THE ASSOCIATION BETWEEN THALASSAEMIC DISEASES AND TRAITS AND POST-STREPTOCOCCAL ACUTE GLOMERULONEPHRITIS

P. TANPHAICHITR, P. BANCHET, B. PETCHCLAI*, P. HATHIRAT, W. SASASNAKUL, C. CHATASINGH and S. HIRANRAS*

Departments of Pediatrics and Pathology*, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand.

INTRODUCTION

In a necropsy study of 20 patients with β-thalassaemia haemoglobin-E disease, Bhamarapravati *et al.*, (1967) found mitral stenosis with Aschoff nodule in one patient. They also observed glomerular lesions associated with obvious acute glomerulonephritis in one and with haematuria and proteinuria in three. Wasi (1971), later on, described a peculiar benign percariditis in 8 patients with β-thalassaemia haemoglobin-E disease after splenectomy who had remarkably elevated antistreptolysin O (A.S.O.) titres. Significantly increased A.S.O. titres were subsequently reported among patients with thalassaemic diseases (Economidou and Constandoulakis, 1971; Sukroongreung and Wasi, 1972; Tuchinda *et al.*, 1972).

These observations of increased susceptibility to β-haemolytic streptococcal infection, especially after splenectomy among thalassaemic patients leading to higher incidences of rheumatic disease and proliferative glomerulonephritis than the normal population was claimed (Wasi, 1971; Sukroongreung and Wasi, 1972).

Our preliminary study showed that thalassaemic patients though susceptible to streptococcal infection, as evident by increased A.S.O. titres, are not, more likely to develop acute glomerulonephritis (A.G.N.) than the rest of the population (Tanphaichitr *et al.*, 1976). Thus, a comparative study was done to determine the incidence of thalassaemic diseases and traits among post-streptococcal A.G.N. cases and that of post-streptococcal acute glomerulonephritis developing among thalassaemic patients.

MATERIALS AND METHODS

The study was performed during October 1975 to May 1976 in 50 cases of post-streptococcal A.G.N. and 56 cases of thalassaemic patients. The ages ranged from 3 to 18 years in both groups.

Urinalysis was done on fresh specimens. Abnormal findings were considered when there was trace amount of blood, more than trace of protein, by labstix, and more than 3 red blood cells (RBC) per high power field (h.p.f.) of centrifuged specimens.

Detection of thalassaemic trait and diseases included haematocrit, reticulocyte count, inclusion body and RBC morphology. The blood smears were constantly read by two haematologists. Haemoglobin typing by agargel electrophoresis was performed in suspected cases.

Abnormal blood smears as evidence of thalassaemic diseases were considered when there were marked to moderate degree of anisocytosis, poikilocytosis, hypochromia, microcytosis, cell fragmentation with the presence of target cells. Mild changes of RBC morphology as above was considered as thalassaemic trait.

A.S.O. titres were performed by the method

as previously described (Petchclai *et al.*, 1973). Titres over 240 Todd units were considered high.

Thalassaemic patients: The urinalysis and A.S.O. titres were done in all cases at least 1 month after the latest blood transfusion. The urinalysis was also done twice or more in each patient, after intervals of 6 to 28 weeks. The patients had neither fever nor signs of active exudative tonsillitis and pyoderma at the time of study. The blood pressure was also recorded.

Post-streptococcal A.G.N. patients: Cases met the criteria for diagnosis as previously described (Tanphaichitr *et al.*, 1973; Meadow, 1975). The case numbers were assigned at the time of blood examination for detection of thalassaemic trait or diseases as shown in Fig. 3. Cases number; 17, 20, 22, 23, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 40, 42, 43, 44, 45, 46, 47, 48, 49 and 50 were those who developed A.G.N. during the period of study. The rest were follow up cases of varying period as shown in Fig. 3.

RESULTS

Thalassaemic patients: There were 26 out of the 56 patients (46.4%) with elevated A.S.O. titres. The elevated titres among each specific group of thalassaemic diseases are shown in Fig. 1. It can be observed from Fig. 2 that 7 out of 11 initial high A.S.O. titres remained constantly high on the second determination. Two out of 11 such patients had decreased titres to a normal range while the other 2 had higher titres on the second examination. Two out of another 15 patients as shown in Fig. 2; whose initial A.S.O. titres fell in the normal range had higher titres on the second determination. Elevated A.S.O. titres were also common among splenectomised patients with β-thalassaemic/haemoglobin-E disease (Figs. 1 and 2).

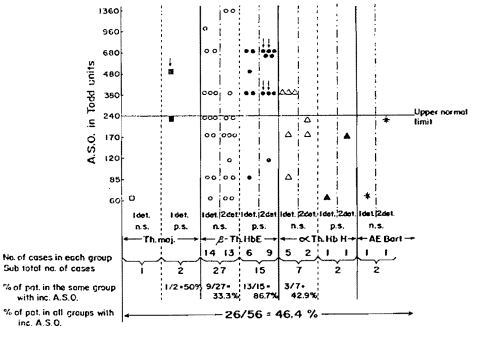

Fig. 1—A.S.O. titres in 56 patients with thalassaemia disease

1 det. = 1determination, 2 det.$^{+}$ = 2 determinations based on the first determination of Fig. 2.

↓ indicated the associated abnormal urine findings.

n.s. = nonsplenectomised patients, p.s. = postsplenectomised patients, pat. = patients.

Th. maj. = Thalassaemia major, β-Th. Hb-E = β-Thalassaemia haemoglobin-E disease, α-Th. Hb. H = α-Thalassaemia haemoglobin H disease.

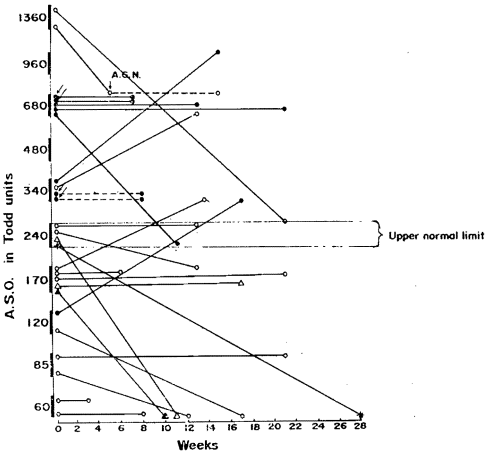

Fig. 2—A.S.O. titres in 26 patients with thalassaemic diseases determined at varying period of time. The symbols, denoting each specific group, are as in Fig. 1. The arrow indicates the patients with abnormal urine findings. The arrow and A.G.N. indicates the patient who developed typical post-streptococcal acute glomerulonephritis.

There were 5 patients (Figs. 1 and 2) who had abnormal urine findings which included trace amount of blood, trace or 1 + proteinuria by labstix. There were only 3 to 10 RBC/

h.p.f. The amount of blood and the numbers of RBC were much less than those found in typical cases of A.G.N. These patients, however, had no history of puffiness, oedema and no hypertension. The subsequent urinalysis, 7 to 8 weeks later (Fig. 2) were normal. The time lapsed for the return to normal urine findings in these patients was sooner than that among typical cases of A.G.N. which usually took 3 to 6 months (Fig. 3).

Post-streptococcal A.G.N.: There was only one nonsplenectomised out of 56 patients (1.8%) who developed typical A.G.N. (Fig. 2). The kidney biopsy revealed diffuse exudative proliferative glomerulonephritis and deposition of C3 complement and polygammaglobulin. The initial urinalysis, 5 weeks prior to the clinical manifestation of A.G.N. was normal despite the high A.S.O. titres of 1,360 Todd units. The subsequent urinalysis were still abnormal 6 months after the attack of A.G.N. The RBC were over 30/h.p.f. and the blood was 1 + to 2 + by labstix.

Patients with post-streptococcal A.G.N.: There were 12 out of 50 cases (24%) whose blood smears showed evidences of thalassaemic trait (Fig. 3). There was only one out of 50 cases (2%) whose blood smear showed evidences of thalassaemic disease (Fig. 3), and the haemoglobin electrophoresis confirmed the diagnosis of β-thalassaemic/haemoglobin-E disease.

DISCUSSION

With the previous findings that A.S.O. titres were elevated among thalassaemic patients increased susceptibility to β-haemolytic streptococcal infection leading to higher incidences of rheumatic disease and acute glomerulonephritis than the normal population seems logical (Wasi, 1971; Sukroongreung and Wasi, 1972). There was only one brief report (Economidou and Constandoulakis, 1971) of 3 cases of acute glomerulonephritis among 137 cases of homozygous β-thalassae-

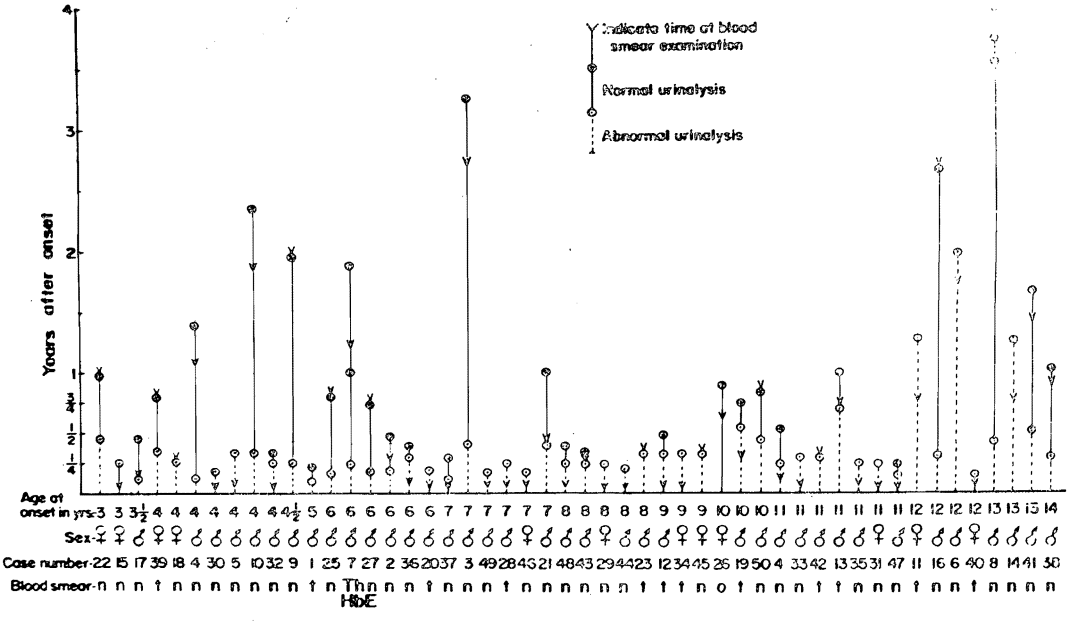

Fig. 3—The clinical course of 50 patients suffering from post-streptococcal acute glomerulonephritis. n = normal blood smear, t = thalassaemic trait, Th. Hb. E = β-thalassaemia haemoglobin-E disease.

mic Greek patients (2.2%). Fifty-eight of them, including the 3 patients with A.G.N., were splenectomised. There has been no other reports of such incidence of A.G.N.; and no single comparative study of thalassaemia among A.G.N. and vice versa until a recent report by Tanphaichitr *et al.*, 1976.

This study eventhough it consisted of 56 thalassaemic patients, smaller in number of patients that than previously studied, showed the same patterns of elevated A.S.O. titres (Economidou and Constandoulakis, 1971; Sukroongreung and Wasi, 1972; Tuchinda *et al.*, 1972). There was only one out of 56 thalassaemic patients (an incidence of 1.8%) who developed typical A.G.N. This incidence is not statistically different from that of 2.2% in Greek patients ($p > 0.05$).

There was only one out of 50 typical cases of A.G.N., an incidence of 2%, who had β-thalassaemic/haemoglobin-E disease. Such incidence is not significantly different ($p > 0.05$) from the incidence of thalassaemic diseases of 0.8% found among the general Thai population (Wasi, 1971).

The incidence of 24% of thalassaemic trait found among typical cases of A.G.N. does not exceed the 35-40% incidence (Wasi, 1971) of that found among the general Thai population.

The 5 cases of transient abnormal urine findings were clinically different from the previous report in a 5-year old black American girl (Robertson, 1972); and in a 56-year old black American woman with β-thalassaemic trait who had a more significant degree of an unknown cause of haematuria despite a normal open renal biopsy finding (Eisenstadt, 1972). We do not think that our 5 patients had subclinical A.G.N.; but more studies such as simultaneous C3 levels in addition to urinalysis and A.S.O. titres should be carried out in order to answer the unexplained transient haematuria.

SUMMARY

This prospective study showed that thalassaemic patients, though susceptible to streptococcal infection, as evident from their elevated A.S.O. titres, are not, as has been suggested, more likely to develop acute glomerulonephritis than the rest of the population. The incidence of thalassaemic trait found among typical cases of acute glomerulonephritis does not exceed that of the general Thai population. There were 5 out of 56 cases of thalassaemic patients having transient microscopic haematuria.

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