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Electrolytes and pH of Mammary Cyst Fluid and Their Relation to Cyst Pathology

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Abstract

The relation between intracystic levels of Na^+ , K^+ , Na^+/K^+ ratio, pH and the cytologic appearance of fluid contents and the histopathology of gross mammary cysts was studied in 182 gross mammary cysts. Na^+ level was inversely correlated to K^+ level ($p < 0.001$). Two types of cysts were identified; the first group (105 cysts) with Na^+/K^+ ratio < 3 and the lining was mainly metaplastic apocrine epithelium, the second group (77 cysts) Na^+/K^+ ratio was > 3 and the lining was flattened ductal epithelium. Na^+K^+ was also found to be inversely correlated with the degree of epithelial hyperplasia of the cyst wall ($P < 0.005$). Poor correlation however was found between cytologic appearance of cyst fluid contents and the degree of hyperplasia.

Introduction

WOMEN with gross cystic disease of the breast are at increased risk of developing breast cancer[1]. It was also elucidated that patients who develop cysts lined by apocrine epithelium may be at greater risk of subsequent breast cancer than those with cysts lined by flattened epithelia[2,3].

Moreover, a relationship exists between cyst fluid composition and the cyst lining epithelium, with apocrine epithelial lining being more associated with higher levels of K^+ than that found in cysts with a mainly flattened epithelial lining[4].

Other reports have also referred to the association between apocrine cells and the low ratio of Na^+ to K^+ in mammary cysts[5,6,7].

The present work is designed to evaluate the relation between the cations of mammary cyst fluid and histopathologic nature of those cysts in a group of patients with gross cystic lesions.

Material and Methods

One hundred eighty two cysts from 140 females aged 20-60 years (mean 37.3

years) were aspirated, analysed and examined histopathologically after surgical excision. Inflammatory cysts were excluded. Patients were sonographed before aspiration to assure a cystic nature. The amount of aspirated fluid ranged between 0.5 and 6 cm.

Biochemical analysis was carried out (on small fraction of the aspirate; only about 20 μ l) by emission flame photometry technique according to Henry et al[8]. A cut point of 3 for the Na^+/K^+ ratio centrifuged samples were stained with Papanicolaou staining. Histopathological examination was carried out for the excised cysts using paraffin section technique.

Results

Cysts varied in size and fluid content. The occurrence was bilateral in 77 cases (55%). The appearance of the aspirate was dark green in 84 of the 182 examined cysts and straw coloured in the remaining 98 cysts.

The chemical analysis of the cyst fluid showed that in 105 (57.7%) cysts the Na^+/K^+ ratio was less than 3. The Na^+ level varied from 18 mEq/L to 322 mEq/L with a mean of 77.66 ± 31.18 while the K^+ level varied from 16 mEq/L to 106 mEq/L with a mean of 63.57 ± 28.80 (Table 1).

Table (1) : Cations and Na^+/K^+ Ratio in Mammary Cysts.

Na^+/K^+	No.	%	Mean Na^+ (mEq/L)	Mean K^+ (mEq/L)
< 3	105	57.7	77.66 ± 31.18	63.57 ± 28.80
> 3	77	42.3	102.18 ± 21.25	17.96 ± 7.34

P < 0.05

In 77 (42.3%) cysts the Na^+/K^+ ratio was more than 3. The Na^+ level varied from 73.5 mEq/L to 180 mEq/L with a mean of 102.18 ± 21.25 while the K^+ level varied from 6 mEq/L to 30 mEq/L with a mean of 17.96 ± 7.34 (see Table 1).

The relation between the lining epithelium and the cyst fluid chemistry is shown in Table (2).

Cytological examination of the cyst fluid showed that 63 cysts (34.62%) had apocrine metaplasia, while histopatholo-

gical examination revealed more prevalent apocrine metaplasia as it was found in 98 cysts (53.4%). Flattened lining with no recognizable apocrine cells was found in 77 cysts (42.3%) while only 7 cysts (4.3%) showed a mixed epithelial lining.

All the cysts lined with flattened epithelium showed Na^+/K^+ ratio more than 3. The cysts lined by apocrine epithelium showed Na^+/K^+ ratio less than 3. while cysts lined with mixed epithelium showed exactly as similar picture as those lined with pure apocrine epithelium.

Table (2) : Relation between Cations, Cations, Na⁺ /K⁺ Ratio and Lining Epithelium in the 182 Mammary Cysts.

Epithelium	No.		Sodium (Na ⁺) and potassium (K ⁺) in mEq/L				
			Na ⁺ /K ⁺ < 3		Na ⁺ /K ⁺ > 3		
		No.	Mean Na ⁺	Mean K ⁺	No.	Mean Na ⁺	Mean K ⁺
Apocrine	98	98	57.8 ± 33.4*	63.2 ± 26.2**	—	—	—
Flattened	77	—	—	—	77	102.18 ± 21.3*	17.96 ± 7.4@
Mixed	7	7	75	42	—	—	—
Total	182		105 (57.69%)			77 (42.81%)	

* P < 0.001

**P < 0.0001

@ P < 0.001

The relation between the lining epithelium and the pH of the cyst fluid is shown in Table (3).

Difference in the pH between apocrine and flat cysts was statistically significant ($P < 0.001$).

Most cysts lined with apocrine cells

(85.7%) showed acidic fluid (pH from 4.8 to 6.4), while only 14 cysts (14.3%) showed alkaline fluid (pH 7.3 to 8.6).

On the other hand, all cysts lined with flattened epithelium showed alkaline pH (7 to 9.2). Mixed epithelium cysts showed a pure acidic pH (5 to 6.8).

Table (3) : The Relation between the Lining Epithelium and pH.

Epithelium	Acidic pH		Alkaline pH		Total No.
	No.	Mean pH	No.	Mean pH	
Apocrine	84	5.96 $\pm$ 0.78	14	8.10 $\pm$ 0.5	98
Flat	—	—	77	8.07 $\pm$ 0.6	77
Mixed	7	6.8	—	—	7
Total No.	91	—	91	—	182

Discussion

The present study has demonstrated the heterogeneity of the mammary cysts of the gross cystic disease both morphologically and chemically, a finding which is shared with Wellings et al, Dixon et al, Yap et al, Miller et al, and Boccardo et al.[4,7,11,12,13]. On the other hand other researchers have been unable to confirm this finding[14].

The present study proved that all the cysts where the Na^+/K^+ ratio was less than 3 were lined with apocrine epithelium and those with a ratio greater than 3 were lined with flattened epithelium. A finding which could be explained by the electron microscopic studies of the breast cyst epi-

thelium which have shown that the apocrine cells contain many mitochondria and apical secretory granules, in contrast to flattened epithelial cells which contain few organelles, so apocrine secretion is formed by expelling the content of the intracellular secretory granules which have high K^+ [15,16].

A significant statistical difference was also found in the intracystic fluid pH between the apocrine lined cysts which had acidic pH and the flat epithelium lined cysts which had alkaline pH. This finding coincides with the findings of Gasty et al [17] and Dixon et al.[2].

Apocrine change has been reported to be more frequent in females at high risk of breast cancer[1,11,18].

This study has shared the conclusion of the availability of detecting apocrine change in GCD as an indicator for a possible malignant change through electrolyte and pH analysis of the cyst fluid content even without biopsy taking. A finding which might help in identifying patients at increased risk of cancer and also helps better understanding of the pathophysiology of GCD.

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