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Renal Amyloidosis as A Complication of Familial Mediterranean Fever in Children

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Familial Mediterranean Fever is a genetic disease transmitted as a complete autosomal recessive gene. The clinical condition presents itself by recurrent febrile attacks associated with abdominal pain, joint manifestations, and, in some cases, erythemetous skin rashes and chest pain. Patients are asymptomatic between attacks. Renal amyloidosis is one of the severe complications of this disease which causes progressive renal destruction ending with uremia and death.

Forty-five renal amyloidosis cases were observed in Children's Hospital of Hacettepe, Ankara in a period of 10 years. Amyloidosis was proved by renal biopsies. A significant number of these cases failed to show full characteristics of FMF.

Commonly, renal amyloidosis has been attributed secondary to several conditions (Hodgkin's disease, tuberculosis, rheumatoid arthritis, macroglobulinemia, immunologic defects, familial Mediteranean fever, etc). The renal amyloidosis cases reported before 1950's were mostly secondary to tuberculosis and suppurative diseases.[1] [2] Because of the worldwide use of antibacterial treatment during the last 20 years, the number of renal amyloidosis cases secondary to tuberculosis, and long standing suppurative organ diseases were significantly decreased.

However, application of subcutaneous renal biopsies and increased knowledge ot FMF during the last two decades unveiled causes of renal amyloidosis other than tuberculosis and suppurative organ diseases.

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Straus[3] indicated that 43 % of rheumatoid arthritis, 39 % of FMF and chronic suppurative diseases were complicated with amyloidosis in childhood. Cohen[4] reviewed 400 cases of amyloidosis and found that FMF was responsible in 40 % of the cases. Heller et al[5], Sohar et al[6 7 8] analyzed a large number of amyloidosis cases and found thata significant number of them were related to FMF. It is a well known fact that FMF is more frequently seen in Armenians, Jews, Arabs and Turks. However, isolated cases have been reported from other ethnic groups.[9 10 11] First probable case of FMF in the Turkish literature was published, by Marmarali[12] under the title of "a peculiar abdominal syndrome," in 1946. This was followed by the publications of other Turkish author's.[13 14 15 16] Sohar et al[6] reported amyloidosis as the sole anatomical finding with no other manifestations of FMF. These authors divided amyloidosis secondary to FMF into two groups:

1. FMF phenotype I, in which clinical attacks preceded amyloidosis.

2. FMF phenotype II, amyloidosis as a sole manifestation of the disease or amyloidosis preceded febrile attacks.

In this paper we aim to present renal amyloidosis related to FMF with a special emphasis on phenotype II.

Material

Forty five cases of renal amyloidosis have been evaluated at Hacettepe Children's Hospital during the last ten years (1961-1971). Diagnosis of renal amyloidosis in these cases have been proved by subcutaneous renal biopsies. The charts of these patients were reviewed with regard to history, family history, laboratory and X-Ray findings. Predisposing factors were also searched. All biopsies were stained with Hemotoxylen-Eosin, PAS and Gention violet.

Results

The cases were divided on clinical grounds into two groups:

1. Patients who showed febrile attacks before renal symptoms.

2. Patients who did not show any evidence of febrile attacks before renal symptoms. (Table I).

There were slight to marked anemia in 25 patients. Erythrocyte sedimentation rates were accelerated in all cases. Protein electrophoresis was examined in 15 cases all of which showed elevated alfa-2 fraction. Plasma urea was elevated in (17/45) patients. Plasma cholesterol levels

TABLE I

BREAKDOWN OF 45 CASES OF RENAL AMYLOIDOSIS

Group	Number
1. Febrile attacks preceded renal amyloidosis	28
2. Renal amyloidosis not preceded febrile attacks	17

were elevated in all cases except three. Clinical findings and age groups are summarized in Table II and Table III. Breakdown of 45 patients according to their clinical manifestations are summarized in Table IV. We were able to keep close contact with the parents of 15 patients. Three of our patients died in hospital. Two patients were followed in out-patient clinics. Eight patients died at home and two were reported by their parents to be in satisfactory condition. At the time this article was prepared, as far as we could find, only one patient out of fifteen had passed the adolescent age, and died when she was 22 years old. She was a girl who had showed symptoms of FMF at the age of 6 and renal symptoms at the age of 18 years. There was also family history of chronic renal failure and death in 3 cases but none of them had renal biopsies.

None of the forty-five patients showed any clinical evidence of suppurative disease or neoplastic diseases. Only one case had Kala-azar, which may very well be a coincidence with renal amyloidosis.

TABLE II

BREAKDOWN OF 45 PATIENTS ACCORDING TO AGE GROUPS

Years	Number	Female	Male
6–12	27	11	16
13–20	18	6	12
Total	45	17	28

TABLE III

BREAK-DOWN OF 45 CASES ACCORDING TO CLINICAL FINDINGS

	Abdominal pain	Joint manifestations	Temperature clavations prior to renal symptoms	Elevated Blood Pressure (minimal) over 90 mm/Hg	Pitting Oedema	Hepatomegaly	Splenomegaly
Number of the cases	27	13	28	4	42	21	4

TABLE IV

BREAKDOWN OF 45 PATIENTS ACCORDING TO THEIR CLINICAL MANIFESTATIONS

	Number of cases	
Fever and joint manifestations and Abdominal pain	9	28 (62,2 %)
Fever (only)	7	
Fever and abdominal pain	11	
Fever and joint pain	1	
Abdominal pain (only)	5	17 (37,7 %)
Joint pain (only)	1	
Joint pain and abdominal pain	2	
No clinical manifestations Prior to renal symptoms	9	

Discussion

Renal amyloidosis in Turkish children is not very rare, but number of publications are not extansive. A large number of cases presented in this article (17/45) did not show temperature elevations prior to the renal amyloidosis. Many of them, however, gave the history of vague abdominal discomfort or pain and some presented a history of joint manifestations during the course of the disease. This may suggest that FMF does not show itself in each case with typical manifestations, before the emergence of renal complication. Primary amyloidosis is practically not seen in childhood. Majority of cases are secondary to a variety of conditions. Some of the cases which have been analyzed in this paper showed full blown symptoms of FMF (9 cases), some showed vague symptoms of abdominal discomfort (5 cases) or joint complaints (one case) and the others did not indicate any symptoms whatsoever to be related to FMF (9 cases). However, a total 28 patients showed temperature elevations prior to renal symptoms.

Renal amyloidosis secondary to FMF shows typical findings of nephrotic syndrome. Blood urea and blood pressure remains within normal limits until renal pathology progresses to chronic renal insufficiency. Our observations indicate that renal symptoms of amyloidosis become apparent around the school age period and disease progress to renal failure and death before second decade ensues.

Conclusion

1. Renal amyloidosis secondary to FMF is not very rare among Turkish children.

2. Significant number of children who have renal amyloidosis secondary to FMF do not show cardinal symptoms of FMF before renal complication.

3. Majority of the patients show symptoms of renal complication after the age of 6 years and succumb to death before the adolescent period ends.

4. Males appear to be more prone than females to renal complication of FMF.

Summary

Familial Mediterranean fever is not very rare among Turkish children.

Renal amyloidosis is a severe complication of familial Mediterranean fever which usually causes renal failure and death during adolescent period.

Forthy-five cases of renal amyloidosis, obsorved in a 10 year survey, all of wich proved by subcutaneous renal biopsies, were presented. Nine patients showed full characteristic features of familial Mediterranean fever. Fever preceded amyloidosis in 7 cases, abdominal pain and fever in 11, fever and joint pain in 1, abdominal pain only in 5, joint pain and abdominal pain in 2 and joint pain in only 1. The remaining nine patients did not show any clinical manifestations of FMF.

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