

Diminished Content of Enterochromaffin Cells in the Rectal Mucosa of an Infant

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Summary. This report deals with an extremely small number of enterochromaffin cells in the rectum of a newborn male. This finding occurred only in 200 biopsies. The correlations to congenital disturbances of the motility of the intestine in the newborn are discussed.

The frequency of these alterations seems to be comparable with other disturbances of cells of the neural crest, as for example pigment anomalies.

Although further biochemical investigations could not be carried out because of technical difficulties, the case seems to be worth publishing for theoretical and practical reasons and in view of the possibility of special treatment.

Key words: Intestinal motility — Enterochromaffin cells — Rectal suction biopsy.

Zusammenfassung. Es wird über einen extrem niedrigen Gehalt an enterochromaffinen Zellen in der Rectumschleimhaut eines männlichen Neugeborenen berichtet, bei welchem seit der Geburt eine mit Obstipation einhergehende Motilitätsstörung des Magendarmtraktes bestand. Eine Störung der Innervation konnte ausgeschlossen werden. Der Säugling verstarb an einer Enterocolitis und sekundären Komplikationen im 7. Monat und mußte vorher über lange Zeiträume parenteral ernährt werden.

Die bekannte Wirkung der Produkte der enterochromaffinen Zellen — Serotonin und Motilin — auf die Motilität des Darmes erlaubt unseres Erachtens die hypothetische Annahme eines kausalen Zusammenhanges zwischen dem erhobenen Befund am enterochromaffinen Zellsystem und den klinischen Erscheinungen. Die Tatsache, daß dieser Befund in bisher über 200 untersuchten Fällen erstmals erhoben werden konnte, scheint eine Mitteilung zu rechtfertigen, da nach unseren heutigen Kenntnissen eventuell zielführende therapeutische Konsequenzen möglich sind. Die mögliche Frequenz solcher Störungen des enterochromaffinen Zellsystems wird diskutiert.

Enterochromaffin cells are not uniformly distributed in the gastrointestinal tract. They are numerous in the duodenum and also in the rectum, as is proved by the higher incidence of carcinoid tumors in this region. In our opinion the accumulation of enterochromaffin cells in the rectum provides a possibility of studying the normal and pathologic features of this special cell system by simple reproducible suction biopsies, thus avoiding general anesthesia. The amount, distribution and functional state of the cells can be correctly ascertained by fluorescence or silver impregnation techniques (Hamperl, 1952; Masson, 1928; Sakharowa, 1972). Both techniques can be employed even in very small bioptic material as is demonstrated by Gootz et al. (1974). The possibility of using both techniques (fluorescence and impregnation) consecutively on one and the same slide permits an exact statement of the biological conditions of the cells system (Lassmann, 1974).

In recent years we have investigated with these techniques more than 200 cases of bioptic material from newborn infants some days or weeks old and from adults. Normally 10 or 20 slices are examined to discover the exact state of the number and distribution of the cells in the rectal mucosa. The content of serotonin in the cells and noradrenaline in the nerves is demonstrated by using special filters and photometric techniques if necessary, and there is a good correlation between the content of granules in the cells and the content of serotonin or motilin.

In recent years several papers dealing with the distribution and frequency of carcinoid tumors in the intestine have been published (Feyrter, 1934, 1951; Masson, 1956; Ratzenhofer, 1961, 1972; Hosoda, 1972; Greenwood et al., 1974; Pears et al., 1974).

But as far as we know a case with an extremely diminished or completely missing content or with disturbances of synthesis in the course of an enzyme defect of the enterochromaffin cell system is still unknown.

In 200 cases examined we observed for the first time an extremely diminished content of enterochromaffin cells in the mucosa of the rectum in a baby 4 months old. This finding was confirmed by fluorescent and silver impregnation techniques, and this finding together with distinct clinical symptoms seems to be worth briefly communicating.

Material and Methods

The biopsy was taken from a newborn male 4 months old at the time with troubles of intestinal motility since birth. Because of the severe general state of the infant the biopsy was taken under general anesthesia and the material was methodically prepared as described by Gootz et al. (1974) in previous papers.

Results

The male infant examined died 7 months after birth in the course of enterocolitis and induced secondary complications. The child had been constipated since

birth, suffering from lack of intestinal motility. It recovered from pneumonia in the 2nd month. Laparotomy was done twice because of clinical symptoms of ileus which could not be confirmed on either occasion; only gas was suctioned out of the enlarged intestine. Enterocolitis, peritonitis, and hemorrhagic meningitis were confirmed at the post-mortem. But the fact that since birth there had been severe troubles of intestinal motility causing the constipation was not mentioned.

Because of the severe constipation a rectal biopsy was taken in the 4th month of life to exclude Hirschsprung's disease. Even the X-ray examination was normal in this respect.

The neurohistologic examination of the bioptic material showed a normal innervation of adrenergic and parasympathetic nerves and ganglia cells. But the most impressive finding was an extremely diminished number of enterochromaffin cells confirmed by fluorescent and silver impregnation techniques (Fig. 1 B).

External circumstances paralysed further biochemical investigations of serum, urine, and blood platelets for the evaluation of serotonin productions and excretion found necessary in the course of our histological findings.

Discussion

The number of enterochromaffin cells differ in normal conditions (Fig. 1). They are numerous in the basal parts of the krypts, and more scattered in the upper parts. An exact statement dealing with the number and distribution of the cells is in our experience only reliable in sagittal section including the whole mucous membrane and 10–20 serial slices should be used.

With regard to the above-mentioned procedure, the findings of an extremely decreased content of enterochromaffin cells for the first time in the newborn male infant is in our opinion extraordinary and worth discussing.

There is a close correlation between the content of serotonin and motilin of these cells and the intraplasmatic granula in the cells as proved in experimental studies. In our case the cells show a normal fluorescence and normal content of impregnated granula, which in our opinion demonstrates that in our case there is a real decrease in the number of cells and this state is not caused by disturbances of synthesis attended by an enzyme defect. On the other hand a correlation between intestinal motility and serotonin content is demonstrated by clinical observations in carcinoid syndrome and by administration of the precursor of serotonin, 5-Hydroxytryptophan (Cerletti, 1958).

Recently the contractile action of motilin and 13.Nle-motilin an analogon was studied (Domschke, 1976). There is a decrease of activity from the duodenum and stomach to the anal parts of the intestine and this behavior seems to be in good correlation with the number and distribution of the enterochromaffin cells. But till now the effect of Motilin on the muscles of the rectum in respect to the higher amount of enterochromaffin cells in this region is not known. But from a functional point of view a higher contractile effect of Motilin in this region seems to be possible.

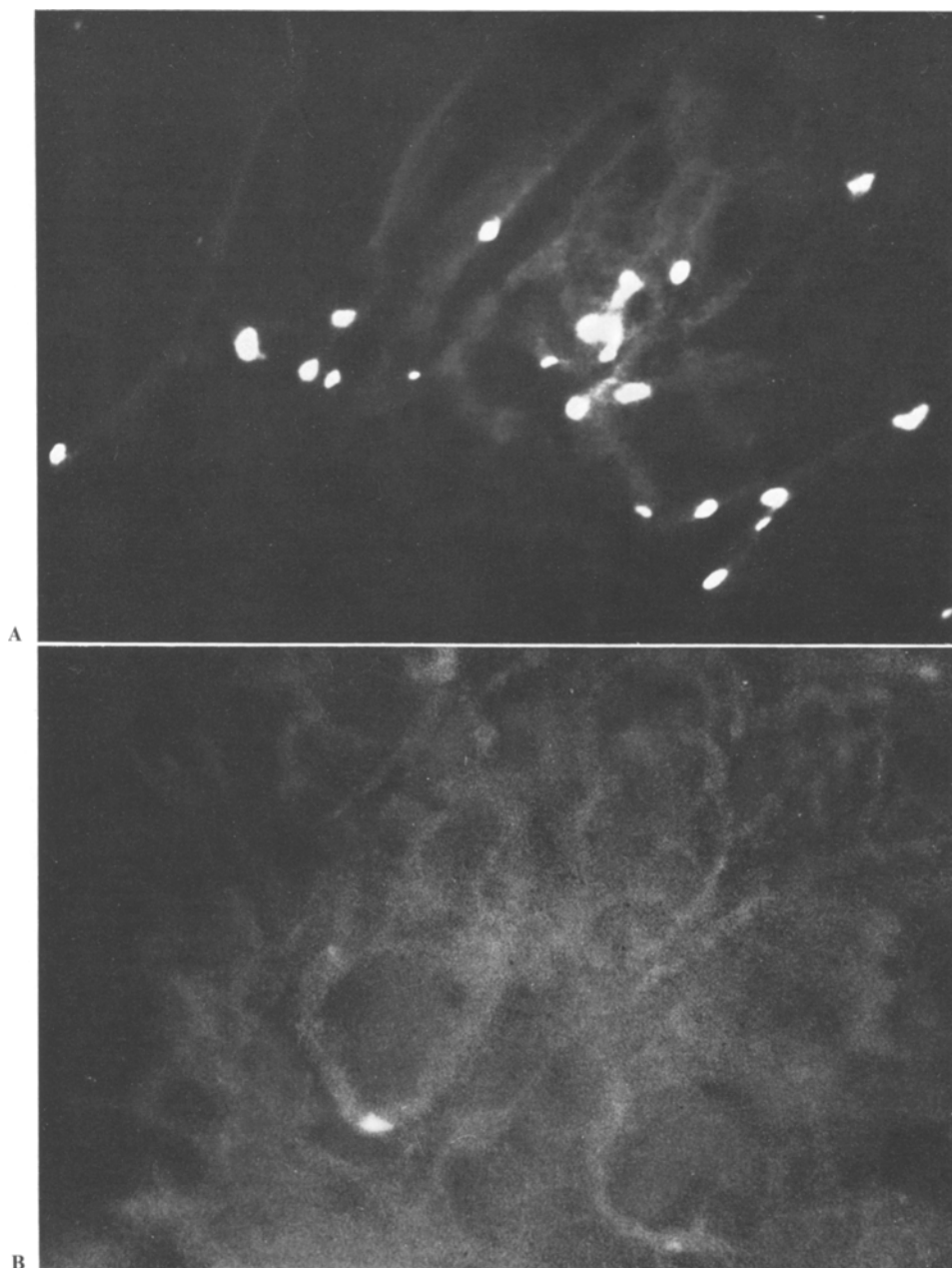


Fig. 1. **A** L95/74 male infant aged 2 months. Psych. constipation. Normal content of enterochromaffin cells in rectal mucosa. $\times 110$ Meth.: Sacharowa. **B** L96/75 female infant aged 4 months. Disturbance of intestinal motility since birth. Extreme diminished content of enterochromaffin cells in the rectal mucosa. $\times 150$. Meth.: Sacharowa

We believe that the morphologic findings in our case are directly related to the clinical observations of intestinal disturbance of motility since birth. The fact that a correlation of clinical symptoms and findings described above has never been put forward seems to be easily explained by the fact that in routine work an exploration of the content or functional state of enterochromaffin cells in the intestine is not practised. On the other hand, in the autopsy report the complications leading to death are explained, but the state of the cells was not given. A further complication regarding the state of the cells in autopsy material is the well-known fact that an exact statement of the number, distribution and functional behaviour of the cells is only possible within 6 h after death, and in most cases the post-mortem is not undertaken within this period.

The incident rate of enzyme defects or decreased number of enterochromaffin cells as an inborn error seems to be very low. Looking for comparable findings, a correlation with that of inborn errors of pigment disturbances seems possible. As is now generally accepted, the cells, the melanocytes and the enterochromaffin cells derive from the neural crest, so the disturbances of migration and enzyme defects seem to be comparable (albinismus partialis or totalis I and II). The incident rate of enzyme defects or disturbances of migration of melanocytes is 1:15,000–1:40,000 (Witkowski and Prokop, 1974).

We believe that defects of the enterochromaffin cell system have a similar sequence.

The fact that such a finding was the first in 200 cases is in our opinion worth publishing in this case. Even a biochemical examination was impossible. The communication of this case should lead to an examination of the enterochromaffin cell system in every case of disturbances of intestinal motility in a newborn infant existing since birth as methods with reproducible results are available. These examinations are of interest not only theoretically but because of possible therapeutic measures by a substitute therapy.

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