clinical features of patients at presentation	*n*	Percentage of patient cohort
Previous infection		
Not found	13	26
Skin only	10	20
Upper respiratory tract only	15	30
Skin and respiratory tract	7	14
Pulmonary	5	10
Reason for consultation		
Fever	30	60
Abdominal symptoms	10	20
Direct symptoms of APSGN	7	14
Complications of APSGN	3	6
Haematuria		
Macroscopic	32	64
Microscopic	18	36
Proteinuria		
All kinds of proteinuria	49	98
Nephrotic syndrome	12	25
Oedema	33	66
Arterial hypertension		
All kinds of hypertension	32	64
Systolodiastolic hypertension	25	50
Diastolic hypertension	7	14
Severe hypertension	4	8
Oliguria	9	18
Dyspnea	9	18
Cardiac failure	7	14
Seizure	2	4
Severe presentation (cardiac failure, severe hypertension±encephalopathy)	11	22
Delay between streptococcal infection and symptoms, days (mean ± SD)		
Respiratory infection	9.2±8.4	
Skin infection	9.5±4.2	
Duration of hospitalization	7.2±3	

APSGN, Acute post-streptococcal glomerulonephritis

admission in 43.7% (14/32 available values) of the children, but no anuria was reported. Thirty-five children had creatinine values above the normal level for the age (>60 μmol/l for children between 2 and 8 years, and >80 μmol/l for children >8 years): mean 71±24.8 μmol/l for children <8 years and 90.5±37.9 μmol/l for children >8 years. Proteinuria was nephrotic (proteinuria/urinary creatinine >3 g/g) in 25% (12/50) of the children, and C-reactive protein was increased in 59.2% (peak mean value of 61 mg/l).

At first measurement, there were increased titres of ASO in 76.3% patients and of ADNaseB in 97.3%. The C3 fraction was decreased in 90% of children (45/50), with the five normal values explained by the delay in making the assessment (10–30 days after the onset of the disease). The type of haematuria, level of proteinuria and inflammatory syndrome were not correlated with immediate severe forms nor with initial renal failure, but the C3 level was correlated to the severity of the disease (Table 3).

Transthoracic echocardiography revealed a dilatation of the left cavity with a functional mitral insufficiency in seven children (14%). Cerebral exploration (computed tomography scan or magnetic resonance imaging) was performed for the two children with hypertensive encephalopathy, revealing cerebral oedema in one patient. A biopsy was performed in a patient presenting with heavy nephrotic proteinuria that lasted for more than 1 week. Histology confirmed the diagnosis of APSGN, showing endocapillary proliferation without any crescent and immunoglobulin (Ig)G and C3 fraction deposits.

The initial evolution was assessed using data collected on the seventh day of hospitalization or at the end the patient's stay in the hospital (mean 6.7 days after admission). At these times, oedema had resolved in 91% (30/33) and hypertension in 98% of cases (31/32). A diuretic therapy (furosemide) had been prescribed for 33/50 children (66%) for a mean of 4.7±2.8 days, and a second anti-hypertensive treatment (nicardipine) had been given to 17/50 (34%) of children for a mean of 4.9±0.1 days. Proteinuria was still positive in 72% (36/50) of the children, and microscopic or macroscopic haematuria was still present in all of the cases. Antibiotics had been given to 98% (49/50) of children, with 28% (14/50) receiving penicillin V and 70% (35/50) receiving another penicillin, mainly amoxicillin.

Children were followed up for a mean period of 5 months (range 0.16–16.1 months), until macroscopic haematuria, proteinuria, hypocomplementemia and renal impairment resolved. No evolutive data were available for seven children lost to follow-up; a large number of the remaining patients presented to the clinics only during the period of clinical symptoms. Haematuria resolved in 7.7±5.7 months (range 0.5–16.1 months) and proteinuria in 3.9±4.7 months (range 0.25–16.1 months). No children had prolonged hypocomplementemia, oedema or high blood pressure during the follow-up. At the last consultation written up in the medical records, all children had normal or slightly elevated (<10%) creatinine value for the age [5].

Discussion

The burden of APSGN is known to be tenfold higher in the children of the Pacific Islands than in their European

Table 3 Effect of the type of haematuria, proteinuria, C3 level and C-reactive protein on the severity of the clinical presentation[a]

Variables	Severe forms	Non severe forms	*p*
Number of cases	11	39	
Macroscopic haematuria	7/11	25/39	0.7
Proteinuria/creatininuria, g/g (mean ±SD)	3.4±2.7 (7/11 available values)	5.4±4.5 (25/39 available values)	0.66
C3 fraction (g/l)	0.2±0.1	0.4±0.4	0.02
CRP (mg/l)	74.5±82.7 (5/11 available values)	60±54 (32/39 available values)	0.86

CRP, C-reactive protein

[a] Severe presentation: congestive cardiac failure, severe hypertension ± encephalopathy

counterparts [6, 7], with the incidence in 2007 being 18 cases per 100,000 children <15 years (data obtained from the census of the population in 2007). The incidence calculated in our study was probably underestimated because many cases are asymptomatic [8–10] and the children referred to the two private hospitals of Papeete were not included in our patient cohort. The reasons for this endemic high incidence of APSGN in French Polynesia are: a larger percentage of children < 15 years of age (26% in 2007) compared to European countries (18% in France in 2007), a high frequency of bacterial infections explained by climatic conditions, home overcrowding (number of people per house in France = 2.1 [11] compared to 3.2 in French Polynesia [12] and 6.6 in the families of the ill children in our study), low social economic level, reduced accessibility to medical care because of geographic conditions and cultural habits (not consulting a medical doctor for minor symptoms). With the symptoms of pharyngitis resolving in 4 days without antibiotics, a lot of untreated streptococcal infections can cause non-suppurative complications [7]. This may explain the particularly strong incidence of APSGN in the Australes Islands (a mean of 133 annual cases per 100,000 children <15 years of age between 2005 and 2007), which are located a long distance from Tahiti (>500 km).

Seasonal incidence variations are usually described in terms of the type of previous infection(s) and to the endemic or sporadic status of the area. In high-incidence or endemic countries, the previous infection is more often skin infection occurring during the rainy season (i.e. October in Morocco [13] and April to June in New Zealand and Chile [8, 14]. In sporadic incidence countries, as in Europe, the previous infection is more often pharyngitis, and APSGN is most prevalent between December and April [15]. Our data follow most closely the pattern of high-incidence, endemic areas [14, 16]: high incidence of APSGN in the rainy season November to May; 30/50 cases (60%) correlated with a high incidence of skin infections during this period (8/10 cases). However, contrary to high-incidence populations, respiratory tract infections were predominant in our study (20/50 cases). This predominance could due to missing information in medical records (no previous infection found for 13/50 patients) or be the first sign of an epidemiologic evolution from endemic to sporadic pattern area, as has been described for many other countries [17, 18]. Scarlet fever, oral abscess, sinusitis and even pneumonia can also cause APSGN [3, 19–23], with increases in ASO [3, 21]. In our study, five children had pneumonia before being diagnosed with APSGN. Even though it is not rare not to find any previous infection to explain the APSGN [24, 25], in our study 26% (13/50) of the children had no skin or respiratory infection before the illness. The same proportions were observed by Blyth et al. in an Australian cohort [26].

Serologic evidence of a recent streptococcal infection is known to be more sensitive than the history of recent infection or positive cultures [27]. The ASO level is elevated less often in acute glomerulonephritis following streptococcal skin infections [25, 28]. In our study, we found increased ASO titres in 74% of all the children and in only 60% of the ones with skin infection. In contrast, the ADNaseB titer increased in a larger number of patients (97%), irrespective of the nature of the preceding streptococcal disease (100% if skin infections, 90.9% if respiratory infections). Therefore, in French Polynesia, where 34% of APSGN cases are caused by skin infections, the two serologic measurements are preferable as a diagnostic tool, as also shown by Blyth et al. [29].

The classical presentation of APSGN is acute nephritic syndrome. However, as reported in the literature [15], the presence of all of the symptoms at the same time (oedema, macroscopic haematuria, hypertension, oliguria) was not frequent among our patient cohort (only 2/50). In five children (10%), the only sign was microscopic haematuria, and five other children were asymptomatic. More severe clinical presentations (congestive cardiac failure, severe arterial hypertension, and/or encephalopathy) were observed in the same proportions as in other endemic areas [14, 26]. The level of the C3 fraction of complement was lower in these severe clinical presentations (0.2±0.1 vs. 0.4±0.4 g/l in non-severe forms, p=0.02), but not in patients with initial renal failure (Table 3). Blyth et al. also

found that the C3 level had no effect on the initial plasma creatinine levels [26]. C-reactive protein, proteinuria and macroscopic haematuria did not correlate with clinical severe forms or with initial renal failure, as has also been reported in the literature [30, 31]. The only patient without proteinuria presented with congestive cardiac failure.

There is no simple treatment for APSGN, and the prevention of streptococcal infections remains the most important control strategy. In our study, penicillin was used in 98% of children to eradicate the GAS carriage. This antibiotic may limit the spread of nephritogenic strains and prevent recurrences. Two children (4%) in our study had an antecedent of APSGN within the 2 years preceding admission to hospital for APSGN. The literature reports recurrences of 0.7–7% [8, 32]. The exact physiological mechanisms that cause recurrences remain unclear. The suppression of immune responses against nephritogenic streptococcal strains due to early penicillin therapy and the absence of a natural immune response against nephritis-associated plasmin receptor (NAPLr) or other streptococcal antigens have been suggested [32].

Conclusion

The limitations to our study are those generally associated with retrospective studies, such as difficulties in finding accurate data in the medical records. Acute post-streptococcal glomerulonephritis is still endemic in some parts of the world, such as in French Polynesia. Our population had the aspects of a high-risk population, but despite a high incidence of skin infections, respiratory infections were predominant. In most cases, this disease is benign, with a good renal prognosis, but severe systemic complications are possible because of major sodium and water retention in the acute phase. The C3 level is the only predictive factor of severe forms, thus it is still difficult to predict the severity of this disease at presentation in endemic countries. Consequently, systematic urinary screening should be performed after any streptococcal infections. Our follow-up was very short, and further studies should be performed to evaluate the outcome of this disease in Polynesia. French Polynesia has to continue to fight against the infectious causal agents.

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