

PINEAL CALCIFICATION AMONG BLACK PATIENTS

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A postmortem histopathological study was done in 233 pineal glands of black patients. Among them, 70 percent showed microscopic evidence of calcification in the pineal parenchyma. The frequency of calcification increased with age. However, the severity of calcification reached the peak in the 60 to 69 year old age group and then gradually declined. As compared to males, females had slightly higher frequency and reached the peak of severity in younger age groups. When pineal calcification was compared among patients with various malignancies, a higher frequency and more severe calcification were observed in patients with carcinoma of the prostate and the pancreas. A lower frequency and less severe calcification were observed in patients with carcinoma of the breast and the cervix. The results of this study emphasize the important role of sex hormone in genesis of pineal calcification.

Pineal calcification has long been observed and it is so common that radiologists use it as a guide to identify the midline of the brain in skull x-rays. However, very little is known about the patho-

physiological significance of this common phenomenon, apparently due to our ignorance of the pineal gland in the long past medical history since it had been considered as a vestigial organ of human body. Its antigonadotrophic function was first suggested by the observed association of pineal tumors in children with precocious puberty and it was recently proved by pinealectomy experiments.¹⁻³ The recent advance in biochemical methodology has enabled scientists to perform more fruitful investigations on the pineal gland and some breakthroughs have been achieved. The information accumulated from animal experiments indicated that the pineal gland functions as a neuroendocrine transducer, translating neural impulses into hormones responsive to rhythmic diurnal phototic stimulation.⁴⁻⁶ There are reasons to believe that the pineal gland serves as a regulator of the entire endocrine system mediated through the hypothalamus and/or pituitary gland. In fact, many hormone related substances have been identified in the pineal tissue. Among them, the most important and well known one is melatonin (5-methoxy-*n*-acetyl tryptamine).⁵ In addition to its antigonadotrophic function, animal experiments also demonstrated inhibitory influences on the pituitary-thyroid axis, the pituitary-adrenal axis, and pituitary secretion of growth hormone.⁷⁻⁹

Pineal calcification may start in early childhood and progress with age.¹⁰ However, this calcification apparently does not disrupt the integrity of secretory pinealocytes and the enzymatic activity

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within the gland appears to persist with the advancing age.¹¹ Its prevalence on skull x-ray films varies greatly in different population groups; a much higher incidence in European whites and a lower incidence in Asians and Africans were reported.^{12,13} A comparison between American whites and blacks on skull x-ray films also indicated significantly higher incidence in whites than in blacks (26.4 percent against 16.1 percent in adult age).¹⁴ However, most of the x-ray studies of incidence may be inaccurate because of the difficulty in identifying minute foci of calcification and the high incidence of calcification in immediate surrounding tissues in the pineal region (capsule, choroid plexus, and habenular commissure) which is indistinguishable to the radiologists. Doubtless, a histopathological study is more desirable to provide more accurate and detailed information on pineal calcification.

There is experimental evidence that the growth of animal malignant tumors can be influenced by both the pineal and melatonin.¹⁵ In humans some conflicting results have been reported on the relationship of malignancy and the weight of the pineal,^{16,17} although pineal enlargement was associated with melanoma and breast carcinoma.¹⁸ However, a systemic study of pineal activity in patients with various forms of malignancies has not yet been done. The purpose of this study is to observe the histopathological distribution of pineal calcification among American black patients. An attempt is also made to evaluate its pathophysiological significance and possible relation with various forms of malignancies.

METHODS

Histopathological examination was done on 233 pineal glands obtained from routine autopsies. All of the pineals were fixed with the brains in 10 percent formalin and were examined in situ with the adjacent brain tissue. Since the center of pineal calcification was observed to be within 2 mm of the midline,¹⁹ a sagittal midline section of the pineal, including posterior and habenular commissures, was taken. Each section was scrutinized for calcification in pineal parenchyma and its surrounding tissues (choroid plexus, capsule, and habenular commissure at the stalk area). The severity of calcification was indicated by the estimated percentage of area calcification. Only those

pineals showing more than 5 percent of area calcification were considered as significant and were included in the tabulation. The observed calcification was then subgrouped according to sex and age for further analysis and comparison.

RESULTS

General Observation

Calcification in the pineal region was not limited to the pineal gland itself. In addition to the pineal capsule, the surrounding tissues, choroid plexus, and the habenular commissure were often the sites of severe calcification. There was no observable relation between the calcification in surrounding tissues and in the pineal gland. Although the calcium deposition could be found throughout the pineal parenchyma, the center or the mid portion of the gland was most commonly and most severely involved. Frequently, the pineal tissue at the stalk area in conjunction with the habenular commissure were also severely calcified. The calcification was often associated with some degree of gliosis and/or fibrosis at the immediate vicinity. However, the remaining pineal parenchyma did not show appreciable degenerative changes. It appeared that a severe pineal calcification was often associated with pineal enlargement and the pineals devoid of calcification were often smaller.

Age and Sex Distribution of Pineal Calcification

Among 233 glands, significant pineal calcification (more than 5 percent of area calcification) was found in 124 glands (53.22 percent); 39 glands showed only minute foci of calcification (less than 5 percent of area calcification); and 70 glands (30 percent) showed no calcification.

The frequency and severity of significant calcification were tabulated according to age and sex in Table 1. As a whole, the frequency of pineal calcification increased with age throughout life and the severity reached its peak in the 60 to 69 year old age group and then slightly declined. When the age distribution was compared between males and females, the frequency of pineal calcification increased steadily throughout the life in males and fluctuated markedly in females. The severity of pineal calcification in males more or

TABLE 1. AGE AND SEX DISTRIBUTION OF FREQUENCY AND SEVERITY OF PINEAL CALCIFICATION

Age (yr)	Males		Females		Total	
	Significant Calcification* (%)	Severity** (%)	Significant Calcification (%)	Severity (%)	Significant Calcification (%)	Severity (%)
0-9	0/2	0	0	0	0/2	0
10-19	1/3 (33.33)	35.00	0	0	1/3 (33.33)	35.00
20-29	1/5 (20.00)	10.00	1/9 (11.11)	10.00	2/14 (14.29)	10.00
30-39	2/10 (20.00)	20.00	6/6 (100.00)	20.00	8/16 (50.00)	20.00
40-49	4/13 (30.77)	21.25	5/15 (33.33)	30.00	9/28 (32.14)	26.11
50-59	11/25 (44.00)	38.18	14/20 (70.00)	29.64	25/45 (55.55)	33.40
60-69	14/25 (58.33)	42.50	13/21 (61.90)	29.61	27/45 (60.00)	36.30
70-79	20/28 (71.43)	31.50	10/20 (50.00)	31.50	30/48 (62.50)	31.50
80+	8/12 (66.67)	28.75	14/20 (70.00)	27.14	22/32 (68.75)	28.18
Total	61/122(50.00)	33.77	63/111 (56.76)	28.33	124/233(53.22)	31.00

*Greater than 5 percent of area calcification

**Mean area calcification of the pineals with significant calcification by percentage

less followed the general pattern. However, it reached the peak in the 40 to 49 year old age group and then remained unchanged in females. Occasionally, severe calcification was seen also in young individuals.

Possible Relation with Malignancy

Among 72 pineal glands from patients with various malignancies, 52 (75 percent) of them showed significant calcification in parenchyma. The frequency and severity were tabulated in Table 2 according to various malignancies. Accordingly, the pineals from patients with malignancy had considerable higher frequency and slightly lower severity of calcification as compared to the general group in Table 1. The pineals from the patients with breast and cervical carcinoma had relatively lower frequency (50 percent for each) of calcification accompanied by remarkably low severity (14.16 and 8.75 percent, respectively). In contrast, the pineals from patients with carcinoma of the prostate and the pancreas had relatively higher frequency and severity of calcification.

DISCUSSION

The general histopathological observation of pineal calcification among black patients in this

study disclosed features similar to those noted in whites.¹⁰ Pineal calcification had been regarded by many as part of progressive degenerative changes of the pineal gland. This concept has been challenged by some recent works. Previous authors demonstrated persistent enzyme activities throughout the adult life in the pineal,¹¹ and there is no evidence of decreasing weight with age.²⁰ In fact, the presence of calcification contributes the increasing weight of the pineal with age and apparently does not lead to a decrease in pineal cellularity.¹⁷ All this suggests that the deposited calcium in the pineal is a by-product of metabolic activity rather than a result of pineal degeneration. Therefore, the amount of deposited calcium in the pineal constitutes a parameter of pineal endocrine activity in the past. This theory is further supported by the result of this histopathological observation.

The incidence of pineal calcification in skull radiographs has been considered relatively low among American and African blacks.^{13,14,21} However, this study indicated that pineal calcification was rather a common phenomenon among blacks (only 30 percent showed no calcification). Apparently, the low incidence on skull x-ray films was due to proportionally large numbers of undetectable calcification in the pineal glands of blacks.

The antigonadotrophic function of the pineal has been recognized.¹⁻³ Some recent works also

TABLE 2. DISTRIBUTION OF FREQUENCY AND SEVERITY OF CALCIFICATION OF PINEALS FROM PATIENTS WITH VARIOUS MALIGNANCIES

Neoplasms	Pineals With Calcification	Frequency (%)	Severity (%)
Breast	3/6	50.00	14.16
Prostate	14/15	93.33	30.66
Gastrointestinal tract	13/16	81.25	24.06
Lung	8/13	61.53	18.84
Kidney	4/5	80.00	13.00
Cervix	2/4	50.00	8.75
Pancreas	5/5	83.33	37.50
Others	5/7	71.43	35.00
Total	54/72	75.00	25.32

suggested that pineal hormones (melatonin and/or peptides) could affect the menstrual cycle by its inhibitory influence on ovulation.²²⁻²⁴ The marked fluctuation of frequency in various age groups and more severe degrees of calcification in the pineals of younger females probably reflect the interaction of the pineal and the relatively unstable female hormones. This view is also in keeping with a report using different methods.²⁰

The relation between pineal calcification and malignancy has been a subject of interest. Kutchrenko²⁵ (1941) first associated the increasing amount of calcium in the pineal with malignancy and Drexler et al²⁶ (1957) observed a higher incidence of pineal calcification in women with breast carcinoma. However, a recent study showed no difference in the weight of pineals from patients with malignant and nonmalignant conditions.²⁷ The results of this study showed lower frequency and severity of calcification in pineals from patients with carcinoma of the breast and the cervix. In contrast, the highest frequency and severity of pineal calcification was observed in patients with prostatic and pancreatic carcinoma which are male or predominantly male neoplasms. This observation probably underlines the role of sex hormones in the genesis of pineal calcification with the presence of some neoplasms. It is apparently to the contrary of some previous reports, but it is in line with the theory of hyposecretion of melatonin in pineals in association with breast carcinoma.²⁸

The histopathological features of calcification seen in the surrounding tissue is rather identical to that in pineal parenchyma. However, its pathophysiological significance may be different. The

calcification in the gland was suggested as metabolic by-product of longstanding hypersecretory activity. The calcification occurred in the stalk area including habenular and posterior commissures, is more interesting from some aspects. Anatomically, the pineal gland is a relatively free-moving body suspending in the subarachnoid cerebral spinal fluid. Its delicate stalk attaches to the diencephalic roof of the third ventricle in the region of habenular and posterior commissures. In ancient precartesian medicine, the pineal gland was regarded as the "memory valve" supported by the observation that men often shook or struck their heads as if to free a stuck valve to remember something.⁴ It is conceivable that the pineal stalk area is more subjected to chronic repeated physical strains of torsion and/or traction, especially for those who involve more violent physical activities in their lives. It is reasonable to believe that the calcification seen in the stalk area is a dystrophic one due to chronic tissue damage. This hypothesis is also supported by the observation made by Poltera and Mugondi²¹ (1976) who found more frequent calcification in the stalk area in African males than in females.²⁰

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