Hyperalaninemia with Pyruvicemia (Preliminary Report)

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Recently Lonsdale¹ has described briefly a six-year-old boy who had recurrent episodes of cerebellar ataxia and a persistent elevation of alanine and pyruvate in blood. However, the site of biochemical lesion of the disorder remains unsolved. In process of screening for aminoaciduria, we also found a similar case associated with hyperalaninemia and pyruvicemia.

Case M.O., a girl born after an uncomplicated, full-term pregnancy and spontaneous delivery. Her neonatal period was uneventful. The parents were healthy and not consanguineous. There were two siblings; one of them (sister) died at 5 years of age showing mental and physical retardation similar to that of the patient. The other sister was living and well. The patient showed a slow progress in mental and motor function since the infancy. During the infancy she had often vomiting. There was no history of convulsions or severe illness.

On admission at the age of 9 years, the patient showed mental retardation and motor dysfunction of severe degree. She was able to sit alone but unable to stand or walk. The extremities were somewhat rigid and the deep tendon reflexes were weak. EEG showed findings of hypsarrhythmia.

Thin-layer chromatograms of serum amino acids showed an increase in alanine. The concentration of serum alanine was found to range from 5.0 to 8.0 mg per 100 ml on repeated examinations (normal value; 1.90 to 5.40 mg per 100 ml). The other amino acids in serum were within normal limits. Fasting blood glucose was 80 mg per 100 ml. Blood pyruvate levels were 2.9 to 4.1 mg per 100 ml (normal value; 0.5 to 1.5 mg per 100 ml). Blood lactate levels were 16.6 to 23.3 mg per 100 ml (normal values; 10 to 20 mg per 100 ml). Paperchromatography of urinary organic acids revealed a remarkable spot of pyruvic acid but no abnormal spots were detected otherwise.

Serum alanine levels following the alanine loading showed an almost normal clearance curve except for the elevation of base level. Glucose tolerance test was normal. But the patient showed a significant rise of blood pyruvate and lactate after glucose loading as compared with controls. The activity of

glutamic-pyruvic transaminase in the liver from the patient was found to be normal. There was no difference in the *in vitro* lactate production from glucose by erythrocytes between the patient and controls.

These findings suggest that the metabolic lesion of the disorder may lie in the entrance of pyruvate into the TCA cycle or the gluconeogenic pathway. Therefore, the liver biopsy specimen from the patient was studied for decarboxylation of pyruvate and pyruvate carboxylase. Decarboxylation of pyruvate was assayed by determining the formation of $^{14}\text{CO}_2$ from pyruvate-1- ^{14}C . Pyruvate carboxylase was assayed by determining the incorporation of $^{14}\text{CO}_2$ to oxaloacetate according to Utter and Keech.² The patient's liver showed a definitely diminished activity of pyruvate carboxylase and normal activity of pyruvate decarboxylation (cf. Table 1). These results indicate that this particular disorder may be due to a partial defect in pyruvate carboxylase and hyperalaninemia is a secondary phenomenon due to the elevation of pyruvate.

TABLE 1. *Activities of pyruvate carboxylase and of pyruvate decarboxylase in the liver of the patient and controls*

	Pyruvate carboxylase		Pyruvate decarboxylase*
	$\mu\text{mole/g}$ of wet weight	$\mu\text{mole/mg}$ of protein	cpm/g of wet weight
Control I, aged 5 years	1.16	0.0368	234×10^3
Control II, aged 14 years	0.87	0.0264	147×10^3
Control III, aged 7 years	0.69	0.0214	
Patient, aged 10 years	0.19	0.0042	149×10^3

* Liver slices were incubated with pyruvate-1- ^{14}C ($0.1 \mu\text{c}/\mu\text{mole}$) and Krebs-Ringer phosphate buffer for 60 min at 37°C and $^{14}\text{CO}_2$ liberated was determined.

References

- 1) Lonsdale, D. Hyperalaninemia with pyruvicemia. *New Eng. J. Med.*, 1968, **278**, 1235.
- 2) Utter, M.F. & Keech, D.B. Pyruvate carboxylase I. Nature of the reaction. *J. biol. Chem.*, 1963, **238**, 2603-2608.