Report

The biochemistry of breast cyst fluids and duct secretions

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Summary

The ratio of potassium to sodium concentrations in breast fluids has led other investigators to the subclassification of cysts into two types: 1) apocrine (secretory) cysts with high potassium and low sodium, and 2) attenuated (flattened) cell cysts with low potassium and high sodium content. Apocrine cells are thought by some to actively secrete potassium. Cell typing is considered important as apocrine cysts are more likely to be bilateral, multiple, recurrent, and serve as markers for epithelial cell atypia.

A retrospective study of the biochemical analyses of 58 cyst fluids and 28 duct secretions obtained by nipple aspiration was conducted. Potassium and sodium concentrations obtained from 12 cyst fluids were statistically correlated with creatinine concentrations. Evidence is presented indicating that micro cysts are initially apocrine in cell type and are more likely in continuity with the terminal ductal-lobular unit. It is postulated that apocrine cysts undergo cellular desquamation and lysis, becoming attenuated cysts. The ratio of potassium to sodium is altered by cell degradation rather than active secretory processes. Biochemical contents of cysts and nipple aspiration fluids are compared.

The biochemistry of breast cyst fluids and duct secretions

Breast cyst fluids have been found to contain large amounts of specific steroids, hormones, and other biochemical substances, the concentrations of which bear a relationship to the relative sodium and potassium content of those fluids [1]. The initial inorganic ion analyses on breast cyst fluids performed by Fleisher et al. in 1973 [2] indicated that 10 of 16 fluids contained sodium in concentrations less than 50mEq/L and potassium in excess of 100 mEq/L. Additional studies followed, not only on cation content, steroid hormone accumulations, protein fractionations, and other biochemical constituents in human breast cyst fluids [3], but likewise in human breast ductal secretions [4, 5].

It was not until 1983 that Bradlow et al. [6] and others [7–9] recommended subcategorization of breast cysts and their biochemical constituents into three types according to the relative content of sodium and potassium. It remained for Dixon et al. [10] to separate cyst fluids into two major groups. In one group, the Na⁺ levels greatly exceeded the K⁺ levels, resembling plasma, and in the second group, K⁺ was the predominant cation. Cyst fluids in the first group contained low levels of the androgen conjugate dehydroepiandrosterone sulfate (DHA sulfate) and the non-secretory (7S) form of immunoglobulin A (IgA) in contrast to the high K⁺ group which contained high concentrations of DHA sul-

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fate and the secretory (11S) form of IgA, suggesting that the endothelium lining such cysts was active and secretory [11]. Additionally, Dixon et al. [12] found that all cysts wherein the Na/K ratio was 2 or less were lined by apocrine epithelium and those with a ratio of greater than 3 were lined by flattened or attenuated epithelium. The usefulness of cyto-
lologic typing, however, was questioned by Bundred et al. [13]. More recently Leis [14] reported that cyst 
typing according to cyst fluid analysis for Na and K corresponded accurately with typing by histologic 
examination of the cells lining the cyst walls but in-
accurately with typing by the cytologic determi-
nation of apocrine cells.

The clinical significance of cyst subtyping has 
emerged from reports that the apocrine type of cyst 
was not only more prone to be multiple, bilateral, 
and associated with a higher risk of cyst recurrence 
[10, 14] but was more likely to serve as a marker for 
epithelial cell atypia [14–16], often associated with a 
higher risk for the development of breast cancer.

An association of apocrine cell type cysts with 
breast carcinomas was given impetus in 1983 by the 
finding of Mazoujian et al. [16] that a glycoprotein 
designated as GCDFP-15 is a specific tissue marker 
of apocrine epithelium and is found in a high per-
centage of breast carcinomas retaining apocrine 
features. Others, however, do not support a direct 
association of gross cystic disease, apocrine type or 
other, with breast cancer [17–21]. Many investiga-
tors, including Leis [14], however, seem to be in ac-
cord with Dogliotti [8] that apocrine cysts secrete 
and probably concentrate many organic and inor-
ganic substances including potassium, serve as a 
marker for precancerous change in the surrounding 
breast tissue, and ‘should be considered at present 
as complex endocrine entities rather than passive 
containers in which fluids are stored’ [8].

It is the purpose of this paper to report on: 1) early 
cyst formation as visualized by contrast ductogra-
phy, and 2) biochemical studies performed by the 
author in 1975 (eighteen years ago) on the fluids of 
breast cysts and secretions obtained by nipple aspi-
ration from the mammary duct system. At that 
time, the author was collecting fluids for cytologic 
evaluation from both the mammary duct system via 
nipple aspiration and from mammary cysts by fine 
needle aspiration. Cytologically, cyst fluid prepara-
tions differed from those obtained through nipple 
levels by the frequent presence of apocrine 
cells and abundant cell detritus. It was in order to 
find a common link between these mammary fluids 
that biochemical evaluations were sought. Accord-
ingly, collected fluids were sent for evaluation by 
chemistry panel with occasional electrolyte panels 
being obtained when the sample size was sufficient. 
Alterations found in the sodium and potassium 
concentrations, in addition to lowered protein and 
albumin concentrations and elevated phosphate, 
uric acid, and creatinine levels in cyst fluids as com-
pared to duct secretions and plasma, led this investi-
gator to surmise that the desquamated intracystic 
cyst lining apocrine cells had undergone desquama-
tion and lysis with release of potassium and intracel-
ular contents. The protein content had apparently 
been degraded by proteolytic enzymes. In conse-
quence of that analysis, biochemical determina-
tions were discontinued and the findings were not 
considered of significant importance for publica-
tion. Recent reports in the literature indicating that 
active apocrine secretion is responsible for the bio-
chemical alterations and changes in steroid and 
protein content of cyst fluids [8, 14] prompted a re-
view of our data. The subsequent review of the data 
obtained from the biochemical analyses indicated 
significant correlations of creatinine concentrations 
with other constituents of breast cyst fluids. As a re-
result, we believe now, as we did then, that the alter-
ations commonly found in the electrolyte and bio-
chemical profiles of breast fluids in cysts are pro-
duced by cyst wall epithelial cell degenerative 
changes rather than secretory processes distinct 
from those of the terminal ductal-lobular units.

Methods

Contrast ductograms performed on 52 women with 
clinical evidence of gross cystic disease were re-
viewed for evidence of micro or macro cyst visual-
ization. Ductograms of patients with spontaneous 
discharge or having gross cysts secondary to papil-
lomas were excluded. Details of the technique for 
performing contrast ductography by the insertion