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CASE REPORT

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A child with a t(11;19)(q14–21;p12) in a pulmonary mucoepidermoid carcinoma

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Abstract We report on a mucoepidermoid carcinoma (MEC) of the lung in a 6-year-old girl with a t(11;19)(q14–21;p12) as the sole karyotypic abnormality. An apparently identical t(11;19) has been reported previously in a MEC originating from the major and minor salivary glands. Our findings indicate that the t(11;19) is intimately associated with the mucoepidermoid phenotype and may be used as a diagnostic marker for this tumour type.

Key words Cytogenetics · Mucoepidermoid carcinoma · Chromosome translocation

Introduction

Mucoepidermoid carcinoma (MEC) is most commonly found in the major and minor salivary glands [1], but also occasionally develops in the mucous glands of the respiratory tract [8]. It is the most common type of malignant salivary gland tumour and the second most frequent pulmonary tumour of bronchial gland origin. Microscopically, MEC is composed of three different cell types, goblet cells, intermediate cells and epidermoid cells, forming a variety of growth patterns. The term "mucoepidermoid" emphasizes the presence of both mucous and epidermoid cells in these tumours. Previous cytogenetic studies of MEC have revealed a t(11;19)(q14–22;p12) as the most characteristic structural abnormality (Table 1) [2–5, 7, 11, 13]. Of a total of 25 MECs analysed cytogenetically, the t(11;19) has been found in 9 (36%) cases (see references in [13]). Interestingly, an apparently identical translocation has also been observed in Warthin tumours [9]. In this paper we describe a MEC of the lung in a 6-year-old girl with a t(11;19)(q14–21;p12) as the sole karyotypic abnormality.

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Clinical history

The patient was a 6-year-old girl who, over a period of 7 months, had four episodes of X-ray-verified pneumonia involving the right lower lung lobe. Bacteriological cultures showed growth of *Haemophilus influenzae*. She had previously had whooping cough without sequelae, and also a few episodes of otitis media. Bronchoscopy revealed a slightly reddish granulomatous tumour occluding segments 8 and 9 on the right side. At operation a well-defined tumour the size of a pea was found within the bronchus to the basal segments of the right lower lobe. A basal segmental resection was performed. Several enlarged lymph nodes in the interlobular grove and in the lung hilus were also removed. The postoperative course was uneventful. After 2 years there were no signs of local recurrence or metastases.

Materials and methods

For light microscopy, 5-µm sections were cut from the paraffin blocks of the tumour. The sections were stained with haematoxylin and eosin and with periodic acid–Schiff (PAS). For immunocytochemical analysis, the avidin–biotin complex (ABC) method was applied to formalin-fixed, paraffin-embedded tumour tissue [5]. The primary antisera and their dilutions were: cytokeratin (1/4, CAM 5.2, Becton Dickinson, Mountain View, Calif.), epithelial membrane antigen (1/100, EMA, Dakopatts) and p53 (1:500, DO-7, Dakopatts).

Fresh tumour tissue was minced into small pieces and digested in a collagenase solution (250 U collagenase/ml) for 1 h at room temperature. After being washed twice in Eagle's MEM, the cell suspension was seeded in 25 cm^2 flasks in Dulbecco's MEM/Ham's F12 (1:1) supplemented with 10% fetal calf serum, 1% 200 mM *L*-glutamine, 200 U penicillin/ml, 50 µg streptomycin/ml, 0.4 µg hydrocortisone/ml, 10^{-10} M cholera toxin, 5 µm insulin/ml, 24 µg adenin/ml and 20 ng epidermal growth factor (EGF)/ml. Cells were harvested after Colcemid exposure followed by hypotonic treatment and fixation in methanol/acetic acid. Slides were subsequently G-banded and analysed according to the recommendations of the ISCN [10].

Fluorescence in situ hybridization (FISH) was performed on unbanded metaphase chromosomes using painting probes for chromosomes 11 and 19 (Oncor, Gaithersburg, Md.). The conditions for hybridization, post-hybridization washes and immunocytochemical detection of the probes were as recommended by the manufacturer. Chromosomes were counterstained with propidium iodide. Slides were examined in a Zeiss Axiophot epifluorescence microscope using the appropriate filter combinations.

Results

Grossly, a 13-mm rounded, exophytically growing and well-demarcated tumour was found obstructing the segmental bronchus. Microscopically, it was composed of cords and islands of squamous cells intermingled with intermediate and mucus-producing cells (Fig. 1). There were numerous mucin-filled spaces. There were few mitotic figures and mild nuclear atypia. The tumour cells were positive for cytokeratin and EMA and negative for p53. The histopathological picture was consistent with a low-grade mucoepidermoid carcinoma. There were no signs of metastases in the regional lymph nodes.

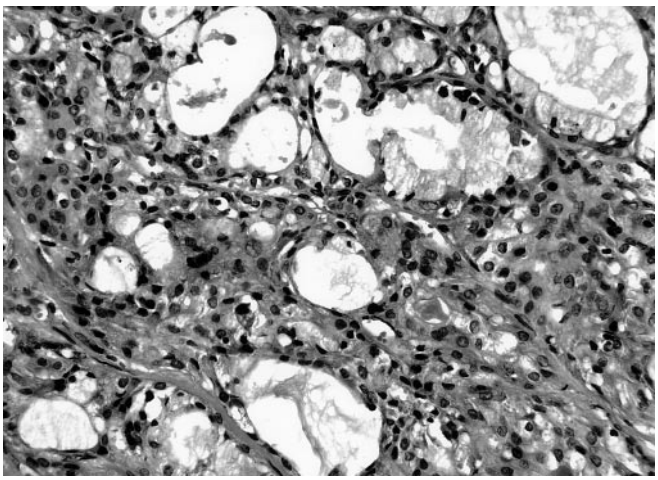

Fig. 1 Photomicrograph of the mucoepidermoid carcinoma (MEC), showing mainly intermediate cells and mucus-producing cells. The appearance is consistent with a low-grade MEC. H&E, ×200

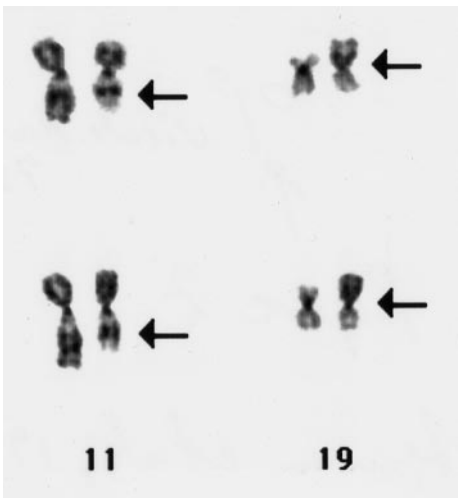

Fig. 2 Partial G-banded karyotypes of the MEC, showing the t(11;19)(q14–21;p12)

Cytogenetic analysis was performed on short-term cultured tumour cells after 8–10 days in vitro. A total of 21 metaphases were karyotyped. Twenty of these showed an identical reciprocal t(11;19)(q14–21;p12) (Fig. 2). In 13 cells the t(11;19) was the sole anomaly. Hybridization with painting probes for chromosomes 11 and 19 confirmed the presence of the t(11;19) in both metaphase and interphase cells. The remaining seven variant cells showed, in addition to the t(11;19), various nonclonal abnormalities, including two cells with trisomy 1, one with trisomy 22, and one with loss of one chromosome 15 and three F-sized markers of unknown origin. There was also one cell with a normal female karyotype.

Discussion

We describe a case of mucoepidermoid carcinoma of the lung characterized by t(11;19)(q14–21,p12). There are two previous reports of cytogenetic analysis of MEC of the lung, and one of these also had an 11;19-translocation [7]. The other case was negative for the t(11;19) and showed, in addition to four cells with a normal karyotype, four metaphases with loss of the Y chromosome, two with an inv(4)(p15q13), and two with monosomy 4 [12]. Thus, two of three pulmonary MECs have shown the t(11;19), demonstrating that this is a common abnormality, not only in MEC derived from the salivary glands but also in MEC originating from the mucous glands of the respiratory tract.

This MEC occurred in a 6-year-old girl; there is only one previous report of a MEC occurring in a child [3], a parotid tumour in a 6-year-old girl, which also showed a t(11;19)(q14–21;p12) as the sole abnormality. In addition, El-Naggar et al. [4] recently described an 18-year-old woman with a 4-year history of an intraoral MEC with a t(11;19)(q21;p13.1) as the sole change. These observations indicate similar pathogenetic mechanisms in MECs found in children and adults.

As is evident from Table 1, the t(11;19) in MEC can occur at any age, in either sexes and in multiple locations, including major and minor salivary glands, mucous glands of the respiratory tract and heterotopic, intranodal salivary gland tissue. The t(11;19) thus seems to be closely linked to the mucoepidermoid phenotype and may be used as a diagnostic marker for this tumour type. Work is now in progress to map the breakpoints physically and clone the genes involved in the t(11;19). This work may also throw some light on the curious occurrence of an apparently identical translocation in some Warthin tumours [9].

The present MEC also contained a few cells which, in addition to the t(11;19), also contained various trisomies (+1 and +22). This pattern is in line with previous obser-

Table 1 Clinical and karyotypic features of 10 mucoepidermoid carcinomas with t(11;19) or variants of there of

Reference/case	Age/sex	Localization	Karyotypes
[11]/CG461	53/F	Retromolar area	40–47,XX,t(11;19)(q14–21;p12)
[11]/CG501	76/F	Hard palate	48,XX,t(11;19)(q14–21;p12),+16,+20
[11]/CG540	59/M	Retromolar area	46,XY,inv(1)(p32–33q42),t(6;15)(p12;q25),der(11)del(11)(p11.2p13)t(11;19)(q14–21;p12),der(19)t(11;19)q14–21;p12)
[2]	57/F	Hard palate	46,XX,t(11;22;16;19)(q14.3–21;q11.2;p13.3;p12)
[3]	6/F	Partotid gland	46,XX,t(11;19)(q14–21;p12)
[7]	35/M	Lung	43–46,XY,der(11)del(11)(p14–15)add(11)(q21),der(19)t(11;19)(q21;p11)
[5]	67/F	Oral mucosa	49,XX,+7,+8,+9,t(11;19)(q21;p13.1)
[4]	18/F	Hard palate	46,XX,t(11;19)(q21;p13.1)
[13]	73/M	Heterotopic salivary gland tissue	46,XY,t(1;7)(p36;q11),t(11;19)(q14–21;p11)
This report/CG729	6/F	Lung	46,XX,t(11;19)(q14–21;p12)

vations of MEC with multiple trisomies, either as the sole anomalies or in combination with the t(11;19) translocation (Table 1) [11]. The fact that in five of ten known cases with t(11;19), or variants thereof, the translocation has been the sole anomaly indicates that it represents a primary cytogenetic abnormality in these cases and that the trisomies are secondary abnormalities related to tumour progression. Follow-up studies will indicate whether the trisomies are positively correlated with poor prognosis in MEC.

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