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Clinical Presentation and Prolactin Level of ANDI (Aberration of Normal Development and Involution) Patients of Breast

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Abstract: ANDI (Aberration of normal development and involution) classification covers most of the benign breast conditions as a result of hormonal influence. Prolactin plays an important role in normal proliferation and differentiation of breast epithelium. The objective of this hospital based study was to find out clinical presentation and prolactin level of ANDI patients. Total 330 patients with different conditions of ANDI visited surgical out patient department of Liaquat University of Medical and Health Sciences from May 2005-May 2006. 200 were selected for their Prolactin levels measurments apart from other clinical, radiological, cytological or histopathological investigations. Only 30 (15%) patients found to have raised Prolactin. 27% of multiple fibroadenoma, 12.5% with recurrent fibroadenoma, 13.3% with cyclical nodularity, 6.5% with mastalgia, 4.8% with fibrocystic disease, 23% with fibroadenosis and 71% with galactorrehea along with fibrocystic disease were having raised Prolactin. The result of our study suggest that Prolactin hypersecretion is likely etiological factor in some of the conditions of ANDI, rest may be due to end organ hypersensitivity to normal circulating Prolactin or other hormones. Pharmacological manipulation of raised prolactin in patients can provide relief from symptoms.

Key words: ANDI · prolactin · fibroadenoma · fibroadenosis · mastalgia · fibrocystic disease · galactorrhea

INTRODUCTION

Mammary glands have physical as well as psychological importance in human females [1].Benign breast diseases constitute the major workload in breast clinics [2]. The histological changes of benign breast diseases are in reality part of spectrum of changes that occur in the life time of breast tissue [3]. A comprehensive classification which puts all of these process of physiological changes, growth, development and involution in a single framework is ANDI (Aberration of normal development and involution) classification [4]. This includes six conditions, two are developmental (Adolescent hypertrophy and fibroadenoma), two are cyclical (mastalgia and clinical nodularity) and two are involutionary (cyst formation and sclerosing adenosis) [5]. Prolactin plays an important role in the proliferation and differentiation of normal breast epithelium [6]. Several studies have shown that serum prolactin level may be increased in patients with breast pain and other benign breast diseases including fibrocystic disease and fibroadenosis [7-9]. It is suggested that patients with benign breast lumps and pain should be screened for clinical or laboratory evidence of hyperprolactinemia [10-12]. Serum prolactin test requires a sample that should be drawn in the morning at least 2 hours after patient awakes as sample drawn earlier may show sleep induced peak level [13]. No restriction of food,fluid and physical activity is required but patient should relax half an hour before test [14, 15]. Reference ranges vary from laboratory to laboratory but are generally within following range. Adult male 0-20 ng ml^{-1}, adult female 0-20 ng ml^{-1}, pregnant female 20-400 ng ml^{-1} [16, 17].

We did not find any study regarding serum prolactin in breast disease in our local surgical literature. Large numbers of female patients attend our surgical out patient breast clinic for benign breast diseases and quite few of them are treated non surgically by different

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pharmacological agents including anti prolactin. Aim of our study was to profile andI patients and to evaluate relation of serum prolactin level with their presentation which in turn helped in management of these patients.

MATERIALS AND METHODS

This study was conducted in breast clinic setting of surgical outpatient department of Liaquat University of Medical and Health Sciences Hospital, during May 2005-May 2006. The study design was observational, prospective and non interventional. Patients of all age group who were attending our breast clinic with any of the six conditions coming under the heading of ANDI were included in our study to profile the presentation of ANDI in our breast clinic.

Patients with recent history of pregnancy, lactation, hormonal intake, or clinical, radiological or histopathological evidence of inflammatory or malignant lesion were not included. All patients with adolescent hypertrophy, multiple or recurrent fibroadenomas, moderate to sever mastalgia, moderate to sever cyclical nodularity, multiple cysts, fibrocystic diseases, galactorrhea and gross fibroadenosis had their serum Prolactin levels recorded from samples taken at least 2 hours post awaking. Patients with solitary fibroadenomas, mild to moderate mastalgia or nodularity and simple cysts were not sent for serum prolactin as they were managed by just reassurance or other simple measures like pain killers and simple excision or aspirationAll patients of less then thirty five years of age with lump or galactorrhea were sent for ultrasonography with high frequency probe. Patients more then thirty five years of age with doubtful pathology were sent for mammography. All patients with lump or lumpiness were sent for FNAC to have documented record of cytology and in doubtful cases true cut biopsy was also performed to exclude malignancy.

A detail Performa pertinent to our study was filled for every patient, in which details about symptoms, examination findings and radiological, cytological or histological findings along with serum prolactin levels were mentioned.

RESULT

A total 330 patients were included in the study. The age range of patients was between 15-50. Maximum numbers of patients were between 2nd and 3rd decades of life (Table 1). Out of 330 patients 6(1.8%) were having

Table 1: Age wise distribution of the patients

Group	Age of the patient	Number of the patients	Patients (%)
A	< 25	198	60
B	25-35	86	26
C	>35	46	14

Table 2: Different conditions of ANDI with raised S. Prolactin levels

S. No	Condition of ANDI	No. of patients	Patients (%)	No. of patients with raised prolactin	Condition with raised prolactin (%)
1	Adolescent hypertrophy	6	3	0	0.0
2	Multiple Fibroadenomas	18	9	5	27.0
3	Recurrent Fibroadenoma	8	4	1	12.5
4	Cyclical nodularity	30	15	4	13.3
6	Mastalgia	48	24	3	6.25
7	Fibrocystic disease	41	20.5	2	4.8
8	Fibroadenosis	42	21	10	23.0
9	Galactorrhea (with fibrocystic disease)	7	3.5	5	71.0
	Total	200	100	30	

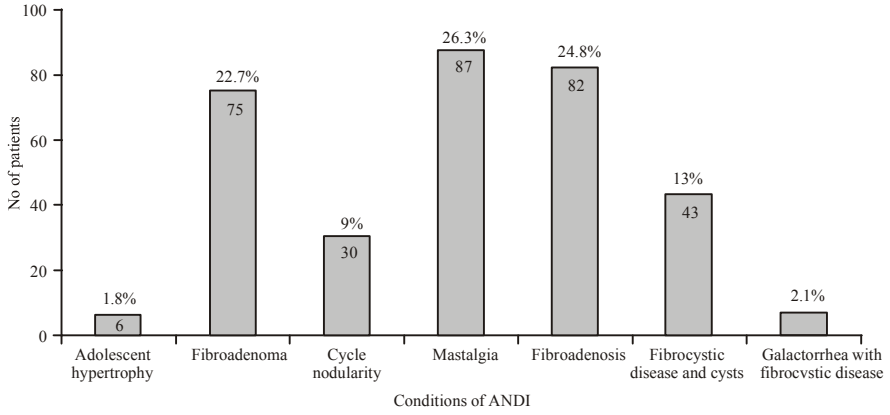

Fig. 1: Graphical presentation of different condition of ANDI

adolescent hypertrophy. 75 (22.7%) patients presented with fibroadenomas which include solitary fibroadenoma, fibroadenoma with adenosis, multiple and recurrent fibroadenomas. 87 (26.3%) patients presented with mastalgia both cyclical and non cyclical. 30 (9%) were having moderate to sever cyclical nodularity. 43 (13%) patients were having fibrocystic disease 2 of them were having solitary cyst. 82 (24.8%) patients had fibroadenosis with or without mastalgia. 7 (2.1%) patients came with galactorrhea with fibrocystic disease Fig. 1. Out of these patients we excluded 100 patients of solitary fibroadenoma, mild adenosis, mild to moderate mastalgia and solitary simple breast cyst for treating them by different means without having their serum Prolactin levels done. Remaining 200 patients were selected for their serum Prolactin levels and laboratory results were obtained. Out of 200 only 30 (15%) patients were having raised S.prolactin level. The range of prolactin was from 28-300 ng ml^{-1} (Table 2).

DISCUSSION

Female patients come to breast clinic with symptoms including breast lumps, nodularity, pain, nipple discharge etc [18]. Benign breast diseases classified by ANDI (aberration of normal development and involution) constitutes the major workload in breast clinic [2]. Benign breast disease results from an imbalance or inappropriate target gland response to changing tide of hormonal stimulation. The presence of fibrocystic increases the risk of cancer by 2.64 times, it is important to find out those women who are at greater risk of developing mammary cancer [19]. On the ground of clinical and experimental studies it has been found to have connection between prolactin and breast pathology especially in carcinoma [12]. So to find out profile of ANDI patients and serum prolactin level is important because of possibility of multiple risk combinations [8]. In our study with 330 patients of ANDI we got maximum number of patients (60%) in age range of 15-25 which is slightly different from most of the studies where benign breast diseases apart from fibroadenoma is most common in 2^{nd} and 3^{rd} decades of life. Commonest symptom with which 26.3% of our patients presented was mastalgia which is similar to the results of Maj Kumar [20] and Uma [18] who also got mastalgia as commonest symptom in their studies. 9% patients came with cyclical nodularity which is almost equal to Uma [18]. Fibroadenosis was there in 24.8% of patients with or without mastalgia, which is higher then studies by Uma [18], Jamal [21]and Mansoor [22] where adenosis was 17.6, 14 and 14.5% respectively, but it is near to the studies by Shabtai [23], Inekwaba FN [24] where adenosis was 23 and 29.3% respectively. 22.7% of our patients were having fibroadenomas which is quite lower then studies by Inekwaba [24], Chaudhuri [25] and Muritlo [26] where presentation of fibroadenoma is 55, 62 and 38% respectively, but it is near to study by Kumar [20]. We got 13% patients with fibrocystic disease which is almost equal to study by Siddique [27] who got fibrocystic disease 13.96%, but it is quite lower then study by Ciatto [28] who got 43.2% patients with fibrocystic disease. 2.1% patients came to us with galactorrhea with fibrocystic disease which is within the range given by Sakiyama [29] i.e. 0.1-32%. We got 1.8% patients with adolescent hypertrophy for which we did not get any comparable reference. Out of 200 patients we selected for serum prolactin levels only 30(15%) were having raised serum prolactin level which is higher then study by Gorin-A [30] who found normal prolactin level in benign breast disease in his study, but it is near to the study by Nicol [31] who had 7% patients of benign breast disease with raised S.Prolactin level. In our study we found maximum number 71% patients with raised prolactin level who were having galactorrhea with or without fibrocystic disease which is within the range given by Sakiyama [29] according to him 49-77% patients with galactorrhea have non puerperal hyperprolactinemia. None of our patient with adolescent hypertrophy of breast has raised prolactin level, which is in favor of results in study by Arscott [32] who said that etiology of pubertal gigantomastia may involve breast tissue hypersensitivity to hormones other than prolactin. 27% of patients with multiple fibroadenoma, 12.5% with recurrent fibroadenoma, 9% with cyclical nodularity and 23% patients with fibroadenosis were having raised serum prolactin level. This result is in favor of study by Strollo [33] who found raised prolactin levels in benign breast disease and hypothesized that raised serum prolactin is interact with oestradiol to give mammary gland hypertrophy. We found 6.25% patients of moderate to sever mastalgia having raised serum prolactin which is quite low then study by Kumar [34] who found significantly high level of serum prolactin in patients with mastalgia. Same is with fibrocystic disease where we got only 4.8% patients having raised prolactin levels which is about ten times less then level found by Peter [35] and Bischoff [36] in their study which is 45.6% and 58% respectively and they consider prolactin as etiological factor of gross cystic breast disease. Our results contradict with Wypych [9] who considers prolactin

hyper secretion as a hormonal reason for benign breast diseases. From results of our study we concluded that ANDI is group of conditions which is more prevalent in young females in our part of world and prolactin hyper secretion is responsible as an etiological factor in some of the cases not in all the cases. It could be end organ hypersensitivity to normal circulating levels of prolactin or other hormones or environmental factors are responsible for benign breast disease. Pharmacological manipulation of prolactin in patients having raised serum levels can provide relief from symptoms. Patients who have raised prolactin levels along with fibrocystic breast disease should be regularly follow up as they are prone to develop breast cancer due to multiple risk factors combination.

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