Roentgenographic-Histologic Patterns of Calcification in Thyroid Nodules

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Synopsis

Roentgenographic and histologic examinations were carried out on excised specimens of 100 cases of malignant thyroid neoplasms and of 98 cases of benign nodules. Industrial film and low voltage were used to obtain the maximum detail. Microscopic sections stained with hematoxylin and eosin were examined in all the cases and the selected 24 sections were stained by von Kossa’s method. Calcium deposits were grossly classified into psammomatous and coarse types. The former was seen in 59 of 100 malignant tumors and in only 2 of 98 benign nodules, whereas the latter was observed equally in both the malignant and benign nodules at the rate of 42%. Roentgenographic-histologic study revealed that most of the psammomatous calcifications were produced by true psammoma bodies, but there were a few exceptions, which were minute calcific deposits in the fibrous stroma and, in the cases of the medullary carcinoma, were calcifications in the amyloid. Several modes of development and distribution of psammoma bodies were found and each example was shown. Coarse calcifications were present in areas of fibrosis and showed various configurations. In only 2 adenomas, calcific deposits were seen along the sinusoidal vascular structures within the tumor parenchyma and fleece-like shadows were obtained on x-ray films. Other types of coarse calcification have no relationship to histologic diagnosis.

The thyroid surgeons, pathologists and roentgenologists are well aware of the fact that calcification within the thyroid gland is seen not infrequently in patients with various thyroid diseases. Grossly it is classified into two types. The more common type is coarse and roentgenologically dense, and in some instances it is visible on the ordinary roentgenograms of the neck. Another type is so fine and of so low density that its demonstration on x-ray films needs careful technique when it is present in small amounts. Attempts have been made to formalize the criteria by which differentiation of benign and malignant nodules may be roentgenographically possible (Holtz and Powers, 1958; Segal et al., 1960; Gerrald-Marchant et al., 1969; Watanabe et al., 1970). Soft tissue roentgenography has been employed by several investigators (Segal et al., 1960; Gasquet et al., 1963; Margolin and Steinbach, 1968; Higuchi et al., 1969) to obtain an optimal contrast and detail.

The present work was undertaken to analyse various patterns of thyroid calcification obtained by roentgenography of excised specimens and to correlate the x-ray findings with histologic features.

Materials and Methods

Roentgenographic and histologic examinations were carried out retrospectively on thyroidectomy specimens of 100 consecutive patients with malignant thyroid neoplasms and 98 with benign nodules including adenoma and adenomatous goiter. The operations were performed at the Second Department of Surgery, University of Tokyo, before the end of November,
1969. Fine-grain industrial film (Sakura X-Ray Film, Type MR) and low kilovoltage were used to obtain the maximum detail. Initially roentgenograms were made on both the paraffin blocks and the remnant surgical specimens. When we had examined 39 specimens of malignant tumors and 41 of benign nodules, we ceased to make any further roentgenogram of the remnant specimens, because it became apparent that almost all the important portions of each specimen had been made into paraffin blocks and therefore the roentgenograms of the blocks provided enough materials for the analysis. In addition, roentgenograms of the remnant specimens were in general difficult to interpret because of their irregularity in shape and thickness and gave very little further information. The numbers of paraffin blocks in each instance were one to 17, averaging 6.7 in malignant tumors and 3.7 in benign nodules. Although specimens which were already demineralized before processing to the paraffin blocks did not show calcific deposits on roentgenograms, they were treated as having coarse calcification and the calcified areas were usually identified on the microscopic sections by their blue staining with hematoxylin. The sections stained by hematoxylin and eosin were examined in all cases and the selected 24 sections each representing any one of the characteristic patterns of thyroid calcification were processed to the silver nitrate staining by von Kossa's method.

Results

I. Roentgenologic classification of thyroid calcification and incidences

Calcium deposits observed in roentgenograms were initially divided into two types; coarse and psammomatous. Their incidences in the benign and the malignant thyroid nodules are shown in Table 1. The incidence of coarse calcification in malignant tumors was the same as that in benign nodules. On the other hand, psammomatous deposits were seen in 59 of 100 malignant tumors, whereas they were present in only two of 98 benign nodules.

Distributed by histologic type, psammomatous calcifications were rich in the papillary and the medullary carcinomas and less frequently seen in the follicular carcinoma. On the contrary, coarse calcifications were observed more often in the follicular than in the papillary and the medullary carcinomas.

Table 1. Pattern of Calcification seen on specimen roentgenogram

<table>
<thead>
<tr>
<th>Histologic diagnosis</th>
<th>Total No. of cases</th>
<th>No. of cases with calcification*</th>
<th>Calcification positive rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Ps+ Co+</td>
<td>Ps+ Co-</td>
</tr>
<tr>
<td>Malignant neoplasms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>79</td>
<td>17</td>
<td>31</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>12</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>5</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Papillary carcinoma associated with</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaplastic carcinoma</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>23</td>
<td>36</td>
</tr>
<tr>
<td>Benign nodules</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma</td>
<td>72</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Adenomatous goiter</td>
<td>26</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>98</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

* Ps+ : Psammomatous calcification positive.
Co+ : Coarse calcification positive.
"Ps+ Co+" indicates cases which had both psammomatous and coarse calcifications.
II. Roentgenographic and histologic appearances of thyroid calcification

A. Roentgenographically psammomatous calcification

Although most of the calcium deposits showing psammomatous pattern on roentgenograms were proved histologically to be true psammoma bodies, there were some other calcific deposits which presented the similar pattern.

Psammoma bodies: As for the development and distribution of psammoma bodies, several patterns were observed. The most typical case is shown in Fig. 1 and 2. The appearance is like very small grains of sand. Its roentgenologic density is too low to be seen on the ordinary roentgenogram of the neck. Most of the calcific deposits on the film represent individual psammoma body, which is usually 20 to 70μ in diameter. They are distributed heavily at the periphery of the tumor and some are seen in the adjacent thyroid tissue. Psammoma bodies of this type are most commonly seen in the papillary carcinoma with histologic evidence of active proliferation. The bodies appear to develop in clusters of cancer cells which have invaded into lymphatic vessels locating in the tumor stroma or in an adjacent thyroid tissue near the primary growth.

Figure 3 shows another example of psammomatous calcification in the papillary carcinoma. It is characterized by a mixture of fine sand-like calcific grains and larger, rounded calcific bodies. Histologic examination revealed that even the fine deposits seen in this case were made up of a clump of several psammoma bodies. The rounded, dense calcific deposits, large up to 1 mm in diameter, appeared to develop by secondary fusing of a number of psammoma bodies or as a result of calcific deposition to degenerated cell mass which was included within a dense fibrosis.

The next two figures (Fig. 4 and 5) show histologic features of different mode of development of psammoma bodies. The bodies appear at the tip of the papillary growth. They are small in amount in a case shown in Figure 4 and are projected on a roentgenogram as faint, scanty calcific deposits. Figure 5 demonstrates a far advanced stage of the similar process, in which papillary growth itself has undergone marked degeneration in a cystic cavity. The psammoma bodies are numerous and conglomerate, so that they give denser and larger psammomatous shadows on the film.

Figure 6 shows a specific type of papillary carcinoma which is characterized by a remarkable extension of cancer cells into lymphatic channels in the thyroid tissue around the primary growth, the extension being often so intense that the whole thyroid may be involved. This type of carcinoma is usually seen in female patients of second decades and has an associated chronic thyroiditis. There are numerous psammoma bodies which have developed in cancer cell mass within lymphatic vessels and hence thin strands of psammomatous shadows are seen throughout the thyroid parenchyma on the roentgenogram.

Calcium deposits other than psammoma bodies: Histologic examination revealed that in a few cases calcium deposits other than psammoma bodies produced shadows very similar to the psammomatous pattern. Those seen mostly in the papillary and the follicular carcinoma are minute calcific deposits in the fibrous stroma as shown in Figure 7 and 8. Most of the fine deposits observed in the medullary carcinoma were proved to be calcification in the amyloid (Fig. 9 and 10).

Psammomatous deposits seen in one case of microfollicular adenoma and in one case of adenomatous goiter (Fig. 11 and 12) were histologically difficult to confirm whether they were true psammoma bodies or calcific deposits to the degenerated cell materials.

B. Roentgenographically coarse calcification

Coarse calcification is seen in the fibrous stroma, septum and capsule of both benign and malignant nodules. In the histologic
Fig. 1. and 2. Typical psammomatous calcification seen in papillary carcinoma. Roentgenographic view of paraffin block (Fig. 1, ×2.5) and histologic appearance of psammoma bodies (Fig. 2, H.E. ×50).

Fig. 3. Psammomatous calcification and associated larger, rounded calcific deposits seen in papillary carcinoma. Calcifications appeared predominantly within and around the tumor capsule. (H.E. ×7, Roentgenogram ×2.5)
Fig. 4. Psammoma bodies developing at the tip of papillary growth in papillary carcinoma. (Kossa, × 50).

Fig. 5. Psammoma bodies of conglomerate form developing at the papillary growth which has undergone degenerative change in a cystic cavity. (H.E. × 50).

Fig. 6. Specific type of papillary carcinoma with remarkable intrathyroid extension of cancer via lymphatic channels and associated chronic thyroiditis. Note numerous psammoma bodies. (H.E. × 20, Roentgenogram × 2).
Fig. 7 and 8. Psammomatous calcification mixed with minute calcific deposits in fibrosis. Calcific deposits are seen on the roentgenogram (Fig. 7, × 2) as slightly larger, dense shadows of irregular spicules. Fig. 8 shows those calcium deposits in fibrosis. (H.E. × 120).

Fig. 9 and 10. Psammomatous shadows seen in medullary carcinoma. They are proved histologically to be mostly calcifications of the amyloid. In Fig. 10, beginning of calcification of the amyloid is seen on the right. (Roentgenogram × 2, Kossa × 120).

Fig. 11 and 12. Psammomatous calcification seen in a case of adenomatous goiter. (Roentgenogram × 2, Kossa × 50).
sections stained with hematoxylin and eosin, only the areas where calcium is deposited extremely are stained dark blue and they correspond well with the figure of calcification on the roentgenogram (Fig. 13). Calcification of low density is, however, actually present in the fibrous stroma around the dense deposits cited above and it becomes apparent on sections stained by von Kossa’s method (Fig. 14).

Roentgenographically coarse calcification appears in various configurations, such as punctate, liner, curvilinear, of irregular spicule or of amorphous plaque of various sizes. Figure 15 shows one of the examples of such coarse calcification. In one area of the block ossification is visible (Fig. 15 and 16), the finding having been observed also in a benign nodule with marked fibrosis.

In general, fibrosis and its calcification tend to be formed in an irregular fashion in the carcinomas and in a rather smooth configuration in the benign nodules. There are, however, exceptional cases and thus the figure of calcification is not a reliable indication of the nature of the nodule.

An extremely dense, amorphous type of calcification, occupying almost the whole nodule, was seen in four cases; one was a well encapsulated papillary carcinoma with minimal capsular invasion, one was a Langhans’ “wucherunde Struma” which had a rapidly growing, non-calcified nodule protruded from a deeply seated, heavily calcified mass, one was a colloid adenoma and one was a benign nodule in which no viable tissue remained.

All the coarse calcifications described above are roentgenographically dense. Fleece-like pattern seen in two adenomas was of low density. Histological examination revealed that this particular calcific deposits were present along the sinusoidal vascular beds in the tumor parenchyma (Fig. 17).

**Discussion**

Although coarse calcifications of moderate size which occur in the thyroid gland are detectable on the ordinary preoperative roentgenograms of the neck and at the macroscopic examination of the excised specimens, psammomatous calcifications and minute calcium deposits are usually overseen at the routine examinations. When roentgenograms of excised specimens were carefully checked and the findings were correlated with the histologic features, both the coarse and psammomatous types of thyroid calcification were detected in unexpectedly high incidences.

As for the diagnostic significance of various patterns of thyroid calcification, the current study has led us to the same conclusion as that stated by previous investigators (Klinck and Winship, 1959; Batsakis et al., 1960; Hisada et al., 1962; Onishi, 1966; Hoshi et al., 1967; Margolin et al., 1967). Namely, only the presence of psammoma bodies has a diagnostic value and they are almost pathognomonic to the thyroid carcinoma. They were found histologically in approximately half of the thyroid carcinomas in our series as well as in other investigator’s series. The important fact is that psammoma bodies were present in a very few cases of benign thyroid disorders, the incidence being one out of 2,153 noncancerous thyroids in Klinck’s series, 10 out of 612 in Batsakis’ study, 1.9% of adenomatous goiters and 2.0% of adenomas in Hoshi’s study, and only 2 of 98 benign nodules in our series.

Coarse calcifications were, on the other hand, found in the similar incidences in both benign and malignant nodules. Furthermore no apparent correlation existed between the configurations of coarse calcium deposits and the histologic diagnoses. Only one exception was a fleece-like pattern of calcification seen in two adenomas, in which calcium deposited along the sinusoidal vascular structures in the parenchyma.

The knowledge on the roentgenographic pattern of thyroid calcification obtained from the present study may be useful in two ways. One is in an interpretation of calcium deposits on the neck x-ray films. We have been working
Fig. 13. Papillary carcinoma with coarse calcification. Roentgenographic feature correlates well with histologic finding. (H.E. × 10, Roentgenogram × 2.5).

Fig. 14. Coarse calcification seen at the fibrous capsule of follicular adenoma. (Kossa × 10, Roentgenogram × 2.5).
Fig. 15 and 16. Various patterns of coarse calcification seen in papillary carcinoma. Calcification of network figure seen on roentgenogram (arrow) is ossification, whose microscopic feature is shown in Figure 16. (Roentgenogram × 2.5, H.E. × 50).

Fig. 17. Calcium deposits along the sinusoidal vascular structures in adenoma. Roentgenogram shows a fleece-like calcification. (Kossa × 15, Roentgenogram × 2.5).
along this line using soft tissue roentgenography. The problem at the present time is how to allow roentgenographic identification of psammoma bodies of non-aggregate form and of low density. Another possible usage is a thyroid specimen roentgenography during the operation, which may prove valuable in the detection of malignant tumor itself, of the presence and extent of intraglandular metastasis and lymph node metastasis. We have already experienced several cases in which this technique was valuable and the details will be reported elsewhere.

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References