Cirrhosis in children from peanut meal contaminated by aflatoxin


The most toxic of the metabolites of Aspergillus flavus known to grow on peanuts is aflatoxin B1. It affects the young of many species of mammals and causes hepatic necrosis followed by bile duct proliferation. There is, however, no information related so far on the toxic manifestations of this compound in human beings. A 3-year study was done on 50 children of the Indian childhood clinic. The investigation was carried out on children who had consumed contaminated groundnut oil and peanut meal for periods ranging from 6 days to 6 months. All were cases of protein-calorie malnutrition with the exception of one normal child and one who had nephrosis. Detailed dietary histories were obtained with particular reference to groundnut oil, peanuts, and peanut meal. There was a history of the consumption of these food items, as children belonging to the lowest income group of the Indian community, a little milk and vegetables. In our weekly clinic, the children were carefully examined, and records of anthropometric and other laboratory measurements were recorded. Repeated liver biopsies were taken every 2 to 3 months, and it is the policy in this clinic to take a liver biopsy after the first examination. In many children, since their liver biopsies were done at 2 to 3-month intervals, in others, because they failed to attend the clinic, it was possible to do only two biopsies within the first 6 months. The liver biopsies were fixed in 10% formaldehyde for paraffin section. The sections were stained with hematoxylin and eosin, and for ultrastructural examination. Muscle biopsy was performed on all 20 children initially and repeated after 6 to 7 months in eight.

Results

None of the 20 children displayed frank jaundice or any signs of acute hepatitis. Although a relatively mild rash was noted in 16 cases, all the children......

10

Materials and methods

In January 1969, all children of the child welfare centre on whose feeding habits were known, and who were 5 years of age or less, were invited to participate in the study. After obtaining informed written consent, each child was given a detailed dietary history, and in addition, a liver biopsy was taken. The children were then divided into two groups, A and B. Group A consisted of 10 children who had consumed groundnut oil and peanut meal for periods ranging from 6 days to 6 months. Group B consisted of 10 children who had not consumed groundnut oil or peanut meal. Each child was given a detailed dietary history, and in addition, a liver biopsy was taken. The children were then divided into two groups, A and B. Group A consisted of 10 children who had consumed groundnut oil and peanut meal for periods ranging from 6 days to 6 months. Group B consisted of 10 children who had not consumed groundnut oil or peanut meal. Each child was given a detailed dietary history, and in addition, a liver biopsy was taken.
After 2 years, six children, including a pair of siblings, still have enlarged firm livers 13 to 5 cm. Liver biopsies were refused by the parents. Of the remaining eight cases, there is no follow-up at this date.


diagnosis of the liver

The first liver biopsy was taken approximately 1 to 2 months after consumption of the toxic meal, when the majority of the children returned to the clinic. It revealed moderate to severe fatty infiltration without any changes in the tubular architecture and the presence of an inflammatory exudate extending into the hepatic parenchyma (Fig. 1).

In four cases, liver biopsies showed severe fatty infiltration and an entirely undisturbed tubular pattern. In two cases, hepatic cells were severely damaged and often showed no nuclear staining with ballooning of cells, focal necrosis and inflammatory reaction were frequently seen. Biopsy taken after 4 months

Fig. 1. Shows severe fatty infiltration of the liver. H&E X 200.
fibrous tissue appearing from the portal tract and infiltrating into surrounding parenchyma followed by severe cellular infiltration in which peribiliary fibrosis was often seen. In two cases, septa extended into the parenchyma, but the lobule was not sealed. Focal necrosis was frequently seen. A portal tract often contained inflammatory cells. Fine connective tissue membranes were seen extending throughout the parenchyma. In some areas, the connective tissue membranes were seen extending throughout the parenchyma. Also in some areas, the connective tissue membranes condensed to form an acinus, producing fibrosis with strand-like inflammatory exudate (Fig. 2). Biopsies taken from children between 10 months and 1 year old showed complete abolition of the lobular architecture with dissection of septa of varying thicknesses. The typical regenerative changes were not seen. In some cases, the bile cells appeared unaltered and showed phasophilia of the persisting cytoplasm. Many cases, focal coagulation occurred in containing cells. Focal necrosis was frequently observed and bile duct proliferation was increased. The fibrous tissue septum surrounding the lobule contained variable numbers of inflammatory cells with moderate ductular proliferation and fat-containing hepatic cells (Fig. 3). The section stained for reticular fibers showed dissection of lobular architecture by septae of varying thicknesses (Fig. 4). Muscle biopsies done on all cases after 1 to 2 months revealed acute fragmentation with loss of striations and cellular infiltration. In the repeat biopsies done after 6 to 8 months, fragmented muscle bundles with interstitial fibrosis, fatty infiltration, and chronic inflammatory cells were seen (Fig. 5).

Discussion

The fact that kwashiorkor rarely progresses to cirrhosis is well documented (8, 9). The etiology of Indian childhood cirrhosis is obscure (4). Since 1961, 3,500 children with protein-calorie malnutrition have been treated by us on an outpatient and inpatient basis with protein-rich peanut meal. In more than 7000, the follow-up has been for more
than 1 year and in several cases for more than 3 years. It was customary to perform a liver biopsy on admission, then 1 month after disappearance of edema with subsequent weight gain, and when the albumin globulin reversal came to normal. We found that fatty metamorphosis of the liver rapidly yielded to dietary protein supplements, and the livers became normal within 6 weeks. In no case has cirrhosis of the liver been noted clinically or on liver biopsy material. We present this observation as a control factor in the absence of a controlled study. In contrast, the children who consumed peanut protein contaminated with aflatoxin showed a gradual transition from an increased central and periporal fat of the liver to formation of fatty cysts to fibrosis and cirrhosis over a period of 1 year. Repeated analyses of these protein-rich foods over the years reveals the aflatoxin content to be less than 30 µg per kg. The urine of cases reported here were consistently negative for aflatoxin. In our animal experiments, it was noted that aflatoxin B1 was excreted in the urine in small amounts within 24 hr. In these 20 children who consumed contaminated meal, the earliest signs (as is usual with infantile cirrhosis also) were gastrointestinal, at which stage the toxic meal was discontinued. Urine was collected for aflatoxin content after a fortnight, when increased hepatomegaly was obvious, and the toxic meal was analyzed. We could in no way correlate the severity of liver pathology with aflatoxin found in urine of 7% of the 250 cirrhotic children studied (5). We have also found aflatoxin in the urine of 10% of normal children (5). The explanation we put forward on the basis of our experience with these kwashiorkor cases is that the exact period of toxic injury - long past by the time characteristic hepato...
Fig. 4. Shows dissection of lobular architecture by septa. Reticular stain × 200.

Fig. 5. Metabolism showing hepatic cytoplasm and fibrosis. HE × 200.
as the occurs, and when the duration of Indian childhood cirrhosis continues. In these children, it is important to be aware for characteristic clinical and histopathological lesions to occur in the liver that produce of aflatoxin in the urine of children and non-
\[...

Malini et al. have reported that pro-
tem depletion in weaning caused the toxic effects of aflatox in the liver. The
\[...

Summary

Generalized abnormalities of gastrointesti-
nal function and incidentally, a number of cases of liver disease, were noted over a period of 4 weeks. The patients showed a general loss of appetite and anorexia in central obesity, and a few weeks with aches and colds. The results are identical to those of Indian childhood cirrhosis.

References

1. Abraham, R. and R. R. A. Gopalan, 
2. P. B. B. S. Seneviratne, M. A. M. 
3. C. D. S. Seneviratne, M. A. M. 
4. T. T. T. J. A. Weeraratne, 
5. M. V. S. C. A. Perera, 
6. T. T. T. J. A. Weeraratne, 
7. A. P. C. A. Perera, 
8. W. D. M. P. Ratnasuriya, 
9. T. T. T. J. A. Weeraratne, 
10. A. P. C. A. Perera, 
11. A. P. C. A. Perera, 
12. A. P. C. A. Perera, 
13. T. T. T. J. A. Weeraratne, 
14. A. P. C. A. Perera, 
15. T. T. T. J. A. Weeraratne, 
16. A. P. C. A. Perera, 
17. T. T. T. J. A. Weeraratne, 
18. A. P. C. A. Perera, 
19. T. T. T. J. A. Weeraratne, 
20. A. P. C. A. Perera,