Is maternal gastrin important in congenital hypertrophic pyloric stenosis?

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Summary

The birth of a normal infant to a woman with Zollinger-Ellison syndrome is described. The cord blood serum gastrin was very elevated. This suggests that maternal gastrin can cross the placenta, a fact previously in doubt in man. The infant did not develop congenital hypertrophic pyloric stenosis. This is further evidence that raised blood gastrin *in utero* is not an important causative factor in the development of congenital hypertrophic pyloric stenosis in man.

Introduction

Injection of depot pentagastrin into pregnant bitches during the second half of pregnancy has been shown to produce congenital hypertrophic pyloric stenosis (CHPS) in their pups (Dodge, 1970; Dodge and Karim, 1976). Controversy remains, however, as to whether gastrin either from mother or infant has a role in the pathogenesis of CHPS in man. Raised serum gastrin levels have been found in infants with CHPS before pyloromyotomy (Spitz and Zail, 1976; Bleicher *et al.*, 1978). In other studies pre-pyloromyotomy serum gastrin levels in infants with CHPS did not differ significantly from those in control infants (Rogers *et al.*, 1975; Moazam *et al.*, 1978; Hambourg *et al.*, 1979; Grodiowski *et al.*, 1980).

It is not known whether maternal gastrin can cross the placenta (Werlin, Grand and Drum, 1978). Werlin and his co-workers showed however that the cord blood gastrin levels in 40 infants with CHPS did not differ from controls, nor was there any difference between the serum gastrin levels of the mothers of each group. Furthermore the mean cord blood gastrin levels of both the patient and control infants

were significantly higher than the mean maternal levels.

We report the birth of a normal infant to a mother with the Zollinger-Ellison syndrome. The cord blood gastrin was very high, but the infant did not develop hypertrophic pyloric stenosis.

Case report

In 1971 a woman aged 28 years presented with a 3 year history of peptic ulcer symptoms and diarrhoea. A selective vagotomy and gastroenterostomy was performed, during which a pancreatic tumour was discovered and excised. Six months later she developed two stomal ulcers. The fasting serum gastrin was 6175 pg/ml (normal range 0-150 pg/ml), confirming a diagnosis of the Zollinger-Ellison syndrome. The patient was treated by a total gastrectomy the same year. She has continued to display elevated serum gastrin levels in the subsequent 10 years, for example 60,000 pg/ml in May 1978, 132,000 pg/ml in June 1979, but remains asymptomatic.

Two sisters have each developed the Zollinger-Ellison syndrome, one of whom had a multiple endocrine neoplasia type I syndrome with multiple parathyroid adenomata and a pituitary adenoma. The patient's eldest son has osteogenesis imperfecta. There is no family history of CHPS.

In 1974 the patient gave birth to a normal baby girl. Cord blood serum gastrin was 1360 pg/ml. The infant did not develop CHPS. One year later the baby's serum gastrin level was 155 pg/ml when the serum gastrin level in the mother was 7650 pg/ml.

Discussion

The ability of maternal gastrin to cross the placenta appears to be species specific. Studies with

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labelled gastrin have demonstrated that gastrin does not cross the placenta in the pregnant rat (Von Berger *et al.*, 1976), but does so in the dog (Bruchner, Snow and Tonkalerud, 1970). It is not known whether maternal gastrin can cross the placenta in humans (Werlin *et al.*, 1978) but the presence of high cord blood serum gastrin in this case strongly suggests that maternal gastrin does cross the placenta.

The cause of CHPS is unknown but it is thought that many genetic and environmental factors, including the important modifying effect of gender, operate together to produce the condition (Dodge, 1973). Since injections of depot pentagastrin given to pregnant bitches in the second half of pregnancy have been shown to produce pyloric stenosis in 28% of pups (Dodge and Karim, 1976), there has been controversy as to whether raised blood gastrin either *in utero* or post-natally may be one such environmental factor in man. The findings of Werlin that infants with pyloric stenosis do not have elevated cord blood serum gastrin makes the possibility that an elevated serum gastrin concentration at the time of delivery is implicated in the pathogenesis unlikely. The failure of the infant described above to develop CHPS could be due to the lack of other environmental and genetic factors such as maleness. Nonetheless the absence of CHPS in this child is further evidence against the hypothesis that intrauterine exposure to a high dose of gastrin is an important causative factor in the development of the condition in man.

Acknowledgment

We wish to thank Dr K. Buchanan for the estimation of the serum gastrin levels in this study.

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