The Turkish Journal of Pediatrics
Volume 20 / Nos. 1-2 / Jan.-April 1978 / pp. 58 – 62

Coexistence of Sickle Cell Trait and Cystic Fibrosis*

Safiye Göğüş, M.D. / Melda Çağlar, M.D.*** / Esat Yılgör, M.D.**** / Çiğdem Altay, M.D.*****

Sickle cell trait, a heterozygous state characterized by the presence of hemoglobin SA, is present in 7 to 9 per cent of American negroes[1] and the incidence of this variant hemoglobin in the Southern part of Turkey in Eti Turks is 15%[2].

Cystic fibrosis is transmitted as a recessive trait. Its frequency is approximately 1 in 1500-2000 Caucasian births.[3] It has also been reported in other races.[3] A study carried out among the live births in Turkey found the incidence to be 1/3000.[4]

The aim of this paper is to report in detail the clinical and pathological observations in a case of cystic fibrosis showing widely disseminated intravascular sickling. To the best of our knowledge no cases of cystic fibrosis associated with sickle cell trait has been reported in the literature.

Case Report

A six month old Caucasian boy, of Eti Turk origin, was admitted to Hacettepe Children's Hospital because of a cough and failure to thrive for the previous five months. His birth weight was 3600 g. His parents were cousins and both were in good health. He was the third child of the family, the other two children had died at the age of four months from bronchopneumonia.

---

* From Department of Peditrics, Children's Medical Center, Hacettepe University, Ankara, Turkey.

**Assistant Professor in Pediatrics, pediatric pathologist.

*** Professor of Pediatrics, pediatric pathologist.

**** Assistant of Pediatrics.

***** Professor of Pediatrics, pediatric hematologist.

On examination he was an ill-looking baby with a weight of 2800 g, height of 60 cm, and head circumference of 38 cm. He could not hold his head up or sit unassisted. By auscultation occasional rhonchi were audible over both lung fields. The liver was soft and palpable 5 cm below the costal margin. The other findings of the physical examination were within normal limits.

Laboratory Data were as Follows: Hemoglobin 15.75 g/dl, Hct 48 %, white blood cell count 13,300 /mm^3, with 67 % neutrophils and 33 % lymphocytes. Erythrocytes were normal in appearance except for slight anisocytosis. Serum electrolytes were within normal limits. X-rays of the chest showed areas of lobular atelectasis and general hyperinflation of the lungs. He was started on penicillin because of a respiratory tract infection. His general condition deteriorated and he expired 10 days after his admission.

At Necroscopy Gross Pathological Findings were as Follows: Mucous plugs in the trachea and major bronchi, bilateral hyperventilation of the lungs and thymus weighing 1 g (the normal weight for this age is 22.9 g). Histologic sections of upper respiratory tract, lungs, pancreas, and gastrointestinal tract demonstrated histopathological changes compatible with cystic fibrosis (Figure 1). In addition, there was chronic

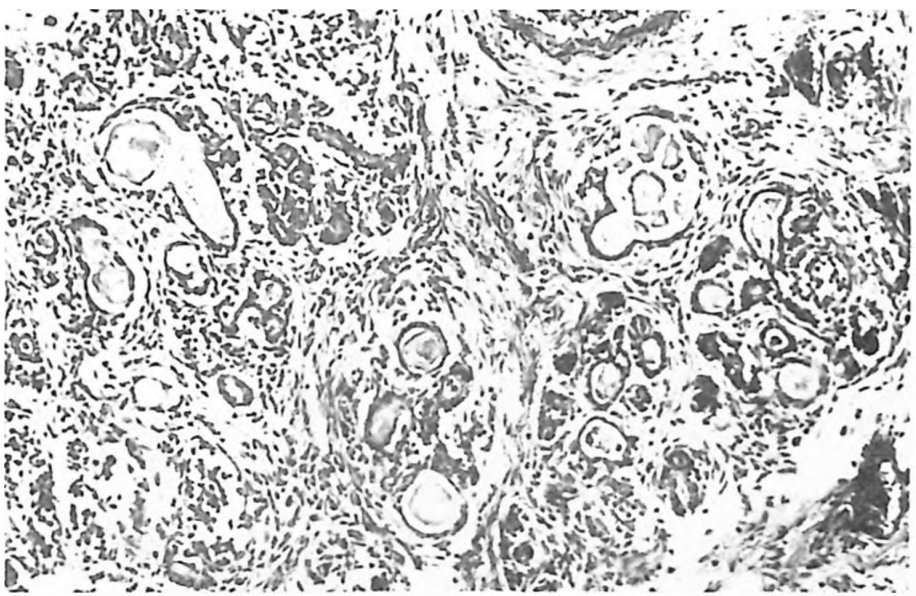

Figure 1

Section of the pancreas showing marked interlobular, interacinar fibrosis and dilated ducts containing eosinophilic inspissated secretion. H & E x100

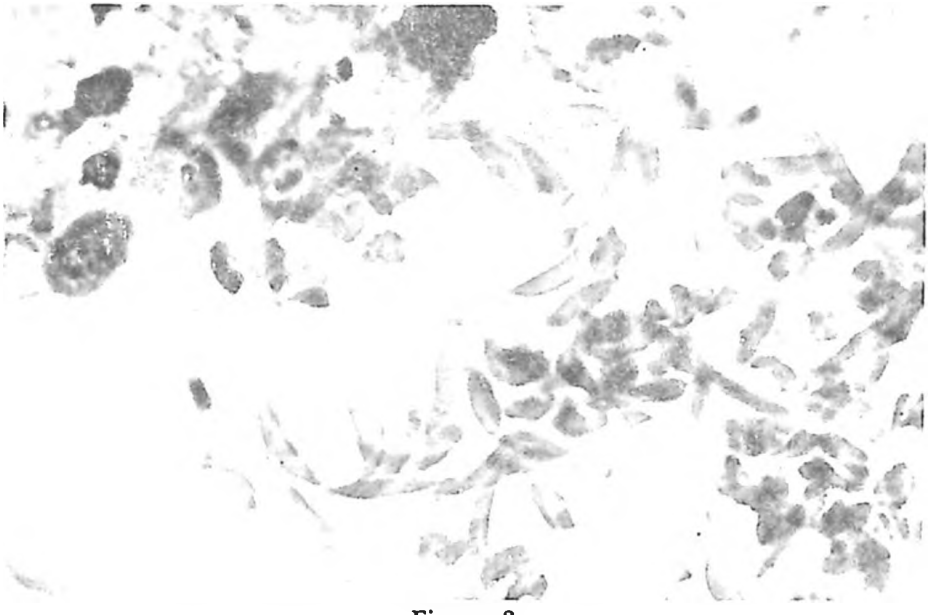

Figure 2
Section of the choroid plexus showing sickled red blood cells in a vessel. H & E x1000

passive congestion, fatty metamorphosis and hemosiderosis in the liver. The thymus showed involution. Generalized congestion of all organs was found and sickled cells were seen in the sinusoids and blood vessels (Figure 2). Some vessels in all organs were packed with aggregates of sickled red blood cells without any infarction. After the examination of the baby's necroscopy, hemoglobin electrophoreses and sickling tests were performed on the parents. Starch gel electrophoreses at pH 9 revealed AS pattern from the mother and AA pattern from the father. Their Hb A_2 and Hb F levels were within normal limits. At that time we assumed that the patient had sickle cell trait.

Discussion

Persons with sickle cell trait do not usually have anemia and they do not show any evidence of hemolytic or aplastic crises. However, haematuria, splenic and pulmonary infarcts as a result of reduced oxygen tension have been reported as the serious medical complications.[5] Other conditions such as acidosis, dehydration, the presence of reducing agents in the blood, high viscosity and hypercoagulability were also suggested to be causes of massive intravascular sickling.[6] These crises stated to be dangerous and even fatal, but the antecedent cause may not always be found.[5, 6]

McCormick[7] in 1961 reported a necroscopy series of 120 patients with proven sickle cell trait. In 15 of the 120 cases, truly massive intravascular sickling unassociated with any infarcts was seen. Additional 22 cases contained one or more obvious visceral infarcts, in the other cases sickled cells were obvious but were not in massive numbers or associated with visceral infarction. The presence of massive sickling suggested that SA was responsible or a contributing factor in death in 15 of these cases.

Our case had emphysema, obstructive bronchitis and broncholitis. These pathological findings would be enough to cause severe hypoxemia. The presence of the polycythemia in this patient indicated a long term hypoxemia due to the lung pathology. One would expect that hypoxemia together with high hemoglobin and hematocrit levels might cause in-vivo sickling phenomenon in a sickle cell trait. Prior to the death of our patient, no symptoms developed which could have been identified as the presence of one of the sickle cell crises. The generalized sickling in this case must be a preterminal event from the progressive anoxia, and at necroscopy, morphologic changes compatible with sickle cell trait were found.[8] Hemosiderosis in liver could be explained with the presence of cystic fibrosis. In a young infant with AS, the protective effects of high fetal hemoglobin must be considered as a factor which would interfere with in-vivo sickling in severe anoxemia. Since our patient was only 6 months old, we assumed that despite of the presence of long term anoxia in-vivo sickling phenomenon in him prior to the terminal event was probably also prevented by a high level of Hb F, although we were unable to test for this. In our case, generalized sickling may be considered as a contributing factor in death. The coexistence of cystic fibrosis and sickle cell trait in this case is interesting; such coexistence should be born in mind and all cystic fibrosis cases from populations in which hemoglobin S is not rare should be searched for this hemoglobinopathy.

Summary

A six month old infant who was diagnosed to have cystic fibrosis and sickle cell trait at post mortem examination was presented and the literature was reviewed for this coexistence.

REFERENCES

1. Myerson, R. M., Harrison, E., Lohmuller, H. W.: Incidence and significance of abnormal hemoglobins: report of a series of 1000 hospitalized Negro veterans. Amer. J. Med. 26: 543, 1959.
2. Altay, C., Yetgin, S., Özsoylu, S., Kutsal, A.: Hemoglobin S and some hemoglobinopathies in Eti-Turks. Hum Hered. 28: 56, 1978.

3. Oppenheimer, E. H. and Esterly, J. R.: Pathology of cystic fibrosis. Review of the literature and comparison with 146 autopsied cases, in Rosenberg, H. S., and Bolande, R. P., editors: Perspectives in Pediatric Pathology, Chicago, 1975 Year Book Medical publishers Vol., 2, p. 241.
4. Gurson, C. T., Sentel, H., Gurgan, M., and Pala, S.: Newborn screening for cystic fibrosis with the choride electrode and neutron activation analysis. Helv. Paediat. Acta 28: 165, 1973.
5. Ober, W. B., Bruno, M. S., Weinberg, S. B., Jones, F. M. Jr., and Weiner, L.: Fatal intravascular sickling in a patient with sickle cell trait: The New Engl. J. Med. 263: 947, 1960.
6. Jones, S. R., Binder, R. A., and Donowho, E. M., Jr.: Sudden death in sickle cell trait. New Engl. J. Med. 282: 323, 1970.
7. McCormick, W. F.: Abnormal hemoglobins. II. The Pathology of sickle cell trait. Am. J. Med. Sci. 241: 329, 1961.
8. Mullick, F. G., Delage, C., and Irey, N. S.: Sickle cell crisis associated with drugs. Arch. Environ. Health 26: 221, 1973.