THE CALCIFIED PINEAL BODY AND CARCINOMA

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THE pineal body or epiphysis is one of the controversial body structures as regards function. However, recent investigation supported by morphologic evidence suggests that the pineal body serves as an endocrine gland,[1] and that it may have an antigonadotropic activity.[2] Because anatomic and physiologic changes have been noted in the endocrine glands of patients with certain carcinomas, it was thought worthwhile to study the pineal body in a series of patients having carcinoma. Since there are no known means of determining or measuring the function of the pineal body, the investigation was limited to roentgen study of pineal calcification. It is the purpose of this paper to record the roentgen findings of pineal calcification in a selected series of patients having carcinoma and those in a control group of patients not having malignant neoplasm.

Material and Method

Selection of patients. All patients having metastatic carcinoma of the brain or skull and all patients having primary carcinoma of the breast, or of the head and neck, who were examined at the Cleveland Clinic between October 30, 1945, and October 27, 1954, were selected for the initial survey. In a review of the charts of 1,172 patients, 164 were found which listed available skull roentgenograms. These 164 patients comprised the *malignant group* for this study. The sites of their primary carcinomas were as follows: breast, 73 patients; lung, 34; prostate, 12; mouth, nose, and throat, 12; lower gastrointestinal tract, 6; upper gastrointestinal tract, 3; pancreas and bile ducts, 3; kidney, 3; uterus and cervix, 3; thyroid, 1; trachea, 1; primary unknown, 13.

None of the patients in the malignant group was less than 30 years of age. Consequently, the 110 patients not having malignant disease who were selected

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as the *control group* for this study were 30 or more years of age and had roentgenography of the skull during the month of January 1953.

Evaluation of roentgen findings. On roentgenograms, pineal calcification usually is seen in the midline above and slightly posterior to the petrous portion of the temporal bone, either as a small single opacity, or as an ovoid cluster, 0.5 to 1.0 cm. in diameter, composed of small calcified areas.[3] In the present study, calcification that was not present in the midline of this region was considered to be outside of the pineal body. To assure consistent, objective evaluation, all roentgenograms for the survey were interpreted by one radiologist (T.F.M.), who was uninformed as to the previous diagnoses.

Results

For purposes of comparison, the charts of both groups of patients were separated into subgroups on the bases of age and sex of the patient (Table 1).

Malignant group. Pineal calcification was present in 108 (65.9 per cent) of the 164 patients, occurring in 48 (66.7 per cent) of the 72 men, and in 60 (65.2 per cent) of the 92 women (Table 1).

Control group. Pineal calcification was present in 64 (58.2 per cent) of the 110 patients, occurring in 40 (69.0 per cent) of the 58 men, and in 24 (46.2 per cent) of the 52 women (Table 1).

Evaluation of Results

The determinable factors that could have influenced pineal calcification in these patients were: sex, age, history of pregnancy, presence of carcinoma.

Sex. In the control group, the incidence of pineal calcification in men (69.0 per cent) was significantly greater than that in women (46.2 per cent). The difference is significant at the 5 per cent level of confidence.[4]

Age. The mean age of the women with carcinoma was 51.9 years, and the mean age of the women without cancer was 48.3 years. There was, however, a greater difference between the mean ages of the two groups of men; the mean age of the men in the malignant group was 63.6 years and that of those in the control group was 45.0 years.

History of pregnancy. The incidence of pineal calcification has been reported to be higher in women who have been pregnant,[5] but pregnancy as a factor did not appear to influence the over-all incidence of pineal calcification in the women of this series. In the control group of 52 women, marital histories were available in 48, 39 of whom had been pregnant. Pineal calcification was present in 18 of the 39 women who had been pregnant, and in 4 of the 9 who never had been pregnant. Similarly, in the malignant group, of the 84 women with available marital histories, 64 had been pregnant and pineal calcification was present in 41 (64.1 per cent) of them; and of the 20 women who never had

Table 1. — *Age and sex distribution and incidence of pineal calcification in malignant group of 164 patients and in control group of 110 patients*

Age range, years	Malignant group, no. of patients						Control group, no. of patients					
	Sex		Pineal calcif.		No pineal calcif.		Sex		Pineal calcif.		No pineal calcif.	
	M.	F.	Men	Women	Men	Women	M.	F.	Men	Women	Men	Women
30-39	0	11	0	8	0	3	21	19	14	7	7	12
40-49	15	27	8	16	7	11	11	13	9	8	2	5
50-59	27	32	18	22	9	10	14	15	9	7	5	8
60-69	24	19	18	11	6	8	9	4	6	2	3	2
70-79	6	3	4	3	2	0	3	1	2	0	1	1
Total	72	92	48	60	24	32	58	52	40	24	18	28
Total	**164**		**108(65.9%)**		**56(34.1%)**		**110**		**64(58.2%)**		**46(41.8%)**	

been pregnant, pineal calcification was present in 13 (65 per cent). The incidence (75 and 76 per cent) of pregnancy in both groups also is similar.

Presence of carcinoma. The incidence of pineal calcification in the 72 men in the malignant group (66.7 per cent) approximates that in the 58 men in the control group (69.0 per cent). However, 60 (65.2 per cent) of the 92 women in the malignant group had calcified pineal bodies as compared with 24 (46.2 per cent) of the 52 women in the control group. This difference is significant at the 5 per cent level of confidence.* This unexpected finding prompted further study of the records of the women with carcinoma.

Seventy-one (77.2 per cent) of the 92 women in the malignant group had carcinoma of the breast. Pineal calcification was present in 43 (60.6 per cent) of the 71 women with carcinoma of the breast, and in 17 (81.0 per cent) of the 21 women with other types of carcinoma. This difference is not statistically significant because of the small number in the latter group.

Thirty-six (60.0 per cent) of the 60 women with metastatic or recurrent carcinoma of the breast had calcification of the pineal body; and of the 31 of of these with metastasis to bone, 19 (61.3 per cent) had pineal calcification. The group of 11 women with carcinoma of the breast but without disseminated disease was too small for the findings to serve as a basis for conclusions concerning the effect of metastasis on the incidence of pineal calcification. However, the type of mètastasis did not appear to exert any important influence.

Complete follow-ups of women with carcinoma of the breast were available in 14 having pineal calcification, and in 5 without pineal calcification. The median duration of life after onset of the disease was 4.4 years in those having pineal calcification and 2.8 years in those not having pineal calcification. The median duration of life after sex-hormone therapy was 1.5 years in nine women with pineal calcification and 3 months in three women without pineal calcification. Although definite conclusions cannot be based on findings in so few patients, those with pineal calcification appear to have a better prognosis and respond better to hormonal therapy. This possible correlation between response to therapy and pineal calcification is worthy of further investigation.

Comment

The calcific deposits in the pineal body, the so-called "brain sand granules" are laminated structures composed mainly of phosphates and carbonates of calcium and magnesium.[6] Although calcific deposition in the pineal body is believed to be the result of its degeneration,[6] there is no proof that calcification is related to hypofunction of this body. In fact, Sander and Schmid[7] noted the theory of Coronini that calcification results from crystallization of hormone. Although personal observations and also Quercy, De Lachaud, and Durand's[8] histologic study of the human pineal body suggest that calcification of this body

*$Chi\ square = 4.21;\ P < 0.05$.

may be associated with a decrease in the amount of pineal parenchyma capable of active function, the physiologic effect of such a decrease is not known.

The administration of pineal extract has been reported to inhibit the growth of experimentally induced cancer in mice,[9,10] and to cause symptomatic improvement in patients having clinical cancer.[7,11] The experimental studies concern a small number of animals, and need further confirmation; the clinical studies fail to provide adequate controls or objective evidence of improvement and include no mortality statistics.

Further inconsistencies were reported by Kitay and Altschule[1] in a review which noted that pineal injection and implantation have been consistently reported to inhibit the growth of spontaneous or induced malignant neoplasms, but that pinealectomy has been reported to accelerate the growth of sarcoma transplants in the rat as well as to inhibit the growth of spontaneous and induced cancers in mice. Thus the possible role of the pineal body in the development of carcinoma is controversial and demands further and more objective evidence.

At the present time, the explanation for the increased incidence of pineal body calcification noted in this series in women with carcinoma is not apparent. To clarify the problem, a better understanding is needed of the function of the pineal body.

Summary

In a selected series of women having carcinoma the incidence of calcification of the pineal body was significantly greater than that in a control group of women without malignant disease in the same age group. The difference in incidences of pineal calcification between men having carcinoma and those not having malignant disease was not significant.

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