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KIDNEY PATHOLOGY IN A PATIENT WITH SEVERE COMBINED IMMUNODEFICIENCY DISEASE*

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SUMMARY: Sanal Ö, Çağlar M, Ersoy F, Coşkun Y, Tezcan İ. (Immunology and Pathology Units, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Kidney pathology in a patient with severe combined immunodeficiency disease. Turk J Pediatr 1994; 36: 319-323.

A 2-month-old SCID patient with mesangial sclerosis of the kidney is presented. Although the ADA status of the patient is unknown, the parents' RBC-ADA levels seemed to be in the heterozygote range. *Key words: severe combined immunodeficiency disease, adenosine deaminase, mesangial sclerosis.*

Severe combined immunodeficiency disease (SCID) represents a heterogeneous group of congenital disorders manifested by profound deficiencies of both B- and T-cell immunity. A great diversity and alterations in clinical, laboratory and pathological findings and genetic inheritance have been observed in SCID[1-7]. An inherited deficiency of adenosine deaminase (ADA) has been shown to be responsible for a substantial proportion of autosomal recessive SCID cases. Several findings in non-lymphoid organs have been described in ADA-deficient SCID patients[5, 8]. Recently mesangial sclerosis of the glomeruli has been reported in a few patients[8].

We present a SCID patient with unknown ADA activity and associated with kidney pathology. However, the parents' red blood cell (RBC)-ADA activity was found to be compatible with the heterozygote range, the determination of which was made after the patient died.

Case Report

A two-month-old girl was admitted to Hacettepe Children's Hospital with complaints of respiratory difficulty, cyanosis and coughing. She was a product of a marriage between first cousins and had an 18-month-old healthy sister.

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The patient's history included a pulmonary infection at one month of age. Her weight, height and head circumference were 3,700 g, 49 cm and 36.5 cm, respectively. The physical examination and x-rays revealed bronchopneumonia. Although antibiotics and gammaglobulin were given, her condition gradually worsened and she died on the 14^{th} hospitalization day.

Laboratory findings: In the peripheral blood there was marked lymphopenia ($< 400/mm^3$), monocytosis and neutrophilia. The serum IgG level was 100 mg/dl, while IgM and IgA were undetectable. Delayed hypersensitivity skin tests were positive for phytohemagglutinin (PHA), and negative for candida. The percentage of E-rosette-forming lymphocytes was very low (3%). Proteinuria was not documented. Although the ADA activity of the patient was unknown, the RBC-ADA activities of the parents determined after the patient's death fell in the heterozygote range (46 and 13 μmol/uric acid/hour/g Hb) [normal values (n = 30) 106 ± 34, range 61-185]. Chest x-rays showed a lung infiltrate on the right. No thymic shadow or bone abnormality could be visualized.

Pathological findings: Postmortem histopathological examination revealed thymic dysplasia, mesangial sclerosis in glomeruli, bronchopneumonia, fatty liver, and congestion in the adrenal medulla, lung and central nervous system.

The thymus weight was 0.2 g. There was no differentiation between cortex and medulla and no clearly identifiable Hassal's corpuscles. Lymphoid cells were rare and sparse. The connective tissue separating thymic lobules was decreased (Fig. 1).

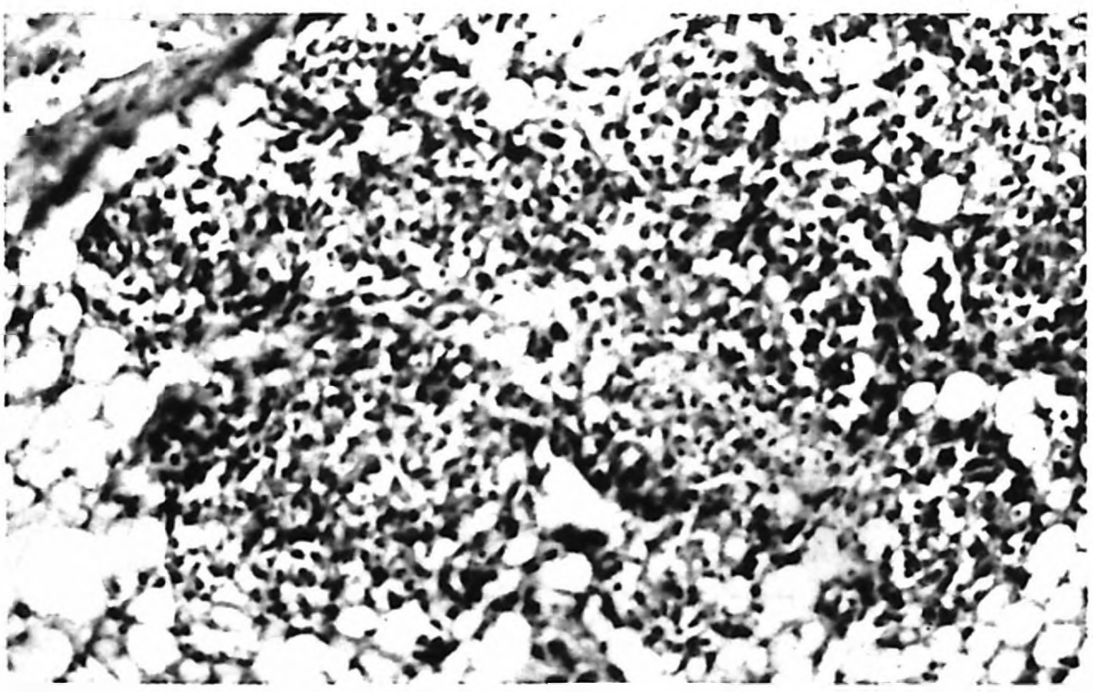

Fig. 1: Microscopic appearance of thymus gland (H + E, x 20).

The peripheral lymphoid tissues were not well developed and lymph nodes were devoid of lymphoid cells. Plasma cells were absent (Fig. 2).

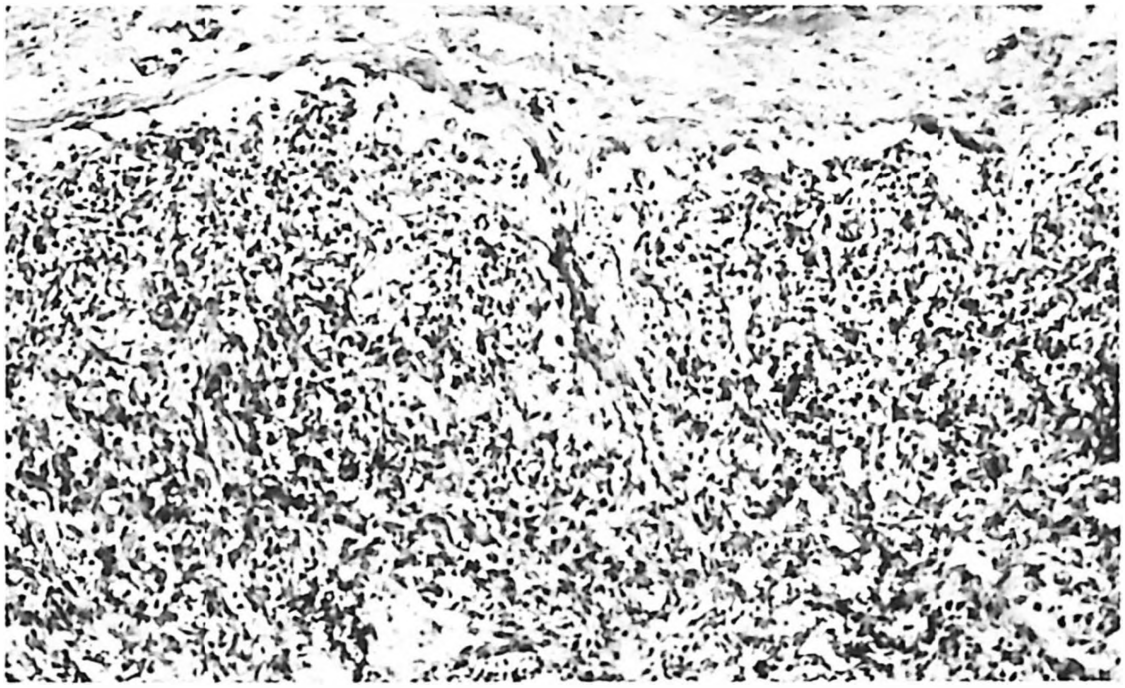

Fig. 2: Lymphoid tissue with no lymphoid or plasma cells (H + E, x 20).

By light microscopy, the kidneys showed increased mesangial fibrillar matrix (mesangial sclerosis) of varying degrees unassociated with cellular proliferation in almost all glomeruli (Fig. 3).

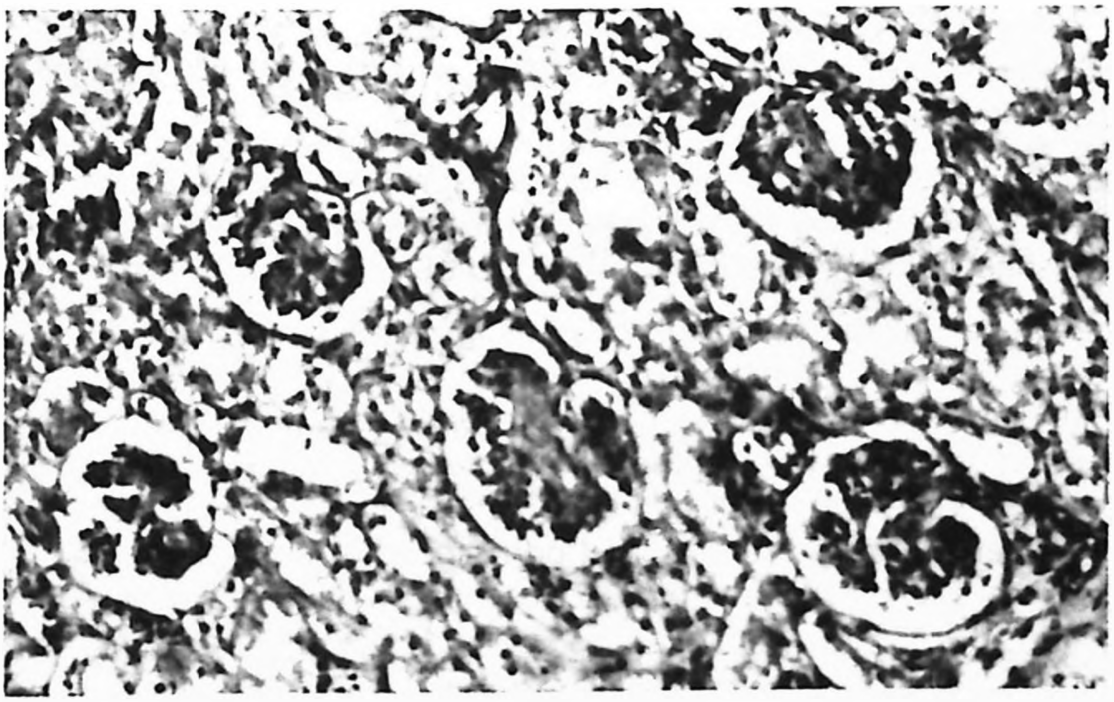

Fig. 3: Kidney pathology characterized by increased mesangial sclerosis (H + E, x 20).

Discussion

SCID cases may occur sporadically, in autosomal recessive form or X-linked form. ADA deficiency has been reported to be present in 25-40 percent of the autosomal recessive cases.

The description of individual cases with SCID shows considerable heterogeneity in immunological findings[1,3,4]. Our patient's serum immunoglobulin levels and E-rosette-forming T-lymphocyte count were very low, consistent with SCID. Further immunological tests could not be performed.

In addition to the histopathological findings consistent with SCID in the thymus and lymphoid tissue on postmortem histopathologic examination, the patient had glomerular sclerosis. Several findings in non-lymphoid tissues have been observed in ADA-deficient SCID cases[6-9]. These include mesangial sclerosis in the kidney, adrenal gland cortical sclerosis and typical alterations in chondro-osseous tissue[8]. Few patients have been reported with kidney pathology associated with ADA-deficient SCID[8]. Ratech et al.[8] reviewed the postmortem pathological findings of non-lymphoid organs in eight patients with ADA-deficient SCID and noticed mesangial sclerosis of the glomeruli in seven out of eight patients. They suggested that the toxic metabolites resulting from the specific enzyme defect may play a role in these pahological changes in the kidneys as in bones and adrenal glands[8-10]. Diffuse mesangial sclerosis is a rather uncommonly encountered clinicopathological entity and is one of the unique subsets of primary-type nephrotic syndrome (NS) occurring in the first year of life[11]. Diffuse mesangial sclerosis may also be an associated nephropathy in syndromic conditions like Drash syndrome (pseudohermaphroditism, Wilms' tumor, glomerulopathy)[12].

The renal pathological finding was not associated with clinical nephropathy in our patient. The fact that NS is a common manifestation of ADA-deficient SCID distinguishes the renal lesion in ADA-deficient SCID from nephrotic syndrome[8].

Our patient had no histopathologic or radiologic abnormality in chondro-osseous tissue, which is an associated finding in ADA-deficient SCID. Although histopathological findings have not been reported in all cases, radiographic changes of bones are not present in all patients with ADA-deficient SCID. Furthermore, bone abnormalities in two ADA-deficient SCID patients reported by Ratech et al.[8] could not be found on histopathological examination. These two patients had been treated with bone marrow transplantation.

Unfortunately we could not determine the ADA activity of the patient, but the parents had RBC-ADA levels compatible with the heterozygote range, indicating that the patient may have had ADA-deficient SCID.

At the present time, it is not known whether the non-lymphoid pathological changes are unique to ADA deficiency. More SCID patients with or without ADA deficiency should be examined to clarify this issue.

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