Lupoid Cirrhosis with Serum Lactic Acid Dehydrogenase Linked to an γA Immunoglobulin

Agarose gel electrophoresis of serum from a patient with 'lupoid' cirrhosis with jaundice showed an abnormal mobility and increased width of the zones of all the isoenzyme fractions of lactic acid dehydrogenase (LDH) (Figure 1). The bulk of the activity (total 2200 Wroblewski units) was found in 2 fractions corresponding to the normal third and fourth fractions. The fastest fractions (I–IV) were found somewhat cathodally to the corresponding fractions in a normal serum, while the most cathodal fraction (V) was found anodally to its normal site (Figure 1). Such anomolous mobility has also been described by KREUTZER, JACOBS and FRANCKE[1]. The abnormal mobility was interpreted as a sign of LDH-isoenzymes being bound to some serum protein with a low charge. To check the validity of this assumption, serum was fractionated by gel filtration in a Sephadex G 200 column. The distribution of the activity among the fractions resembled that of a homogenous protein fraction eluted from the column somewhat before γG, while LDH is normally eluted after γG (Figure 2). The finding corroborated the assumption that the LDH-isoenzymes in the case under discussion were components of a complex of higher molecular weight than that of normal LDH.

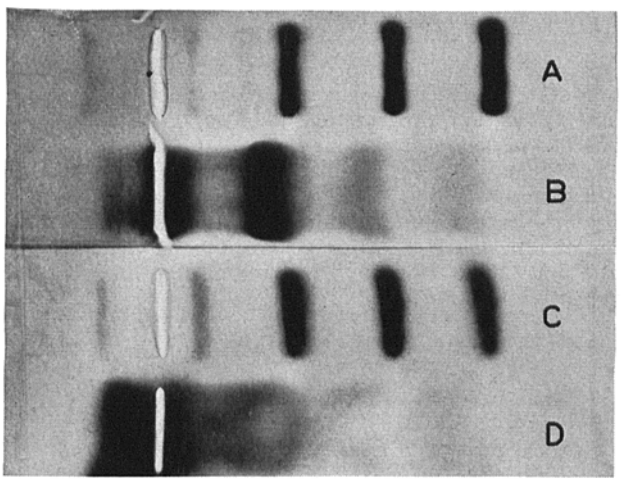

Fig. 1. Normal (A) and abnormal (B) LDH-isoenzymes after electrophoresis in agarose gel without antiserum and normal (C) and abnormal (D) LDH-isoenzymes after electrophoresis in agarose gel containing 10% rabbit anti human γA. Anode to the right.

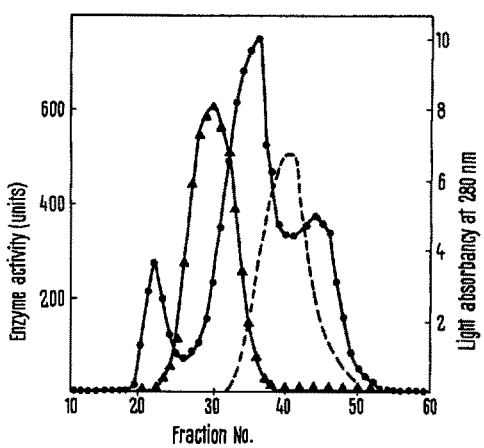

Fig. 2. LDH-activity and protein concentration in fractions of serum obtained by gel filtration. ▲ LDH-activity of the case with lupoid cirrhosis. ● Protein concentration of the same case. Broken line denotes the position of normal LDH-activity in the chromatographic pattern.

Paper electrophoresis of the serum showed a low albumin concentration (3.1 g/100 ml) and a massive polyclonal increase of γ-globulin (2.5 g/100 ml). Immunochemical analysis showed the serum concentration of γG, γA and γM to be 195, 220 and 250% respectively of normal. A low concentration of the β_{1C}-globulin (42% of normal) and a high titre of 'antinuclear antibodies' were laboratory data which supported the diagnosis of lupoid cirrhosis and which directed our thoughts to the possibility of antibodies with LDH interaction. The hypothesis was tested by serum electrophoresis in agarose gel containing rabbit anti human immunoglobulin. The bulk of the abnormal LDH-complexes was immobilized in this gel and the activity was found just cathodally to the application slit. Further analysis showed that the LDH-fractions did not migrate in specific anti human γA, but did so in anti γG and anti γM. None of these antisera affected the mobility of normal LDH-isoenzymes (Figure 1).

In order to find out whether the patient's serum contained LDH interacting immunoglobulins in excess, equal volumes of this serum and of serum from another patient with myocardial infarction (LDH about 2000 U, mainly fractions I and II) were mixed. Electrophoresis showed a marked increase of the 2 fastest fractions, but all of the fractions showed the same abnormal mobility and diffuse outline as in the pattern of the serum from the patient with lupoid cirrhosis. No LDH-fraction with normal mobility could be demonstrated in the mixture. This shows that a considerable amount of free LDH-binding protein occurred in serum and also that normal LDH could be bound. It might therefore be assumed that the patient's own LDH was also normal and that the abnormal LDH pattern was due to the presence of an abnormal γA fraction. The data indicate very high specificity and strong interaction between an γA-fraction and LDH. Since the complex LDH-γA was not dissociated on gel filtration in neutral pH, it is probable that the complex is not formed in vitro but occurs in vivo in the patient's blood. Whether one can speak of an LDH-'autoantibody' is a question of nomenclature.

Résumé. Dans un cas de cirrhose lupoïde, nous avons trouvé chez les isoenzymes de la lactico-déshydrogénase de sérum une mobilité électrophorétique anormale et une augmentation de leur poids moléculaire. Nous avons pu montrer que cette anomalie est la suite d'un complexe que forment les fractions d'enzyme avec une immunoglobuline de type γA. La présence d'un excès de la protéine liant des isoenzymes a été demontrée par l'addition de la lactico-déshydrogénase normale.

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[1] H. H. KREUTZER, PH. JACOBS and C. FRANCKE, Clin. chim. Acta *11*, 159 (1965).