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New Biochemical Aspect of Idiopathic Pulmonary Haemosiderosis in Infancy

By

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A case of idiopathic haemosiderosis in an infant is reported. The condition was characterized by a lower than normal urinary hydroxyproline excretion. The ratio of free to peptide hydroxyproline was normal but the glycosaminoglycan fractions displayed an unusual distribution in that increased amounts of hyaluronic acid were excreted and it was this compound which represented the dominant fraction. The phenomenon is suggested to be indicative of a disturbance in collagen metabolism.

Although idiopathic pulmonary haemosiderosis has been described more than 100 years ago [14], its aetiology and mechanism are still not clear. We have observed a case with a probably new biochemical aspect of the disease.

REPORT OF A CASE

M.B. a female infant of 3400 g had been born spontaneously of a normal pregnancy. Except for a striking pallor, her development had been undisturbed for 5 months when she was treated for bronchopneumonia in another hospital. To our department she was admitted at 8 months of age, with dysponea, cyanosis, increased pallor, exhaustion, low fever and cough. Physically the chest was clear; over the basis of the heart a soft systolic murmur could be heard.

X-rays of the lungs showed bilateral diffuse mottled densities, mainly on the right side, of confluent character. The left heart was slightly enlarged (Fig. 1). ECG and PCG did not reveal signs of congenital heart disease or cor pulmonale.

Beside the pneumonia, the other predominant finding was an anaemia of the iron deficiency type, with Hgb, 3.5 g/100 ml; haematocrit, 20%; RBC, 1.800.000; WBC, 9.600, with a normal differential count; reticulocyte count 0.5%. Serum bound iron value was 18 μg/100 ml; ESR 30 mm/hr. Red blood cell volume also showed hypochromic microcytic anaemia.

Pneumonia aggravated by anaemia was diagnosed and combined antibiotic treatment and blood transfusions were prescribed. There was substantial improvement, the anaemia had been cured and the systolic murmur diminished after the infant was discharged.

During the next month she was admitted twice for the same complaints as before, but the anaemia then was slighter (Hgb, 8.6 g/100 ml and 7.5 g/100 ml; haematocrit, 30 and 23%; RBC 3.000.000; serum bound iron 20 and 18 μg/100 ml, respectively). X-rays showed diffuse bilateral reticular and miliary type changes (Fig. 2). In 2 weeks the pulmonary shadows had cleared up remarkably (Fig. 3).

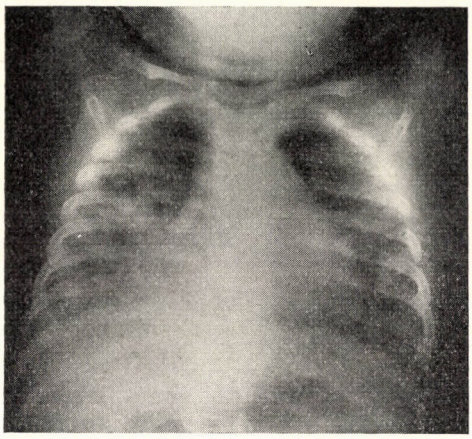

FIG. 1

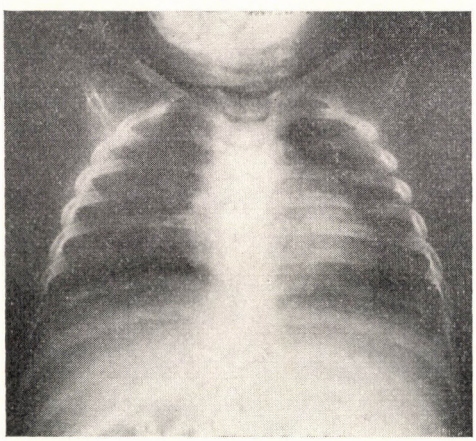

FIG. 2

At the time of the fourth admission we regarded the condition as idiopathic pulmonary haemasiderosis on the basis of clinical, radiological and laboratory data. The diagnosis was confirmed by the detection of siderophages in mucus obtained by bronchoscopy and gastric lavage.

Results of electrophoretic and immunoelectrophoretic examinations, direct and indirect Coombs reactions, milk cutaneous reaction, demonstration of cold, thrombocyte and leukocyte antibodies, proved normal. Respiratory function was not studied, arterial pO_2 and pCO_2 were normal.

Repeated determination of total hydroxyproline in urine by the method of

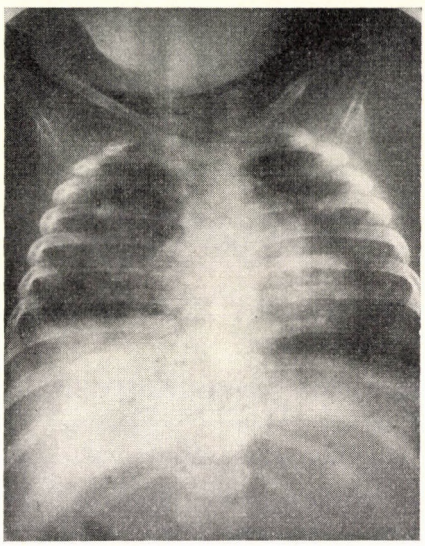

FIG. 3

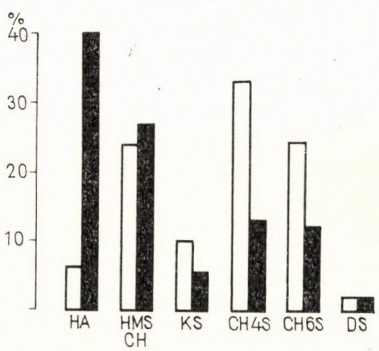

FIG. 4. Light columns represent the values for the control group, black ones the values for the patient. The control data were obtained from 10 healthy infants of similar age. HA = Hyaluronic acid; HMS = Heparan sulphate; CH = Chondroitin; KS = Keratan sulphate; CH 4 S = Chondroitin 4-sulphate; CH 6 S = Chondroitin 6-sulphate; DS = Dermatan sulphate

KIVIRIKKO et al. [4] yielded 22 mg daily or 230 mg/g creatinine, lower than normal (5, 1, 15, 8). The ratio of free to peptide hydroxyproline was 8, approximately normal. Total urinary glycosaminoglycan (GAG) excretion was 4—6 mg/day, normal for her age [6].

The different fractions of GAG [13] showed an unexpected distribution (Fig. 4). As compared with controls, there was

a striking increase in the excretion of non sulphuric GAG (Normal group, 30%; patient, 66.5%). The increase was mainly due to the highly elevated excretion of hyaluronic acid (40%). While normally the dominant GAG in urine is Ch—S, in the urine of our patient hyaluronic acid dominated.

Antibiotics, steroids and blood transfusions had only a transient effect.

Discussion

Idiopathic pulmonary haemosiderosis is characterized by repeated intrapulmonary haemorrhage with subsequent pulmonary haemosiderin deposits, haemoptysis and secondary anaemia. The onset is mostly in childhood.

The pathogenesis of the disease is unknown. Heiner [3] reported on a few instances of the syndrome seemingly related to sensitization of cow's milk protein. According to Ceelen [2] the fundamental defect is a hypoplasia of pulmonary elastic tissue. Soergel and Sommers [9, 10] suggested a congenital defect in the function and development of alveolar epithelium. Others supposed disturbances in pulmonary vasomotor function. Steiner [11, 12] considered the condition to represent an immunoallergic disorder.

In our opinion the decreased urinary excretion of peptide hydroxyproline and the increased excretion of hyaluronic acid are suggestive of a primary defect in pulmonary connective tissue, probably by a disturbance in the metabolism of collagen.

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References

1. Allison, D. J., Walker, A., Smith, O. T.: Urinary hydroxyproline: creatinine ratio of normal humans at various ages, Clin. chim. Acta **14,** 729 (1966).
2. Ceelen, W.: In: Handbuch der speziellen pathologischen Anatomie und Histologie, ed. Henke, E., Lubarsch, O. Vol. 3, Part III. Springer-Verlag, Berlin 1931.
3. Heiner, D. C., Sears, J. W., Kniker, W. T.: Multiplex precipitins to cow's milk in chronic respiratory disease. Amer. J. Dis. Child. **103,** 634 (1962).
4. Kivirikko, K. I., Laitinen, O., Prockop, D. J.: Modification of a specific assay for hydroxyproline in urine. Analyt. Biochem. **19,** 249 (1951).
5. Morrow, G., Kivirikko, K. I., Prockop, D. J.: Catabolism and excretion of free hydroxyproline in infancy. J. clin. Endocr. **27,** 1365 (1967).
6. Németh Csóka, M.: A turbidimetric method for the determination of chondroitin sulphuric acid by rivanol. Biochem. biophys. Acta (Amst.) **50.** 585 (1961).
7. Orii, T.: The urinary acid mucopolysaccharides in normal children. Hoppe-Seyler's Z. physiol Chem. **349,** 816 (1968).
8. Prockop, D. J., Kivirikko, K. I.: Relationship of hydroxyproline excretion in urine to collagen metabolism. Ann. intern. Med. **66,** 1243 (1967).
9. Soergel, K. H.: Idiopathic pulmonary hemosiderosis. Pediatrics **19,** 1101 (1957).
10. Soergel, K. H., Sommers, S. C.: Idiopathic pulmonary hemosiderosis and related syndromes. Amer. J. Med. **32,** 499 (1962).
11. Steiner, B.: Essential pulmonary haemosiderosis as an immunohaematological problem. Arch. Dis. Childh. **29,** 391 (1953).
12. Steiner, B., Nábrády, J.: Immunoallergic lung purpura treated with azathioprine. Lancet **1,** 140 (1965).
13. Tanaka, Y., Gore, I.: Cellulose column chromatography for the fractionation and isolation of acid mucopolysaccharides. J. Chromatogr. **23,** 254 (1966).
14. Virchow, R.: Die krankhaften Geschwülste. Part 2. August Hirschwald, Berlin 1864.
15. Yonuoszai, M. K., Andersen, D. W., Filler, L. H., Fomon, S. J.: Urinary excretion of endogenous hydroxyproline by normal male infants. Pediat. Res. **1,** 266 (1967).