AMYLOID IN JUVENILE ARTHRITIS. DO WE STILL NEED TO WORRY

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Abstract:
The long term complications of rheumatologic diseases are fortunately becoming rare with the advent of better diagnostic and disease modification strategies in current clinical practice. We present a young female with renal amyloidosis following juvenile idiopathic arthritis of polyarticular type.

Keyword: Juvenile arthritis, renal amyloidosis, polyarticular arthritis

Introduction:
Secondary amyloidosis used to be one of the fatal complications of JIA especially systemic and polyarticular type. Prevalence of secondary amyloidosis in JIA is 1-10% and the risk is due to long lasting inflammation. Mortality was identified in girls who had onset of arthritis early in life. After 15 years of arthritis, the frequency of amyloid increases to 7.4%. It rarely occurs as early as one year after onset of arthritis but could develop as late as 23 years after onset.

Case report
A 22 year old female, who was a known case of polyarticular type of JIA, on poor treatment compliance, of disease duration 10 years, presented to us with complaints of joints pain and swelling and swollen lower limbs for past 3 months. The lower limb swelling worsened for past one week with associated abdominal pain. She also complained of breathlessness on exertion (NYHA class 2). She had no history of chest pain, decreased urine output or fever. She was non diabetic and non hypertensive. On the day of admission, her physical examination revealed bipedal pitting edema, peri orbital edema, pallor and sinus tachycardia. Recorded blood pressure was 96/70mmHg. On auscultating respiratory system, there was diminished breath sound on the right base with no added sounds. Her abdomen was distended with demonstrable free fluid. Her musculoskeletal examination showed symmetrical polyarthritis of small and large joints of both upper and lower limbs with flexion deformity of MCP joints and swan neck deformity of fingers. She also had halux valgus on both sides.
Clinical Examination:
Her haemoglobin was 8.6g/dl, TLC 5100, platelets 1.2 lakhs, ESR 160mm/hr. Blood urea and serum creatinine were 24 and 0.9mg respectively. Total bilirubin was 0.9mg/dl and serum albumin 2.9 g/dl. SGOT, SGPT and SAP were within normal limits. Total cholesterol was 280mg/dl. Urine routine showed 4+ albumin with no deposits. Urine PCR was 1.45. RF 320 IU/ml, CRP 28mg/dl. Chest X ray was normal. Ultra sonogram abdomen reported normal sized kidneys with bilateral increased renal echoes, chronic medical renal disease and minimal free fluid in abdominal cavity and both pleural spaces.

ECHO was normal. Ophthalmic examination proved no uveitis. Nephrologist opinion was sought. Renal biopsy was done and acellular amorphous deposits in mesangium and blood vessels were made out. They were positive with Congo Red stain, giving an apple green birefringence under polarised light. Diagnosis of renal amyloidosis was made.

Sections showing histopathology of renal biopsy tissue stained with haematoxylin and eosin. Both viewed under 40X magnification. Figure A shows three glomeruli with acellular amorphous deposits in the mesangium. Similar deposits are seen in blood vessels. Figure B shows glomerulus and renal tubules with acellular amorphous deposits.

Discussion:
JIA is the most common rheumatic disease of childhood. RF positive polyarthritis is defined by ILAR criteria as arthritis cumulatively affecting 5 or more joints during the first six months, in the presence of two positive tests of RF performed at least 3 months apart. In addition, exclusion criteria specified in the ILAR criteria should be applied. Mean age of onset of polyarticular RF positive JIA is 9-11 years and girls outnumber boys. Characteristic pattern of joint involvement is symmetrical polyarthritis. Amyloidosis is a disease resulting from extracellular deposition of fibrils of aggregated proteins in different organs and blood vessels. SAA is a precursor protein in reactive amyloidosis and an acute phase protein that is mainly produced in liver by stimulation of various cytokines. The persistent augmentation of inflammatory pathway through innate immune system might be crucial in deposition of amyloid protein leading to clinical picture in JIA of renal amyloid. Clinical manifestation vary depending on the organ involved in amyloidosis and by far the most commonly involved organs are the kidneys. Renal amyloid usually presents with proteinuria with or without renal impairment. Our patient had both glomerular and
blood vessel deposition of amyloid protein, which forecast a poor prognosis than a tubular deposition. Control of underlying disease is critical in treating amyloidosis and treatment with chlorambucil improved survival in JIA associated amyloidosis and recently TNF alpha blockers and IL-6 receptor antibodies have been reported to regress amyloid in some patients.

**Conclusion:**
Renal amyloidosis should be considered in the differential diagnosis of patients with a potential to cause amyloidosis and in patients with proteinuria, CKD and normal or large sized kidneys. Secondary amyloidosis due to JIA has dramatically decreased due to early recognition of disease and better management modalities including newer biological therapies. This case has been reported for its rarity of presentation of renal amyloidosis in polyarticular form of JIA.

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