Nuclear diameter in parathyroid carcinomas

J M JACOBI,* H M LLOYD,* J F SMITH

From the *Department of Medicine (University of Queensland), Royal Brisbane Hospital, Brisbane, Queensland, Australia, and the Department of Morbid Anatomy, The Medical School, Clinical Sciences Faculty, University College London

SUMMARY Nuclear diameter was measured and mean nuclear diameter calculated in 18 parathyroid carcinomas. In 11 of the 18 tumours mean nuclear diameter was above the range previously reported for 55 parathyroid chief cell adenomas and provides a useful discriminant in histological diagnosis.

The histological diagnosis of parathyroid carcinoma is based on well accepted criteria¹ but may still present difficulties in individual cases. One feature observed in parathyroid carcinoma cells is a high nuclear:cytoplasmic ratio,¹ which suggests that measurement of nuclear size may provide useful information. Studies of nuclear diameter in parathyroid adenomas^{2,3} showed a range of mean values extending well above the normal and correlating with DNA content, tumour mass, and plasma calcium. As part of a study of parathyroid carcinoma nuclear diameters were measured in a series of 18 such tumours, reported recently in detail⁴ and compared with the findings in adenomas (chief cell variety).

Material and methods

Histological sections from 18 parathyroid carcinomas were available. The table gives relevant clinical details and other data.

Nuclear diameter was estimated with the aid of a Wild ocular graticule, 0.2 mm square, divided into 100 squares. The graticule was calibrated with a stage micrometer for use on a Wild M-40 microscope. At $\times 40$ magnification one small square of the graticule was $4 \mu\text{m}$ across. Nuclear diameters were measured by comparison with the $4 \mu\text{m}$ squares. Diameters equal to or greater than $2 \mu\text{m}$ were measured to the nearest $1 \mu\text{m}$. Fields were selected in which cells were arranged homogeneously, avoiding the edge of the section, distorted areas, and areas of haemorrhage. Endothelial cells were not included. In general, nuclei seemed to be round or slightly oval. In the case of oval nuclei a mean diameter was estimated, but nuclei

with the larger diameter more than double the smaller were excluded. The rate of exclusion did not vary greatly between tumours. About 1000 nuclei were measured in each carcinoma and subtotals were recorded on a Ferrari-Statistest mechanical counter for each nuclear diameter from $2 \mu\text{m}$ to the largest observed ($16 \mu\text{m}$).

The measurements were carried out by the same observer throughout the study and mean nuclear diameter was calculated for each carcinoma. Correlation coefficients were calculated for mean nuclear diameter, tumour weight, and plasma calcium, using log values. Mean nuclear diameters for the carcinomas were compared with those for adenomas³ by analysis of variance, and group mean values were compared by Student's *t* test. In further comparisons of the two types of tumour kurtosis and skewness were calculated for the distribution of nuclear diameters in each tumour.

Results

Mean nuclear diameter in the parathyroid carcinomas ranged from 5.549 to 10.131, the group mean value being 8.111 (SD 1.387). In parathyroid adenomas the range for mean nuclear diameter was 4.228 to 7.907,³ the group mean value being 5.831 (0.853). The difference between the group mean values was highly significant ($t = 8.34$; $p < 0.001$). In 11 of the 18 carcinomas mean nuclear diameter was greater than $8 \mu\text{m}$, which lies between 2 (1.706) and 3 (2.558) above the group mean value for adenomas and is above the range for adenomas. The mean variance for carcinomas (1.396) was greater ($p < 0.001$) than that for the adenomas (0.638).

In individual tumours the distribution of nuclear diameter was positively skewed in 9 of 18 carcinomas

Table Data for parathyroid carcinomas

Case No (UCH series number) ⁴	Tumour weight (g)	Plasma calcium (mg/100 ml)	Mean nuclear diameter (μm)
1 (15)	10.0	14.2	5.930
2 (51)	8.5	15.0	5.549
3 (65)		17.9	8.153
4 (114)	2.7	12.7	8.377
6 (169)		15.7	8.408
7 (176)	8.4	11.8	9.114
8 (197)		16.6	6.784
9 (208)	8.5	14.2	7.739
10 (266)	5.0	15.6	9.774
11 (278)	1.0	11.4	7.234
12 (321)		16.0	9.251
14 (421)	11.0	19.0	9.657
15 (454)	3.2		8.293
16 (544)	4.8		10.131
17 (568)	14.0		8.801
18 (586)	6.25		6.095
19 (611)	4.0		9.434
20 (632)	15.0		7.273

and in 13 of 55 adenomas. Negative skewness was not observed in either group and mean skewness did not differ between the two groups. Peaked distribution curves (kurtosis > 3) were seen in 15 of 18 carcinomas and in 33 of 55 adenomas. Flattened curves (kurtosis < 3) were seen in three of 18 carcinomas and 22 of 55 adenomas. Mean values for kurtosis did not differ between the two groups.

MEAN NUCLEAR DIAMETER, TUMOUR WEIGHT, AND CLINICAL FEATURES

Evidence of severe hyperparathyroidism (high plasma calcium; overt bone disease in 15 cases) was characteristic of the series. Two cases (4 and 15) were associated with kidney stones (without bone disease) and one with myopathy (case 11). The correlation between tumour weight and plasma calcium nearly reached significance ($p \approx 0.05$), the data being incomplete. Correlation coefficients for tumour weight and plasma calcium with mean nuclear diameter were negligible. The presence of metastases or local infiltration did not seem to affect mean nuclear diameter.

Discussion

The findings in this study show that mean nuclear diameter is a useful discriminant between adenoma and carcinoma. There were no significant differences overall in skewness and kurtosis, but the variance in carcinomas was greater than in adenomas. Mean nuclear diameter has not yet been studied in the same way in primary chief cell hyperplasia. There were significant correlations between mean nuclear diameter, tumour weight, and plasma calcium in the adenomas³ but not in the carcinomas.

Parathyroid carcinoma is often associated with severe hyperparathyroidism and overt bone disease. Adenomas associated with overt bone disease as a subgroup showed a higher mean nuclear diameter than that for other adenomas.³ Hence in general mean nuclear diameter may be an index of functional activity of the parathyroid tumour cell, benign or malignant. The present findings, however, shed new light on the origin of carcinomas, which are believed usually to arise from normal glands.

In a previous study of parathyroid adenomas² nuclear diameter was correlated with ploidy measured by the Feulgen method. The high mean nuclear diameter of parathyroid carcinomas suggests high DNA content also. Studies of ploidy could provide information on the degree of malignancy and prognosis in these carcinomas as in carcinomas of other organs already investigated.⁵

References

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Requests for reprints to: Dr HM Lloyd, C Floor Clinical Sciences Building, Royal Brisbane Hospital, Brisbane 4029, Queensland, Australia.