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# Cytogenetic Observations on a Carcinoma of the Cervix Uteri with Double Minute Chromatin Bodies*

N. B. ATKIN and MARION C. BAKER

*Department of Cancer Research, Mount Vernon Hospital, Northwood, Middlesex HA6 2RN, United Kingdom*

**Abstract**—*In contrast to previous carcinomas at this site studied by chromosome banding techniques, no abnormalities or relative excess of the No. 1 chromosomes were found in a stage I carcinoma of the cervix. A feature of the tumour metaphases, however, was the presence of double minute chromatin bodies, including some rather larger bodies in a few of the metaphases. It is suggested that the absence of changes involving the No. 1 chromosomes might be related to the early stage and good prognosis of the tumour.*

## INTRODUCTION

IN A RECENT study, each of 26 consecutive cervical carcinomas that yielded satisfactory chromosome preparations was characterized by changes involving chromosome 1: either a relative excess of normal chromosomes or one or more abnormal chromosomes were present [1]; the preparations were not good enough to allow full karyotype analyses. The tumour described here has yielded rather better G-banded metaphases; in contrast to the previous tumours, abnormalities of chromosome 1 were not detected, but a feature of the tumour cells was the presence of double minute chromatin bodies (DMs).

## MATERIALS AND METHODS

*Case report*

The patient, aged 58, presented with a stage I poorly differentiated squamous cell cervical carcinoma. She was treated by radium insertions followed 8 weeks later by Wertheim's hysterectomy; histological examination of the operation specimen failed to reveal any residual tumour.

*Chromosome studies*

Direct preparations of biopsy material from the untreated primary tumour were G- and C-banded as previously described [1].

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## RESULTS

Chromosome counts showed a modal number of 80 (Table 1). Analysis of ten G-banded metaphases showed only a minor degree of variation. A representative karyotype is shown in Fig. 1. Most metaphases had three extra copies of chromosomes 14, 19 and 20; two extra copies of chromosomes 3, 5, 7, 8, 10, 15 and 21; and one extra copy of chromosomes 1, 2, 6, 9, 11, 13, 16, 18, 22 and the X. A single marker was commonly present: a small metacentric which was probably an isochromosome for 4p or 5p (Fig. 1). C-banded metaphases showed consistent appearances; there was no evidence of any structural changes involving chromosomes 1, 9 or 16.

*Double-minute chromatin bodies*

These were present in all metaphases examined. They showed the variation in size and number typical of these bodies, but in a few metaphases a moderate number of rather larger minutes (the diameter of each minute being about 1 $\mu$m), with or without a moderate number of typical DMs, were seen (Table 2; Fig. 2). In C-banded metaphases, both the larger and the smaller chromatin bodies failed to show any evidence of heterochromatin. The larger bodies occasionally showed a ring-like appearance (Fig. 2b).

*Table* 1. *Chromosome counts on* 28 *tumour metaphases*

| | Number of chromosomes | | | |
|---|---|---|---|---|
| | 79 | 80 | 81 | 82 |
| Number of metaphases | 3 | 12 | 9 | 4 |

*Table* 2. *Incidence of double minutes (DMs)*

| | Number of DMs | | | |
|---|---|---|---|---|
| | | | 3–16 larger DMs | |
| | 10–160 typical DMs | 3–9 typical DMs | with similar number of typical DMs | without typical DMs |
| No. of metaphases | 60 | 7 | 5 | 2 |

## DISCUSSION

The first interesting feature of the present tumour, unlike the cervical carcinomas previously studied, is the failure to detect either any structural abnormality involving chromosome 1 or a relative excess of normal chromosomes 1. It is possible that there has been a small undetected translocation of part of a chromosome 1 onto another chromosome; however, it is clear that none of the common abnormalities involving chromosome 1, viz. $1p-$ or a translocation involving $1p$, $1q+$ or $i(1q)$, commonly found in carcinoma of the cervix [1] was present.

The second notable feature is the presence of DMs, including some that were larger than usual. DMs have been described in a variety of human and murine tumours; we have found them in occasional carcinomas at most of the common sites, virtually all the tumour cells containing small double bodies which are pale-staining with the C-band technique, show some slight variation in size, and considerable variation in number from metaphase to metaphase (sometimes well over 100 being present). The larger DMs which were seen in seven metaphases of the present tumour numbered up to 16, and also failed to show any C-positive material. The metaphases in which they were present had few if any typical, smaller, DMs, suggesting that they represent an alternative form of the latter; in this they resemble the 'C-minus' chromosomes (metacentrics lacking C-positive heterochromatin) described by Levan and colleagues [2] which appeared coincidentally with a reduction in the number of DMs in a subline of a mouse ascites tumour that had carried DMs for some years. A similar appearance was shown by a metaphase from a human blood culture maintained for over 1 yr *in vitro* in which there were a few DMs and a larger number of double 'fragments' of varying size; it was suggested that the DMs might have originated from the latter [3].

DMs represent one of the more intriguing phenomena found in tumour cells (they have not been described in normal cells). They are Feulgen-positive but do not appear to possess centromeres [4, 5], the daughter halves of the DMs being distributed at random to the daughter cells (thus resulting in variation in number from cell to cell). It has been suggested that they are of viral origin [6]; or they might have originated from host chromosomes and represent an amplification of gene sites resulting in increased malignancy [7]. It has also been suggested that they are ring chromosomes, commonly acentric [3]. (Another phenomenon which appears to bear a relationship to DMs is the homogeneously-staining region observed in human neuroblastoma cell line chromosomes [8] which were

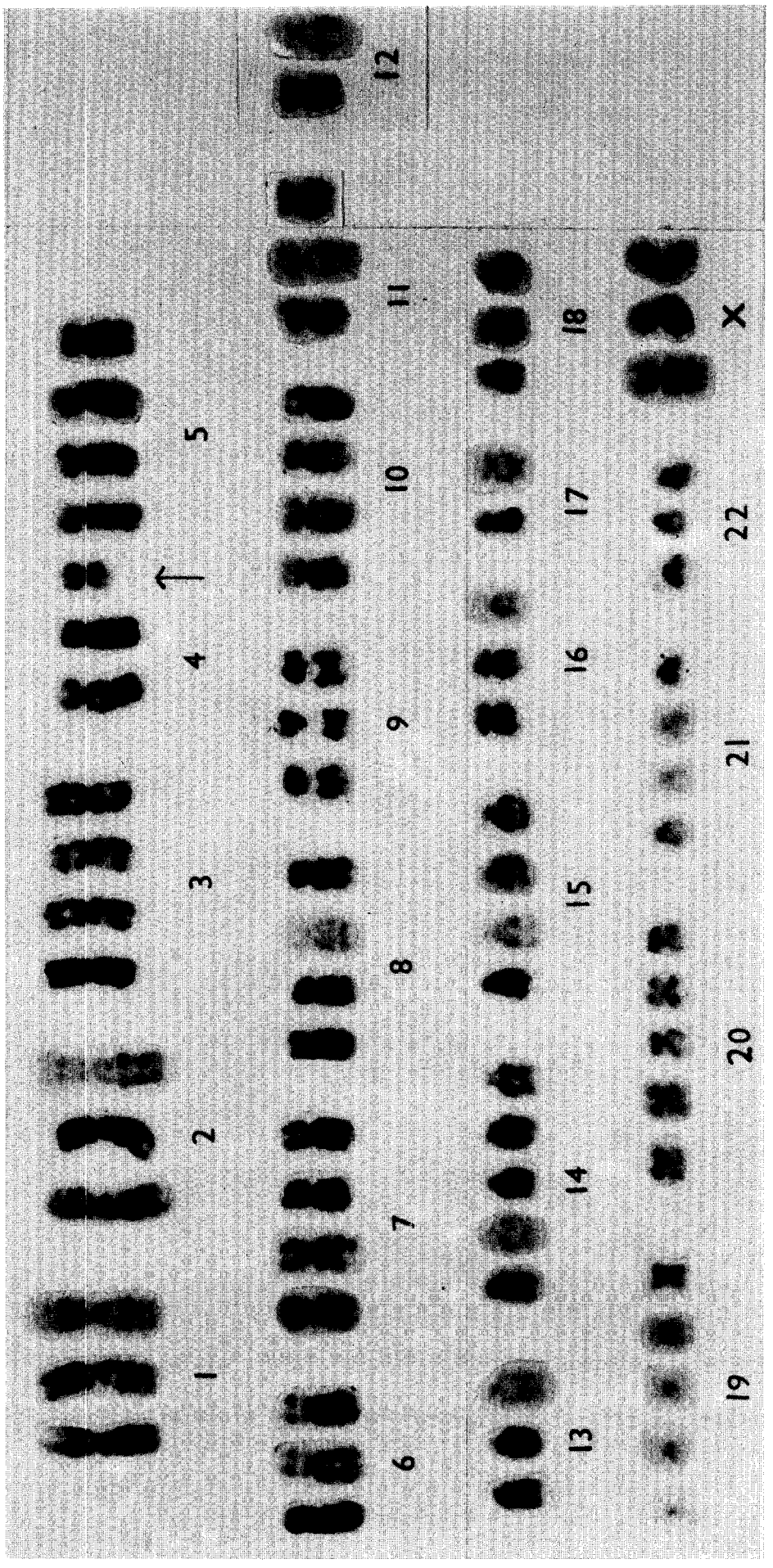


*Fig.* 1. *Representative G-banded karyotype,* 80 *chromosomes. Arrow indicates abnormal chromosome (?isochrosome for* 4*p or* 5*p).* ×4450.

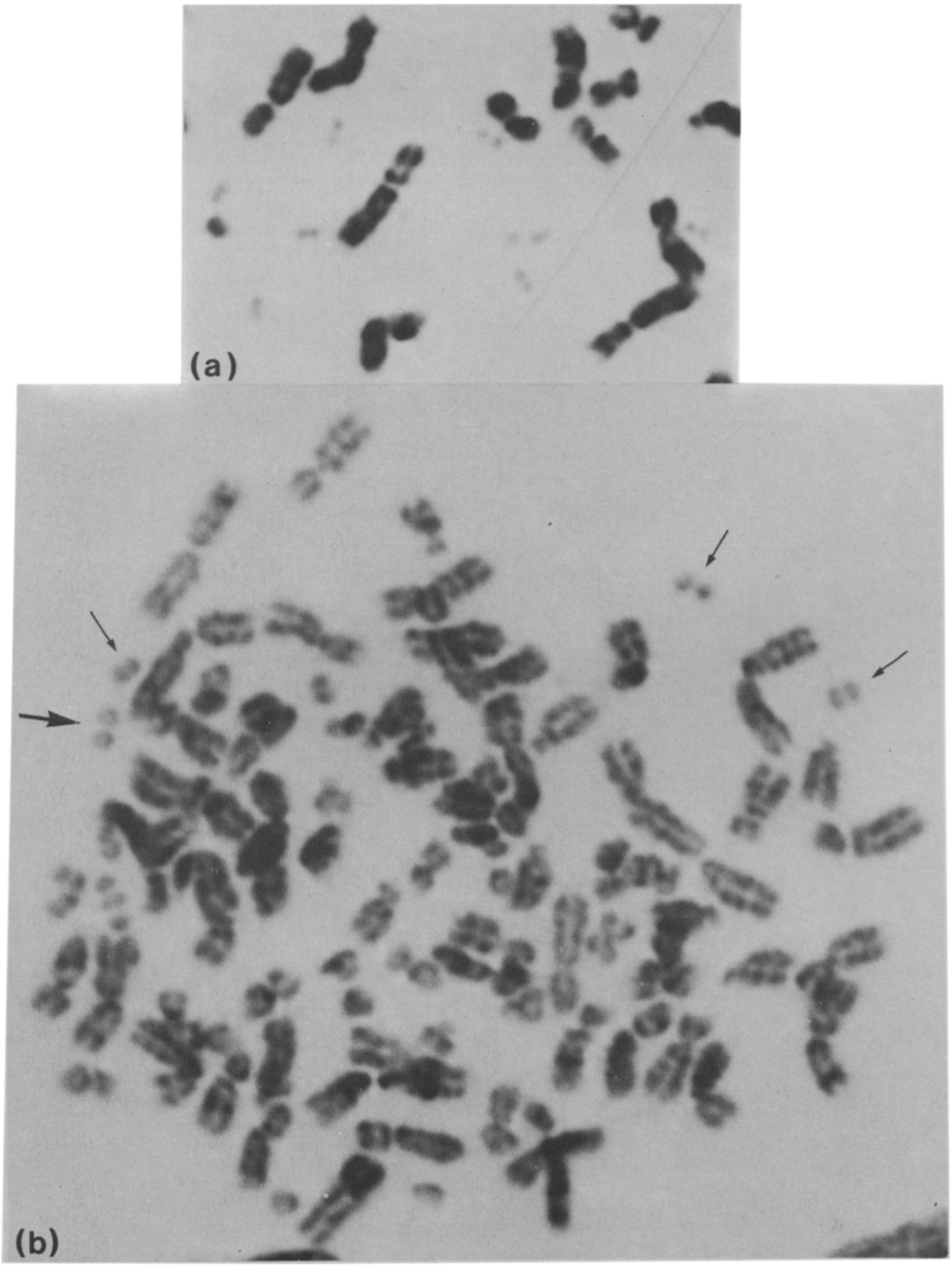


*Fig. 2.* (*a*) *Part of metaphase showing typical DMs;* (*b*) *metaphase with larger DMs; four are indicated by arrows, the thick arrow indicating one with a ring-like appearance. G-banded.* ×4450.

found to segregate independently of DMs present in the same cell line [9]).

If indeed no excess of chromosome 1 material or structural abnormality of this chromosome is present in the tumour described here, unlike the previous cervical carcinomas that we have studied, we may speculate that the DMs, both small and large, are performing a function with respect to the determination of the malignant characteristics of the cells which is similar to that performed by the chromosome 1 imbalance in the previous tumours. Another possibility is that the absence of chromosome 1 excess or abnormality might be related to a rather low degree of malignancy: the tumour appeared to have been confined to the pelvis and to have been completely eradicated by the radiation therapy; also, its chromosome number in the triploid–tetraploid region places it in a relatively favourable category [10].

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