The New England Journal of Medicine

Established in 1812 as The NEW ENGLAND JOURNAL OF MEDICINE AND SURGERY

VOLUME 313 DECEMBER 19, 1985 NUMBER 25

Original Articles

Special Article

Medical Intelligence

Case Records of the Massachusetts General Hospital

Editorial

Correspondence

Overseas edition printed in England by Ambassador Press Ltd., St. Albans, Herts, and published by the Massachusetts Medical Society, 13 Colina Road, London N15 3JA.
Registered as a newspaper at the Post Office. ISSN 0028-4793

PLASMA ATRIAL NATRIURETIC FACTOR IN PATIENTS WITH CIRRHOSIS

To the Editor: Despite intensive study, mechanisms of disturbed renal sodium handling in patients with cirrhosis of the liver have not been completely elucidated. Evidence that hyperaldosteronism can-

not totally account for the retention of sodium and water in cirrhosis has prompted an increasing interest in other hormonal systems.[1] Within the past several years the existence of a circulating natriuretic hormone[2,3] and its importance in sodium retention in patients with cirrhosis[4-6] have been proposed. The inability to measure and define this putative natriuretic hormone adequately, however, has impeded advances in investigating its role.[7]

Recently, the atrial natriuretic factors have emerged as novel regulatory peptides with natriuretic, diuretic, and smooth-muscle-relaxant properties.[8-11] We have demonstrated the occurrence of alpha-human atrial natriuretic factor — the authentic 28-amino acid–residue portion of the precursor hormone in human plasma[12] — and have observed elevated levels of atrial natriuretic factor in patients with hypertension[13] and patients with congestive heart failure (Arendt RM, et al.: unpublished data). Here, we present data on plasma levels and the structure of atrial natriuretic factor in patients with cirrhosis.

Nineteen patients with cirrhosis were evaluated; ascites was not evident in nine, was moderate in five, and was tense in five. The patients with ascites received spironolactone (100 to 400 mg daily by mouth). Twenty patients with no evidence of cardiovascular, renal, pulmonary, or gastrointestinal diseases served as controls. Measurement and molecular-weight analysis of plasma atrial natriuretic factor were performed as previously described.[12] Plasma levels of atrial natriuretic factor were significantly higher in the patients with cirrhosis than in controls (5.9 to 29.1 vs. 3.5 to 18.3 fmol per milliliter; median, 13.2 vs. 9.6 [$P<0.05$, two-tailed Mann–Whitney test]). Concentrations in the patients with tense ascites ranged from 7.4 to 16.5 fmol per milliliter and did not differ from values in the other cirrhotic patients. After spironolactone was discontinued in the patients with ascites, atrial natriuretic factor increased by an average of 47 per cent.

It has been hypothesized that an inability to elaborate a natriuretic hormone adequately contributes to sodium retention in cirrhosis.[1] However, plasma levels of atrial natriuretic factor in our cirrhotic patients were found to be even higher than normal. Moreover, the increase after discontinuation of spironolactone treatment does not indicate impaired release of atrial natriuretic factor in cirrhosis. This finding supports the opinion that the postulated natriuretic hormone found to be decreased in patients with cirrhosis is not identical with atrial natriuretic factor.[14]

Despite normal or elevated plasma levels of atrial natriuretic factor, structural defects of this peptide could be responsible for diminished natriuresis in cirrhotic patients. Different processing of the precursor hormone[11] might result in peptides with less diuretic and natriuretic effect. High-performance gel-permeation chromatography, however, has not revealed the existence of precursor hormones. Neither gamma-human atrial natriuretic factor — the N-terminal–extended fragment containing alpha-human atrial natriuretic factor — nor other precursors could be detected. Thus, we have found no evidence for absolute deficiency or abnormal processing of atrial natriuretic factor in cirrhosis.

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