

The encapsulated follicular carcinoma of the thyroid

A clinicopathologic study of 35 cases*

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Summary. In a retrospective study of 86 follicular carcinomas of the thyroid gland, 35 lesions were classified as encapsulated carcinomas (40.7%). In two of these, lymph node metastases were detected initially. Another patient presented with distant metastases. The biological behaviour of these 35 tumours was studied over a long-term follow-up period (0.4–19.1 years, mean 10.3 years) which featured three cases of death from thyroid carcinoma 0.4–5.0 years after thyroidectomy. Another patient suffered from local recurrence of a follicular carcinoma 13.9 years later. The morphological and clinical findings of those five patients who initially presented with metastases and/or whose follow-up registered the local recurrence of thyroid cancer or death as a result of it, were compared with the remaining 30 cases which were of a benign clinical course. Statistical analysis showed that the prognosis of encapsulated follicular carcinoma is more serious when tumours occur in patients older than 65 years of age and when the tumour diameter is 5.0 cm or more. There was a tendency towards poorer prognosis in those tumours exclusively composed of oxyphilic epithelium.

Key words: Encapsulated follicular carcinoma – Thyroid carcinoma – Follicular carcinoma

Cancer of the thyroid gland covers a broad spectrum of tumours, all entirely different as regards their degree of malignancy. There is no doubt that the nomenclature of the WHO (Hedinger and Sobin 1974) with a rather small number of tumour categories has proved to be useful, but it has been shown by different authors that at least in some of these categories subtypes of thyroid carcinomas with different prognoses can be isolated (Hedinger 1983).

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Therefore a meaningful classification of thyroid carcinomas must take into account not only their morphological characteristics but also the biological behaviour of the different growth variants of neoplasms (Crile and Hawk 1971). Such factors apply not only to papillary thyroid carcinomas, in which prognosis varies depending on the size of the primary lesion (occult, intrathyroid, extrathyroid) (Woolner et al. 1961) but also to follicular carcinomas: in this case, encapsulated angioinvasive tumours behaving as carcinomas of low malignancy have to be discriminated from widely invasive follicular carcinomas, commonly accepted as carcinomas of intermediate malignancy (Crile 1968). This distinction is justified by several clinical investigations over long follow-up periods (Woolner 1971; Franssila 1975). However, not only have sporadic cases of fatal outcome in encapsulated follicular carcinomas been reported, but death from these variants occurred with an incidence rate of up to 17% in more comprehensive studies (Crile 1968). Thus it seems questionable to designate such carcinomas as early cancers (Lang and Georgii 1982; Lindsay 1960) as the occult papillary neoplasms have correctly been termed (Lang and Georgii 1982).

The purpose of the present study was to determine the incidence of encapsulated follicular carcinomas in biopsy material over an eighteen year period and to examine their biological behaviour by means of a long-term follow-up.

Material and methods

Using routine histological techniques, surgical specimens of thyroids containing follicular tumours were studied. These cases had been under observation for an eighteen year period at the Institute of Pathology of the University of Hamburg (1963–1981). All cases were re-examined. In all encapsulated tumours of equivocal histological nature, additional sections from the paraffin-embedded tissue blocks were analysed. With tumours less than 5 cm in diameter an average of 5.7 (minimum 3) capsule sections were made and with the larger tumours 7.7 were taken (minimum 5). These were then histologically analysed. The final diagnosis of encapsulated follicular carcinoma was made in only 35 lesions in which either tumour invasion of capsular vessels or invasion of the tumour capsule could be evaluated histologically. The medical records of all of these 35 patients were reviewed and all cases kept under observation up until January 1983.

Results

Eighty-six of 3,684 follicular tumours of the thyroid gland proved to be carcinomas. Of these, 35 encapsulated follicular carcinomas (40.7%) and 51 widely invasive follicular carcinomas (59.3%) were diagnosed.

Distribution by age and sex

The female: male ratio of our 35 patients with encapsulated follicular carcinomas (EFC) was 4:1. The overall mean age was 46.7 years, ranging from 20 to 78 years, as compared with 57.2 years with a range of 18 to 83 years amongst our 51 patients suffering from widely invasive follicular carcinomas (WIFC). This difference proved to be statistically significant (Student *t*-test, $p < 0.001$).

Clinical presentation

In 28 of the 35 patients, the preoperative presentation was that of a nodule, palpable on physical examination. In each case, scintigraphy demonstrated a cold nodule. In 6 cases, tumours were discovered during the course of routine pathological examination of the gland following surgery for unilateral or bilateral goitres. One patient initially presented with a spontaneous fracture of the neck of the right femur; histological evaluation revealed a bone metastases of a follicular thyroid carcinoma (Fig. 1; Table 1, Case 1).

Pathology

In each of the 35 surgical specimens, the tumours occurred as single foci. With two of these, occult sclerosing papillary carcinomas were evident as second malignancies, one ipsilaterally, the other contralaterally to the encapsulated follicular carcinomas.

The mean diameter of the lesions was 4.1 cm with a range of 2.0 to 10.0 cm. In each case, the macroscopic aspect was that of an entirely encapsulated mass (Fig. 2).

In 23 cases the tumour was completely intrathyroid. In the remainder it was situated in the marginal zones of the thyroid, protruding through the capsule. With ten patients there was only a bare rest of atrophic residual thyroid parenchyma to be seen on the side of the tumour.

Statistical analysis gave no indication whatsoever of any clear correlation between the size of the tumour and the age of the patient (Fig. 3). With 16 of the 35 reclassified tumours, the primary diagnosis had been encapsulated follicular carcinoma since the histological evaluation had, at the time, demonstrated capsular or vascular invasion. With the remaining 19 tumours which had, at the outset, been diagnosed as adenomas, it was only the histological classification, upon examination of another ten sections from the paraffin-embedded tissue blocks, which registered the malignancy criteria mentioned.

Histological analysis of the slides available of all 35 EFC revealed tumour invasion of capsular vessels in 19 cases, showing disruption of the vascular wall by masses of tumour epithelium, often forming polypoid projections into vessel lumens (Fig. 4). In seven cases, malignancy was evidenced by the presence of sharply defined tumour infiltrations into the capsule. Two additional cases showed a complete disruption of the capsule with contact between the tumour epithelium and adjacent thyroid parenchyma (Fig. 5). Vascular invasion and capsular invasion were observed simultaneously in seven cases.

According to most reports on the subject, mitoses are usually counted within the most cellular areas of a tumour, for which reason we deliberately refrained from taking this variable to evaluate our own material which comprised the marginal zones of the tumours. The same can be said of a quantitative analysis of cellular atypia in our 35 tumours.

As regards the tumour architecture, 14 lesions were micro- or macrofollicular throughout, ten tumours were entirely trabecular or solid and eleven showed a mixed microfollicular and trabecular pattern. Of these, one tumour

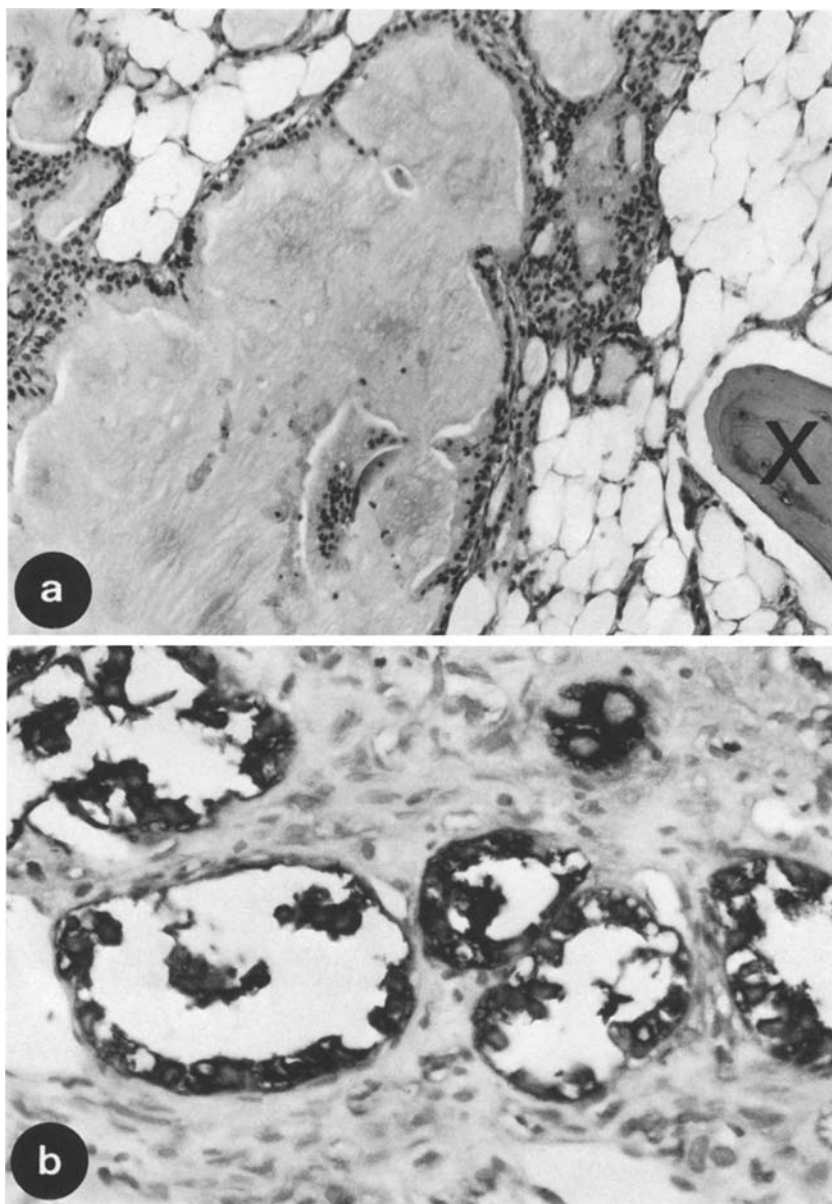


Fig. 1 a, b. Bone metastasis of an encapsulated follicular carcinoma (Table 1, Case 1). **a** H and E $\times 115$ (trabecula X), **b** Thyroglobulin $\times 460$

showed small foci of dedifferentiation with anaplastic tumour epithelium as well as extensive tumour necrosis.

Out of the total of 35 neoplasms, nine tumours displayed oxyphilic metaplasia and one clear cell metaplasia throughout. Two additional tumours showed focal oxyphilic and clear cell differentiation.

Table 1. Morphological and clinical findings of five cases of EFC, in which metastases, recurrences and/or deaths from carcinoma were observed

Case	Age Sex	Symptoms	Tumour size (cm)	Morphology	Therapy	Follow-up
1	76F	Collum femoris fracture with osteolytic metastasis	5	Angioinvasive, microfollicular, oxyphilic, abundance of psammoma bodies (no papillae, no ground-glass nuclei)	Total thyroidectomy, hormone substitution, radioiodine therapy, yet metastases did not accumulate ¹³¹ I	Further bone metastases discovered postoperatively: solitary, painful skull metastasis excised; trabecular and solid carcinoma; death due to cachexia from tumour 5 months following surgery
2	59F	Bilateral goitre for 30 years, over past 3 months increase in size, dyspnoea	6	Capsular invasive, microfollicular: cervical lymph node metastasis	Subtotal thyroidectomy, selective excision of cervical lymph node metastasis, hormone substitution, radioiodine and external radiation therapy	Still alive 16.7 years after surgery with no indication of recurrence
3	78F	Enlarged thyroid for 40 years, growth over past 2 months	6	Angioinvasive and capsular invasive, mixed microfollicular and solid, oxyphilic, cervical lymph node metastasis	Subtotal thyroidectomy, selective excision of cervical lymph node metastasis, hormone substitution	2.2 years following surgery, pathological fracture of humerus: trabecular and solid carcinoma, external radiation treatment; 5 years following surgery refracture: non-iodine avid, multiple bone and pulmonary metastases, death due to cachexia; obduction: 10 cm large local recurrence with invasion of trachea and oesophagus, extensive distant metastases formation
4	72F	Unilateral goitre for 30 years, increased in size 3 years ago	10	Angioinvasive, mixed trabecular and solid, oxyphilic	Subtotal lobectomy (primary diagnosis: adenoma)	13.9 years following surgery local recurrence: scintigraphy indicated cold nodule, 3 cm in diameter, painfully sensitive to touch beneath thyroidectomy scar: needle biopsy showed collections of oxyphilic follicular cells with dense cellularity and marked anisonucleosis, no excision of tumour
5	65F	Dyspnoea due to goitre for 3 months	6	Angioinvasive, predominantly microfollicular including small nests of anaplastic cells, extensive necrosis	Subtotal thyroidectomy, radioiodine therapy, yet metastases showed no iodine avidity, hormone substitution	Immediately subsequent to surgery: bone metastases discovered (skull, thorax): death due to cachexia from tumour 0.4 years following surgery



Fig. 2. Macroscopic view of an encapsulated follicular carcinoma showing all-round capsule confinement intact. Attached thin remainder of atrophic parenchyma

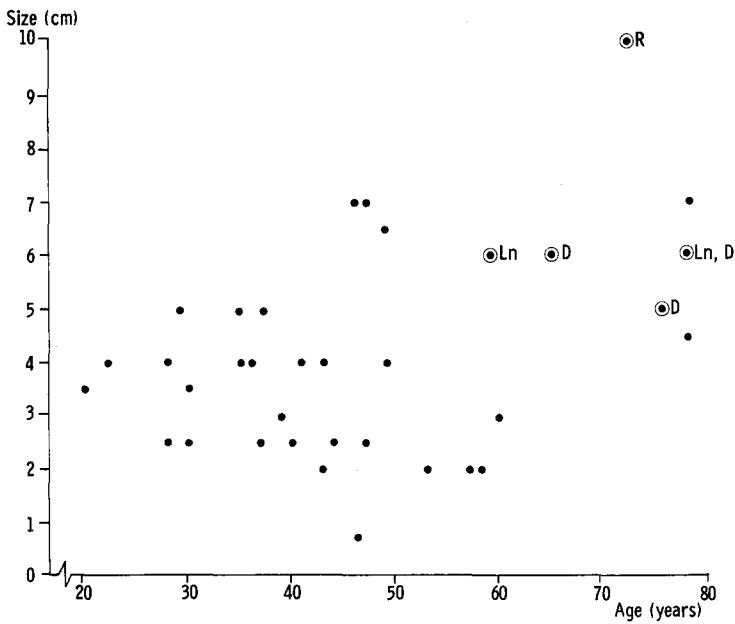


Fig. 3. Correlation between tumour size and age of patient at the time of surgery on 35 patients with encapsulated follicular carcinomas. Cases of cervical lymph node metastases (*Ln*), local recurrence (*R*) and death due to carcinoma (*D*) encircled

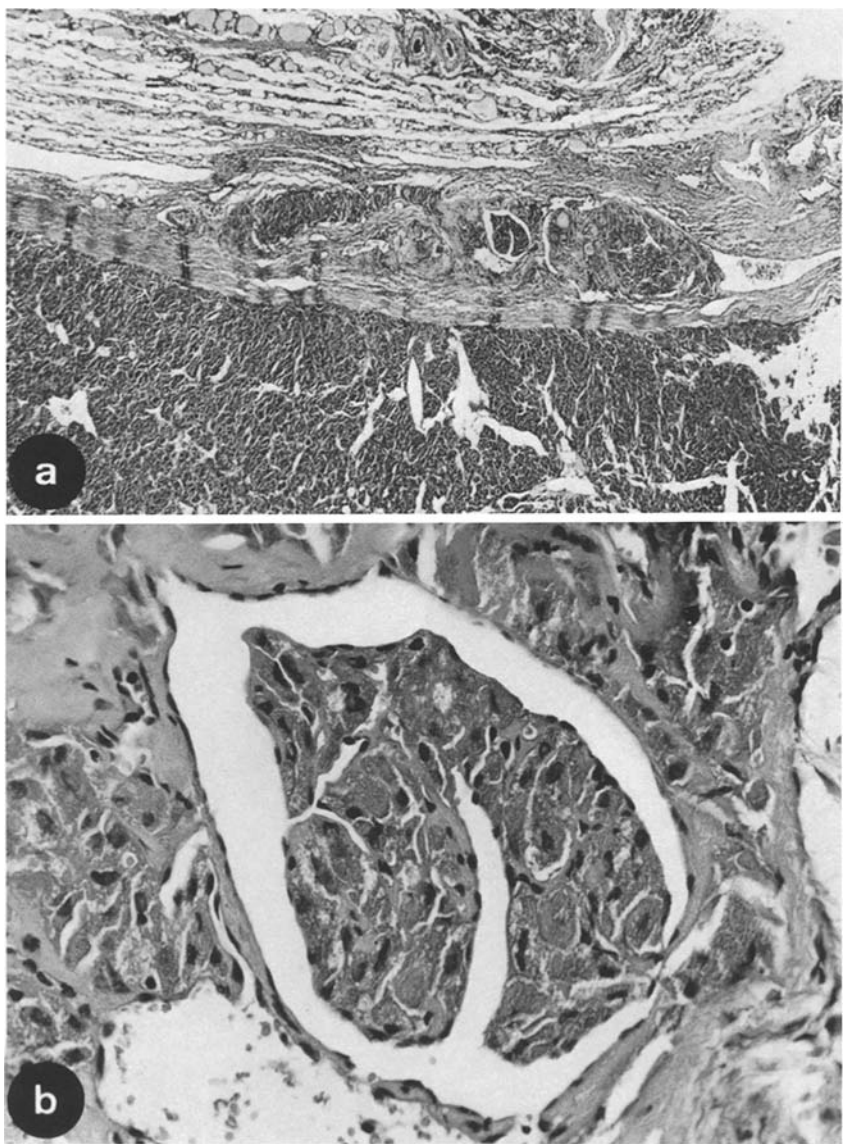


Fig. 4a, b. Vascular invasion with encapsulated follicular carcinoma. Intravascular tumour masses covered by endothelium, showing narrow attachment to vessel wall in places. MG **a** $\times 40$, **b** $\times 400$

Initial lymph node metastases were demonstrated in only two cases. In both, patients who had each undergone surgery at one stage for a cold nodule and unilateral goitre, enlarged lymph nodes of the jugular chain were found intraoperatively and removed. In both cases, histological examination detected metastatic follicular carcinomas (Table 1, Cases 2 and 3).

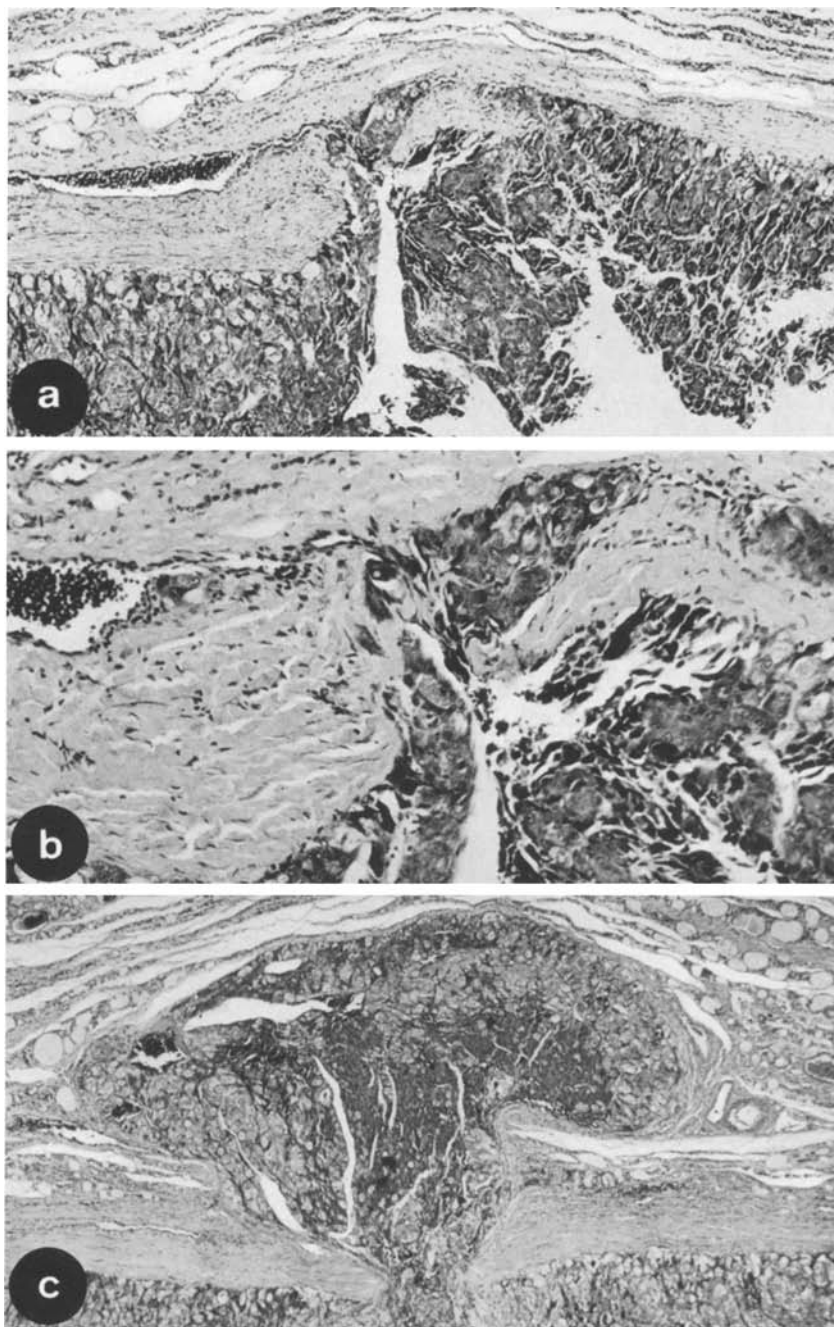


Fig. 5. **a, b** Limited capsular invasion with encapsulated follicular carcinoma. Tumour islands in capsule of neoplasm in continuity with the main mass. Right angular rupture of collagenous fibre bundles at point of tumour invasion. MG **a** $\times 56$, **b** $\times 160$ **c** Absolute capsule disruption with fungus like protrusion of tumour epithelium into adjacent parenchyma. MG $\times 40$

Therapy

Surgical and non-surgical therapy performed on our patients varied considerably depending on the initial pathological diagnosis. In 19 cases, originally diagnosed as follicular adenomas, therapy consisted either of unilateral subtotal thyroidectomy (13 cases) or enucleation of the tumour (six cases). With the remaining 16 patients, all diagnosed at the outset as suffering from carcinomas, total lobectomy was carried out ipsilaterally to the tumour with the subtotal or total resection of the contralateral lobe. Selective lymph node excision was performed only in the two instances noted above. All 16 patients were given TSH suppressive thyroid hormone substitution. In six of these 16 patients, no further non-surgical attempts at ablation of the residual thyroid tissue were made. In seven patients, only additional radioiodine treatment was applied and in three instances, a combination of radioactive iodine and external radiation therapy was used.

Follow-up

Of the 35 patients with EFC, all have been traced (mean follow-up period 10.3 years, range 0.4–19.1 years). Thirty patients are still living and five have died.

Of the 19 cases originally diagnosed as adenomas, 18 are alive. Of these, 17 are living without evidence of thyroid disease. In one patient, there was evidence of a local recurrence of the thyroid tumour 13.9 years following surgery (Table 1, Case 4). The only death occurred in an 81 year old woman 2.8 years following thyroidectomy; this was due to a metastasising adenocarcinoma of the rectum. Autopsy showed no trace of thyroid cancer.

Of those 6 patients who underwent subtotal thyroidectomy, four are alive and free of disease. Two patients died 0.4 years (Table 1, Case 5) and 5.0 years (Case 3) following surgery as a result of distant widespread metastases. The latter was one of the two patients who initially presented with lymph node metastases.

Of the seven patients who underwent subtotal or total thyroidectomy and radioiodine therapy, follow-up showed six subjects to be alive and free of cancer. One patient from this group died from distant widespread metastases 0.4 years postoperatively (Table 1, Case 1). This was the only patient initially presenting with distant metastases.

Of three patients who underwent a combination of thyroidectomy, radioiodine treatment and external radiation, two are alive and free of disease. In one of these cases, lymph node metastases had been observed intraoperatively (Table 1, Case 2). Another patient from this group, 53 years of age, died 6.0 years following thyroidectomy as a result of post-operative bleeding after a dilatative surgical procedure had been carried out for laryngeal atresia as a result of external radiation therapy.

The morphological and clinical findings of the five patients who initially presented with metastases and/or whose follow-up record registered local recurrence of carcinomas or death as a result of the same are listed separately in Table 1. Among these, malignancy was evidenced by capsular invasion

in one case, by angioinvasion in three cases, and by both angioinvasion and capsular invasion in one case. Complete capsule disruption was not observed in any of these five cases.

A statistical analysis of our data showed that the average diameter of the tumours of these five patients was larger (6.6 cm) than with the 30 patients whose postoperative development proved to be benign (3.72 cm) ($p < 0.001$, Student *t*-test). Parallel to this, a comparison was made between the average age (73 years) of these five patients at the time of thyroidectomy and that of the remaining 30 patients (42.8 years). Here again, the difference proved to be statistically significant ($p < 0.0001$).

Discussion

Since the first description by Cohnheim in 1876, it has been a well known fact that encapsulated follicular tumours can metastasise. The importance of vascular invasion as a criterion of malignancy of these lesions was first outlined by Graham in 1924. It was Warren (1931 and 1956) who later pointed out that the invasion of the capsule and vascular invasion do not necessarily coexist. The differences in the biological behaviour of encapsulated atypical follicular tumours with or without vascular invasion have been depicted in detail by Hazard & Kenyon (1954a and b). Since then, invasion of the capsule or the blood vessels are generally regarded as prerequisites for the diagnosis of encapsulated follicular carcinomas. Only in some of the earlier series are atypical follicular tumours given as being encapsulated follicular carcinomas (Lindsay 1960; Woolner et al. 1968), without proof being furnished of the criteria described above. Thus, in carrying out comparative studies to assess the biological behaviour of the encapsulated follicular carcinoma, referral to such surveys is necessarily restricted.

These lesions were originally described as malignant adenomas (Graham 1924), localized carcinomas in follicular adenomas (Warren and Meissner 1953), angioinvasive adenomas (Hazard and Kenyon 1954b), and localized follicular carcinomas (Hirabayashi and Lindsay 1961). In the following years, the term "encapsulated follicular carcinoma" (Crile 1968; Selzer et al. 1970; Franssila 1971; Lang and Georgii 1982; Kahn and Perzin 1983) ["abgekapseltes follikuläres Carcinom" (Georgii 1977), "eingekapseltes follikuläres Carcinom" (Hofstädter and Unterkircher 1980)] has been generally adopted in order to increase accuracy.

In the 35 encapsulated follicular carcinomas of the material we examined, histological evidence of vascular invasion confirmed the diagnosis in 26 cases. In seven cases diagnosis was based only on histological evidence of capsular infiltration which only in two cases took on the appearance of complete disruption of the capsule, showing contact between tumour epithelium and adjacent thyroid tissue. This assessment of *capsule infiltration as a criterion of malignancy in our retrospective study* is confirmed by the findings in one of our patients with regional lymph node metastases (Case 2, Table 1) and by the study of Kahn and Perzin (1983) who reported development of metastatic disease in one patient who had invasion into

the capsule – the capsule being sectioned *in toto* – as the only histological evidence of malignancy. These authors regard invasion into the tumour capsule alone as a sufficient criterion to diagnose malignancy and consider it to be a histological marker for a biologically aggressive tumour. It should be mentioned, however, that this criterion is inconsistent with the WHO classification of thyroid tumours (Hedinger and Sobin 1974), according to which only “extension through the capsule” is considered to be a hallmark of malignancy.

We agree with Franssila (1983 [personal communication]) that tumour islands within the tumour capsule sometimes represent real tumour invasion but that it is not usually possible to differentiate histologically between invasive islands and islands of non-invasive adenoma tissue that have been entrapped within the capsule due to capsular infolding or capsular fibrosis. In order to avoid overdiagnosis of malignancy, *in prospective studies* only follicular tumours with *complete capsular penetration* should be diagnosed as carcinomas (Lang et al. 1980, Löhns 1983 [personal communication]). *In practice*, several deeper sections from the block should be made and new blocks from the capsular area should be prepared when tumour tissue is observed within the capsule of an adenoma. If no tumour tissue is seen outside the capsule or within blood vessels, the tumour should be called benign. It is possible that some of these tumours really represent very low grade encapsulated follicular carcinomas, but their risk for metastasis or death is minimal (Franssila 1983 [personal communication]). The percentage of 40.7 of encapsulated carcinomas of the total number of follicular carcinomas examined by us lies within the range of 17.6% (Franssila 1971) and 60.0% (Hirabayashi and Lindsay 1961) given in other studies. We would also confirm the average age of patients suffering from encapsulated follicular carcinomas as being some ten years younger than of those affected by widely invasive follicular carcinomas (Franssila 1971; Woolner 1971; Beaugie et al. 1976; Lang and Georgii 1982). In fact, it is this age difference and the traces of a capsular type of limiting structure in up to 24% of the widely invasive follicular carcinomas, as described by Lindsay (1960), Woolner et al. (1961), Franssila (1971) and confirmed by our own material (Pfannschmidt et al. 1984) – which makes it possible to see the encapsulated follicular carcinoma as precursor to the widely invasive carcinoma.

Early lymph node metastases, as observed in two of our patients at the time of thyroid resection, are a rare form of encapsulated follicular carcinoma (Hirabayashi and Lindsay 1961; Lang et al. 1980). They are sometimes found in association with pulmonary and bone metastases (Beaugie et al. 1976). Multifocality of encapsulated follicular carcinoma and intraglandular lymphatic dissemination, both characteristic of the intrathyroid papillary carcinoma were not found in any of our cases. The joint occurrence of an encapsulated follicular carcinoma and an occult papillary carcinoma observed in two of our patients is exceptional. In neither encapsulated tumour was there cytological or histological evidence of the papillary carcinoma. The occult papillary tumours were thus in both instances genuine examples of second tumours and could in no way be seen as the outcome of

intraglandular dissemination of an encapsulated papillary carcinoma (Schröder et al. 1984).

Observations on the course of the disease have been made in other studies which have suggested that with encapsulated follicular carcinomas, 75% of all recurrences evolve within the first five years following thyroidectomy (Hazard and Kenyon 1954b), whereas death often only occurs 10–22 years subsequent to surgery as a result of the haematogenous formation of metastases (Hirabayashi and Lindsay 1961; Woolner 1971; Beaugie et al. 1976). Any reliable statements about the biological behaviour of such tumours can, therefore, only be made in conjunction with long-term follow-up periods.

The deaths of three patients out of the 35 under study (8.6%) is still below the incidence figure of 11.8% given by Beaugie et al. (1976) and that of 15.6% of Crile (1968), yet is higher than in studies of other authors which frequently included test series with no deaths at all. In all three instances, blood borne metastases were either present initially or occurred during the course of development of the disease. Such formations were obviously indicative – as with the widely invasive follicular carcinomas – of an advanced tumour and were in each case the cause of the lethal outcome of the illness. In comparison, the illness progressed differently with each of the two patients with initial cervical lymph node metastases. One patient (Case 2) had no recurrence of disease after radioiodine treatment and external radiation therapy (follow-up period 16.7 years) yet the other patient (Case 3) refused back-up therapy and died five years after surgery from extensive haematogenous metastases, the local recurrence measuring 10 cm in diameter.

Because of the small number of encapsulated follicular carcinomas presenting with metastases or causing death, there are hardly any parallels with which to compare the morphology of tumours of benign and malignant clinical development. Hazard and Kenyon (1954b) found some indication that the rate of growth as evidenced by the number of mitoses in the most cellular and atypical areas may affect the subsequent behaviour of the tumour. In addition, these authors saw a tendency towards a poorer prognosis in tumours with marked atypia. Indicative of this was the one case we observed in which, within the primary tumour, undoubted foci of anaplastic tumour cells were identified; within 5 months of surgery, the patient died from an extensive formation of bone metastases (Case 5). Along with Hazard and Kenyon (1954b) we nevertheless feel that an exact assessment of anaplasia is difficult and its prognostic value in the individual case is minimal. In the same way, we see no correlation between the grading of our 35 encapsulated follicular carcinomas (follicular, follicular and solid, solid) and the clinical course of the disease.

Contradictory observations have been made by various authors on the frequency of oxyphilic tumours (Thompson et al. 1974; Tollefsen et al. 1975; Ruchti et al. 1976). In our material 25.7% of the encapsulated follicular carcinomas showed oxyphilic metaplasia but this change was found in 66.7% (2/3) of the tumours which resulted in death. The findings of Hazard

and Kenyon (1954b) are similarly indicative; four tumours found were formed of oxyphilic cells, two of which pursued a malignant course within a five year span.

Hofstädter and Unterkircher (1980) established a correlation between the number of capsule penetrations per capsule length and the prognosis. The evaluation of the number of capsular and vascular invasions demonstrated in our material retrospectively presents a problem, since in no case was it possible to carry out a comprehensive histological classification of the total tumour circumference. One could of course conjecture that with the 19 tumours defined as adenomas in the primary diagnosis, the number of capsular or vascular penetrations was smaller than with the remaining 16 cases, where these criteria of malignancy were detected early on together with the primary microscopic findings. The tumours in these two groups differ in their biological behaviour in such a manner that in the first group, there was no case of either lymph node metastases or death due to carcinomas, whereas in the second, two patients suffered from initial lymph node metastases and one from initial distant metastases and a total of three patients in this group actually died from carcinomas. Bearing in mind the restriction involved in evaluating the number of capsular and vascular invasions, our evidence could be interpreted to show that the biological behaviour of the encapsulated follicular carcinomas in our material is determined by the quantitative extent of these invasions.

We can give definite confirmation of the evidence presented by Crile (1968) to the effect that the prognosis of encapsulated follicular carcinomas becomes more serious when this tumour occurs in elderly patients. The average age of patients with a benign clinical course of disease was 42.8 years, whereas the average age of those who suffered from lymph node metastases, recurrences or distant metastases was 70.0 years. There were no patients younger than 65 years of age who died of this type of cancer, whereas 50% of the over 65 year old patients died of carcinomas.

In Crile's study (1968), the prognosis was worse in men than in women. Our own observations indicate just the opposite although the differences are not conclusive in either study. Analysis of our results points to a significant correlation between the size of the tumour and its biological behaviour. The average diameter of tumours of benign clinical course was 3.7 cm as opposed to 6.6 cm of those who showed one of the criteria of malignancy. No patient suffering from a tumour with less than a 5 cm diameter died as a result of the carcinoma whereas with tumours measuring 5 cm or more in diameter, 25% of the patients died from carcinomas. It is likely that there is a correlation between the size of the tumour and the age of the patient, yet given the small number of cases under study, this cannot be demonstrated conclusively.

Conclusions for therapy

The results of our study indicate that surgical intervention in the form of subtotal lobectomy of the affected side for the treatment of encapsulated

follicular carcinomas (Crile 1968) is, in the majority of cases, adequate – a recommendation made by a number of authors already. Yet in rare instances, encapsulated follicular carcinomas are also obviously capable of lymphogenous and/or haematogenous metastases. Cervical lymph node metastases would appear to have no significant effect on the prognosis, nor do they present any difficulties as far as surgery is concerned. Although the clinical course of both patients we described suffering from cervical lymph node metastases points to the significance of back-up radioiodine therapy, it is impossible to make any inference as regards therapy, given the small number of cases under study.

In comparison, haematogenous metastases indicate a progressive stage in the development of a tumour, in which surgical resection of the thyroid often only proves to be palliative. In fact all three patients in our series with initial or later distant metastases died of their tumours.

Because of the possibility of distant metastases forming in the early stages of encapsulated follicular carcinomas, it seems that primary total thyroidectomy is the form of surgery to be selected in high-risk patients in ensuring an adequate post-operative radioiodine diagnosis and, if necessary, corresponding therapy.

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