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View from Beneath: Pathology in Focus

Histological changes during progression of adenoid cystic carcinoma

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Abstract
Eight cases of adenoid cystic carcinoma were reviewed to determine whether and how the histological features of the tumour vary with the progress of the disease. The tumours were classified by their histological patterns as tubular, cribriform, trabecular or solid. The relative amount of each pattern seen in routine light microscopic sections was calculated histomorphometrically and compared in the primary tumour and recurrent and/or metastatic lesions in the same case. In the early stage, the tubular pattern predominated. Later, the highest percentage shifted to the cribriform, then to the trabecular and finally, in the late stage, to the solid pattern. There was no reverse direction of histological transformation from the solid to the tubular pattern. These results may help to explain previous reports that the tubular pattern usually represents a favourable prognosis, the solid pattern a poor prognosis and the cribriform pattern an intermediate prognosis.

Introduction

The histological features of adenoid cystic carcinoma are varied. Eneroth *et al.* (1968) reported that adenoid cystic carcinomas could be divided into two histological patterns: cribriform and solid. Perzin *et al.* (1978) classified these neoplasms into three basic patterns: tubular, cribriform and solid. Chomette *et al.* (1982) described three histological patterns: trabecular, cribriform and basaloid.

The correlation between the histological patterns of adenoid cystic carcinoma and the clinical features has long been studied. Several authors (Perzin *et al.*, 1978; Chomette *et al.*, 1982; Gates, 1982; Goepfert *et al.*, 1983; Matsuba *et al.*, 1986) have reported that the prognosis is best for the tubular type, worst for the solid type and intermediate for the other types. However, Spiro *et al.* (1974) stated that the clinical stage of the tumour was much more prognostic than its histological grade.

In previous studies (Perzin *et al.*, 1978; Nascimento *et al.*, 1986), only one tissue specimen obtained from the primary

TABLE I
CHANGES OF HISTOLOGICAL PATTERNS IN CASE 1 (A 54-YEAR-OLD WOMAN)

Date of histological examination	Site of specimen	Histological pattern (%)		
		Crib	Trab	Solid
1973	Oral floor	0	100	0
1982	Oral floor	0	76	24
1986	Oral floor	0	19	81

Crib: cribriform
Trab: trabecular

TABLE II
CHANGES OF HISTOLOGICAL PATTERNS IN CASE 2 (A 70-YEAR-OLD MAN)

Date of histological examination	Site of specimen	Histological pattern (%)		
		Crib	Trab	Solid
1980	lt-Nasal cavity	100	0	0
1980	lt-Cervical lymph node	32	68	0
1981	lt-Nasal cavity	100	0	0
1982	lt-Lung metastatic lesion	100	0	0
1982	lt-Nasal cavity	100	0	0
1983	lt-Nasal cavity	91	9	0

Crib: cribriform
Trab: trabecular

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TABLE III
CHANGES OF HISTOLOGICAL PATTERNS IN CASE 3 (A 66-YEAR-OLD MAN)

Date of histological examination	Site of specimen	Histological pattern (%)		
		Crib	Trab	Solid
1979	lt-Submandibular gland	12	88	0
1983	rt-Lung metastatic lesion	0	93	7
1983	lt-Submandibular lesion	0	100	0

Crib: cribriform
Trab: trabecular

TABLE IV
CHANGES OF HISTOLOGICAL PATTERNS IN CASE 4 (A 56-YEAR-OLD MAN)

Date of histological examination	Site of specimen	Histological pattern (%)		
		Crib	Trab	Solid
1980	lt-Submandibular gland	78	14	8
1983	lt-Submandibular gland	36	46	18

Crib: cribriform
Trab: trabecular

TABLE V
CHANGES OF HISTOLOGICAL PATTERNS IN CASE 5 (A 62-YEAR-OLD WOMAN)

Date of histological examination	Site of specimen	Histological pattern (%)		
		Tubular	Crib	Trab
1983	lt-External ear canal	82	18	0
1984	lt-External ear canal	80	20	0

Crib: cribriform
Trab: trabecular

TABLE VI
CHANGES OF HISTOLOGICAL PATTERNS IN CASE 6 (A 48-YEAR-OLD WOMAN)

Date of histological examination	Site of specimen	Histological pattern (%)		
		Tubular	Crib	Solid
1983	Base of tongue	97	3	0
1985	Base of tongue	0	86	14

Crib: cribriform

TABLE VII
CHANGES OF HISTOLOGICAL PATTERNS IN CASE 7 (A 48-YEAR-OLD WOMAN)

Date of histological examination	Site of specimen	Histological pattern (%)		
		Crib	Trab	Solid
1982	rt-Nasal cavity	57	0	43
1985	rt-Nasal cavity	0	0	100

Crib: cribriform
Trab: trabecular

TABLE VIII
CHANGES OF HISTOLOGICAL PATTERNS IN CASE 8 (A 43-YEAR-OLD MAN)

Date of histological examination	Site of specimen	Histological pattern (%)			
		Tubular	Crib	Trab	Solid
1982	rt-Nasal cavity	26	34	40	0
1985	rt-Nasal cavity	0	23	77	0
1986	rt-Nasal cavity	0	0	49	51
1986	lt-Lung metastatic lesion	0	67	19	14
1987	rt-Nasal cavity	0	0	47	53

Crib: cribriform
Trab: trabecular

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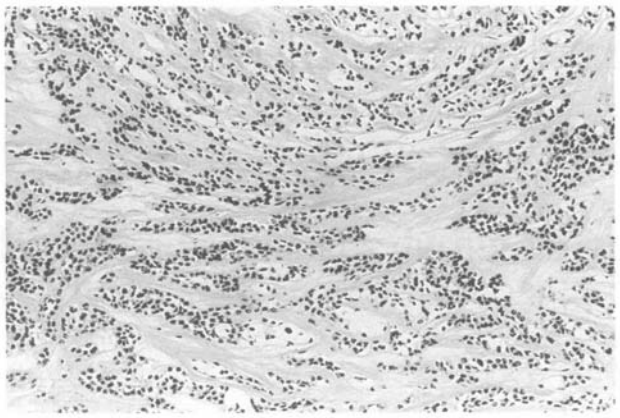

FIG. 1

Case 1: The photograph shows the trabecular pattern of the primary tumour of 1973. H&E stain, × 200.

lesion, but not from recurrent and/or metastatic lesions, was used for the histological classification of the tumour. Moreover, since the histological categories of the tumours were determined from their predominant histological patterns, the classification was difficult in some cases because of the coexistence of other patterns in the same tumour (Perzin *et al.*, 1978; Chaudhry *et al.*, 1986). Therefore, the histological data obtained from these materials and methods might not reflect correctly the histological features of the tumour.

In this study, to correlate the histological features of the tumour with the prognosis, we attempted to review all available histological slides obtained not only from the primary tumour but also from recurrent and/or metastatic tumours in the same case, and to determine whether and how the histological features of the tumour varied during its natural history. More specifically, the percentage of the area of each histological pattern was calculated histomorphometrically in all light microscopic sections and compared at various stages.

Materials and Methods

Of the patients with adenoid cystic carcinomas resected at Osaka Medical College, eight who had a recurrence after one year or more and/or metastases were reviewed. There were four male and four female patients, who were between 43 and 70 years of age (average 55.9). Three of the eight tumours arose from the nasal cavity, two were in the submandibular gland, one in the oral floor, one in the external auditory canal and one at the base of the tongue.

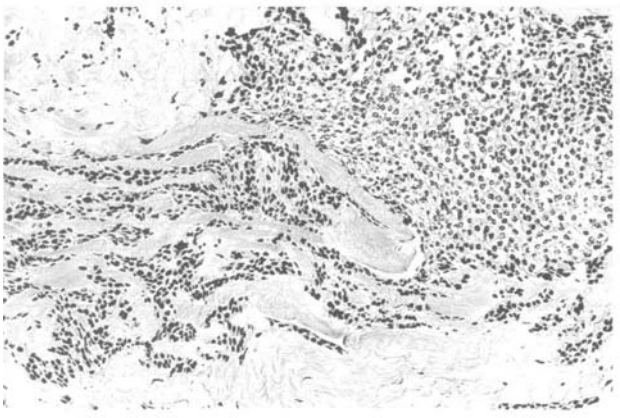

FIG. 2

Case 1: The photograph shows mixed features: a solid pattern (right half of the photograph) and a trabecular pattern (left half) in the recurrent tumour of 1982. H&E stain, × 200.

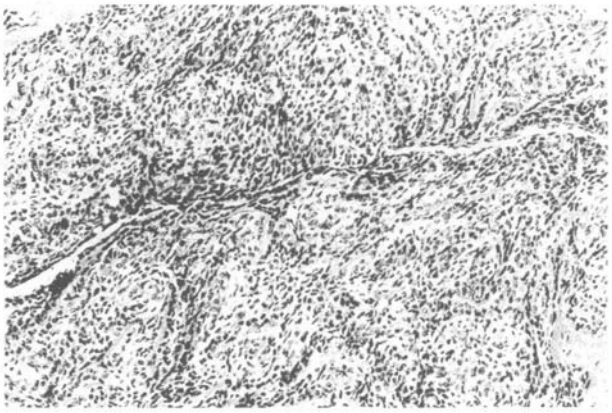

FIG. 3

Case 1: The photograph shows a solid pattern in the tumour of 1986. H&E stain, × 200.

For the clinical analysis, the following items were recorded from the chart: age at the time of diagnosis, sex, clinical history, primary site of tumour, site of recurrence, site of metastasis, date and site of biopsy, and treatment modality. All of the histological slides obtained from primary, recurrent and metastatic lesions in each case were used for the histomorphometrical analysis. Histological classifications were according to the four patterns described by earlier investigators (Perzin *et al.*, 1978; Chomette *et al.*, 1982): tubular, cribriform, trabecular and solid. In this study, the trabecular pattern included all cord-like structures seen in connection with the solid pattern as well as with the tubular and cribriform patterns. Since all four histological patterns are often seen in various proportions not only in the same tumour, but even in the same slide, the percentage of each pattern was calculated in the same slide. The total area of the tissue section in the slide and the area of each histological pattern were measured by Luzex III (Nikon Co. Japan), and the percentage of the total area of the tissue section which each occupied was calculated.

Results

The results are presented in Tables I–VIII. The histological changes of Cases 1, 6 and 7 are also shown in Figures 1–7. In seven of the eight cases, the tumour recurred after more than two years, and the histological features were to a greater or lesser degree different from those of the primary tumour. In the other case (Case 5) in which the tumour recurred after one year, the histology of the recurrent tumour was similar to that of the primary tumour. The histological differences between the

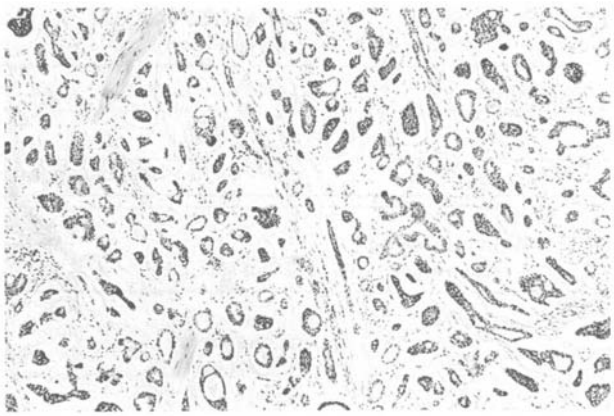

FIG. 4

Case 6: The photograph shows a predominantly tubular pattern in the primary tumour. H&E stain, × 100.

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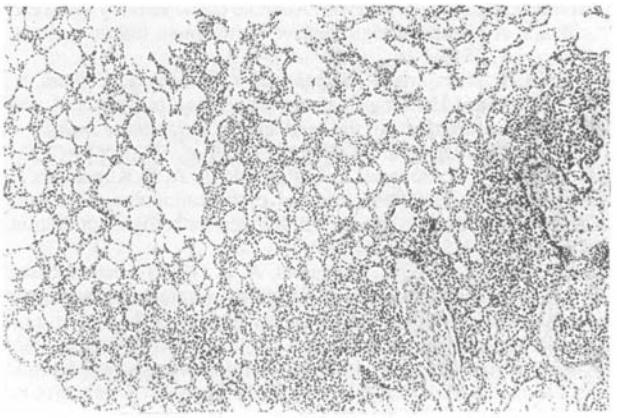

FIG. 5

Case 6: The photograph shows mixed features: mostly a cribriform pattern (left)) and a small area of solid pattern (right lower field) in the recurrent tumour of 1985. H&E stain, × 100.

primary tumour and the recurrent tumour after three years were slight in Case 2, moderate in Case 4 and marked in Case 7. The results described above show a certain tendency. The percentages of the histological patterns of adenoid cystic carcinoma increased in the following order in recurrent tumours: tubular, cribriform, trabecular and solid. No such shift of percentages of histological patterns occurred in the reverse direction. In the metastatic lesions, the histological transformation progressed in the similar direction to that in recurrent tumours.

Discussion

Some authors (Perzin *et al.*, 1978; Marsh and Allen, 1979) have already pointed out that in some cases of adenoid cystic carcinoma the histological features of recurrent and/or metastatic tumours differ from those of the primary tumour. Perzin *et al.* (1978) noted that some tumours which originally had a tubular pattern later showed a cribriform or solid pattern and that others changed from a cribriform to a solid pattern. Marsh and Allen (1979) reported that six of the 21 patients from whom histological material was available from recurrent and/or metastatic lesions developed a tumour of higher grade; that is, a tumour appearing cytologically more malignant, than the primary lesion. From the results of their immunohistochemical study, Chen *et al.* (1988) hypothesized that in the tumourigenesis of adenoid cystic carcinoma, as neoplastic cells differentiate and proliferate, a solid pattern is first formed, next a cribriform or trabecular pattern appears, and the latter two patterns may change

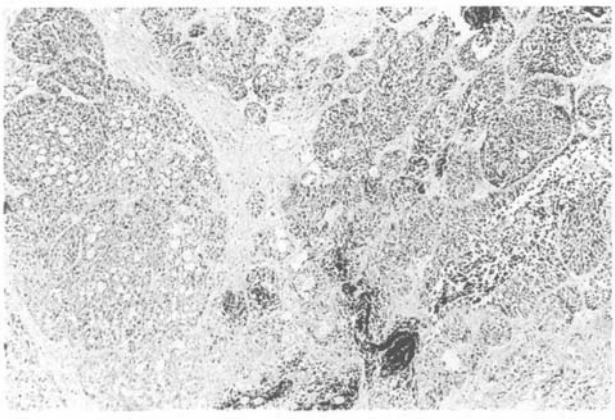

FIG. 6

Case 7: The photograph shows mixed features: a cribriform pattern (left half of photograph) and a solid pattern (right half) in the primary tumour of 1982, H&E stain, × 100.

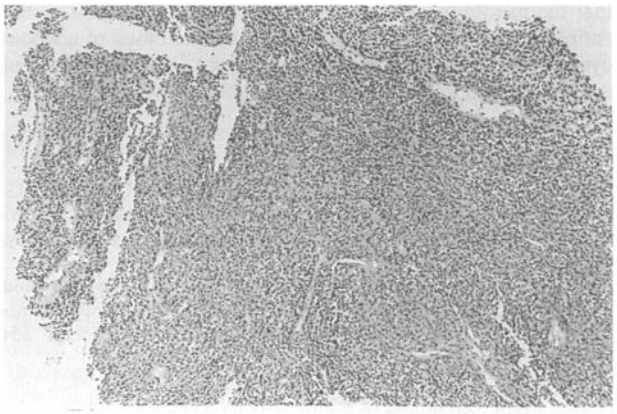

FIG. 7

Case 7: The photograph shows a completely solid pattern in the recurrent tumour of 1985, H&E stain, × 100.

into each other. Consequently, they concluded that since most adenoid cystic carcinomas contain a mixture of histological features, the growth patterns of adenoid cystic carcinoma very likely represent a dynamic state.

In this study, we attempted to assess objectively how the histological features of the tumour change during the clinical course of the disease and to correlate the histological features with the prognosis. We found that the percentage of each histological pattern of the tumour shifted from the tubular pattern through the cribriform and trabecular patterns to the solid pattern during the clinical course. The histological transformation did not progress in the reverse direction. It was also noted that the histological transformation in metastatic lesions progressed in the similar direction to that in recurrent tumours. Our findings do not contradict those of Perzin *et al.* (1978) and Marsh and Allen (1979), as mentioned before. The present result is of interest because it is suggestive of the direction of the histological transformation of adenoid cystic carcinoma.

Several investigators (Eneroth *et al.*, 1968; Perzin *et al.*, 1978; Chomette *et al.*, 1982) have stated that the tubular pattern represents the most differentiated form of adenoid cystic carcinoma and the solid pattern is a poorly differentiated form. In addition, some authors (Perzin *et al.*, 1978; Morinaga *et al.*, 1986) have reported that cell atypia and mitosis are seen more frequently in the solid pattern than in other patterns. In our previous study (Saka *et al.*, 1991), we analysed nuclear DNA content of the region occupied by a predominant pattern in each adenoid cystic carcinoma, and clarified that the $S+G_2M$ fraction was significantly higher in solid pattern than in cribriform or trabecular pattern tumours and the polyploid cell rate was significantly higher in the solid pattern than in the cribriform pattern tumours. The results may indicate that proliferative activity is higher in the solid pattern than in the other two. Judging from these previous studies, our present results indicate that the histological transformation of adenoid cystic carcinoma tends to progress towards the poorly differentiated form of the tumour. In other words, they may indicate that as the histological pattern of adenoid cystic carcinoma becomes poorly differentiated, the neoplasm proliferates more vigorously, then recurs and/or metastasizes. This may explain the previous reports (Perzin *et al.*, 1978; Chomette *et al.*, 1982; Matsuba *et al.*, 1986) that the prognosis of adenoid cystic carcinoma is best when the pattern is tubular, worst when it is solid and intermediate when it is cribriform.

It is thought that the factors which cause the histological transformation of the tumour generally include the histological environment around the tumour, the immunological defense mechanisms of the host and the biological aspects of the tumour itself, and that the degree and speed of transformation can be determined by the degree of involvement of all these factors. There were only eight patients in this study, and it is not certain

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that the histology of one tissue section represents that of the entire tumour. Further examinations of more cases of adenoid cystic carcinoma are necessary to discuss a certain tendency of the histological transformation of adenoid cystic carcinoma.

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