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DNA Ploidy and S-phase Fraction in Pulmonary Carcinoids

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AN ABNORMAL DNA content and a high S-phase fraction (SPF) has been found to correlate with a poor prognosis in several human malignancies [1, 2]. We evaluated these parameters in a series of 18 typical and one (patient 11) atypical pulmonary carcinoids, tumours considered of low grade malignant potential, metastases being reported in 5–15% [3]. DNA ploidy and SPF were evaluated by flow cytometry on paraffin-embedded specimens according to Hedley *et al.* [4].

11 tumours (58%) were diploid, seven (37%) aneuploid and one (5%) tetraploid (Table 1). All aneuploid tumours had a DNA index close to 1 (1.1–1.2). The SPF was not evaluable in three specimens. The median SPF value was 9.1% (range 4.9–19%). 11 (69%) tumours had high (> 7%) SPF values. Mean SPF was higher in aneuploid {[mean (S.D.)] 12.4 (4.8)%} than in diploid [8.4 (2.6)%] tumours. One patient (no. 8) died from metastatic disease in the liver and another (no. 12) relapsed in the lung. The former showed a diploid DNA profile while the latter had an aneuploid one. Both tumours were typical carcinoids and had a high SPF. No relationship among DNA ploidy, SPF and histologic characteristics was observed.

Data on ploidy in neuroendocrine tumours are scanty and contradictory [5–9]. In our study, DNA ploidy was not apparently associated with clinical prognosis of pulmonary carcinoids, although the follow-up period is relatively short. It remains to be clarified whether the DNA index close to 1 found in aneuploid tumours has some significance, i.e. is related to a less malignant phenotype or predictive of low metastatic potential. About 50% of our carcinoids had a high SPF, a characteristic that in other tumour types is associated with poor prognosis [2].

We conclude that DNA ploidy and SPF might contribute to a better definition of the biological characterisation of pulmonary carcinoids, but do not seem to provide clinically useful prognostic information.

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Table 1. Features of pulmonary carcinoids

Patient	Sex	Age (years)	Follow-up (months)	DNA index	SPF (%)	Stromal Invasion	Nucleoli	Mitosis	Necrosis	Pleomorphism
Diploid										
1	F	48	19	1.0	5.0	–	–	–	–	–
2	M	58	13	1.0	6.9	–	+	–	–	+
3	M	61	14	1.0	7.4	–	–	–	–	–
4	F	53	30	1.0	9.5	–	–	–	–	–
5	M	36	9	1.0	4.9	–	+	–	–	–
6	M	66	7	1.0	9.3	+	++	+	–	+
7	F	27	67	1.0	6.2	–	–	–	–	–
8	M	56*	42	1.0	8.7	+	++	–	–	++
9	F	52	61	1.0	12.2	–	–	–	–	–
10	M	13	70	1.0	9.7	–	±	–	–	±
11	M	50	7	1.0	12.9	–	+	+	+	–
Aneuploid										
12	M	51*	25	1.1	13.3	–	–	–	–	–
13	M	46	83	1.2	19.0	–	–	–	–	–
14	M	29	28	1.2	NE	+	+	–	–	±
15	F	60	59	1.1	NE	–	+	–	–	+
16	F	37	41	1.1	14.2	+	+	–	+	+
17	F	38	42	1.2	NE	+	–	–	–	+
18	M	67	7	1.1	8.9	–	++	–	–	–
Tetraploid										
19	F	55	11	1.9	6.8	–	–	–	–	–

* Had metastases.
– = Absent, ± = doubtful, + = present/mild and ++ = present/marked. NE = Not evaluable, SPF = S-phase fraction.

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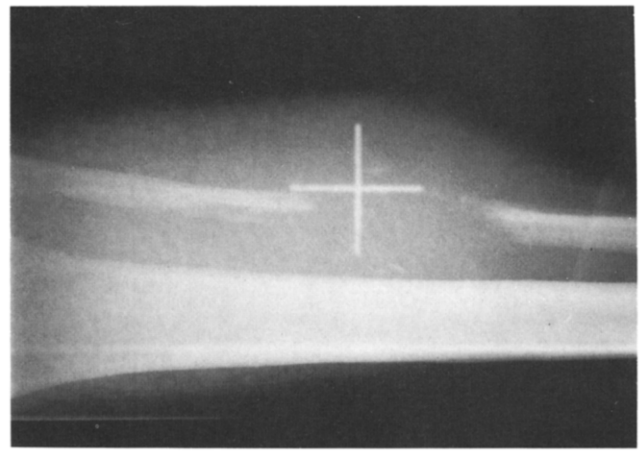

Fig. 1. Lesion in the left fibula in high-grade angiosarcoma of bone.

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Failure of Palliative Radiotherapy in High-grade Angiosarcoma of Bone

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HAEMANGIOENDOTHELIAL SARCOMA (angiosarcoma) of bone is an uncommon tumour of vascular endothelium, comprising between 0.13 and 0.17% of primary bone tumours [1, 2]. Metastatic disease develops in almost all patients with high-grade tumours [3, 4].

A 54-year-old man presented to our unit with a 6-month history of increasing pain in his left hip and leg. X-rays revealed destructive lesions in both the left ilium and left fibula (Fig. 1). He then developed acute left ventricular failure. Haemoglobin was 8.8 g/dl. Both history and clinical examination did not suggest blood loss, and he responded to treatment for cardiac failure. Investigations revealed no other disease sites and biopsy and immunocytochemistry led to the diagnosis of high-grade angiosarcoma of bone.

Because of severe pain, he received radiotherapy on a cobalt-60 unit with parallel opposed fields. The fibula received a midplane dose of 50 Gy (in daily 3.3 Gy fractions) and the left pelvis a midplane dose of 40 Gy (in daily 2.7 Gy fractions). His pain improved only transiently and 2 months later spread to his low back. X-rays revealed collapse of the body of the fourth lumbar vertebra. The patient then developed refractory cardiac failure and died, 5 months after the initial diagnosis.

Cardiac metastases were found at necropsy and decalcified bone sections revealed areas of residual angiosarcoma at both the irradiated sites. Splenomegaly (with increased iron stores and foci of extramedullary haemopoiesis), a hypercellular bone marrow with red marrow extension and an increase in immature myeloid cells were also present. These were felt to indicate a co-existent myelodysplastic disorder, a previously unreported association with this tumour.

We found no clinical or pathological evidence of a response to irradiation and suggest that other treatments be explored for this aggressive tumour.

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