The Pathology of Childhood Thyroid Tumours in the Russian Federation after Chernobyl

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Abstract The histological verification of thyroid carcinoma that have occurred in children in the contaminated areas of the Russian Federation after Chernobyl has been performed by pathologists from Obninsk and Cambridge. Formalin fixed material and paraffin blocks of 10 cases of childhood thyroid cancer were received from different hospitals in Russia during 1993-1995. 4 of the cases were female, and 6 male. In one of these cases the material available in Cambridge unfortunately showed no tumour. Of the other 9 cases, all were papillary carcinomas. 5 showed the solid follicular pattern, predominant in younger children in the UK and forming the great majority of the recent childhood cases in both Belarus and the Ukraine. 2 were predominantly oxyphil carcinomas which were classified with papillary carcinomas on both architectural and cytological grounds, and 2 showed the features of the classic type of papillary carcinoma, predominant among the older children in the UK. All children came from areas contaminated by fallout from the Chernobyl accident, with 6 from Bryansk 1 from Kaluga and 3 from Tula. All cases were confirmed by immunohistochemistry and in situ hybridisation for thyroid differentiation markers. The oncogenes ret, met and p53 were also studied by immunohistochemistry.

1. Introduction

Thyroid carcinoma is relatively rare in childhood [1]. However it is currently assuming greater importance, because of a greatly increased frequency in children exposed to fallout in the areas around Chernobyl [2-5]. We performed histological verification of 10 cases of thyroid carcinoma in children from contaminated areas of Russia and compared the histologic features with those from children in the UK.

2. Materials and methods

Paraffin blocks and 10% formalin fixed material of primary thyroid tumours, surrounding thyroid tissue and metastases to regional lymph nodes were requested from different hospitals in Russia. Histological sections of material available were examined by using routine haematoxylin-eosin staining, immunohistochemistry and in situ hybridisation to confirm the histological diagnosis. Primary antibodies for calcitonin and thyroglobulin were applied, (Dako anti-human calcitonin 1:2,000 dilution and Dako anti human thyroglobulin 1:10,000 dilution), followed by the indirect

peroxidase technique. In situ hybridisation methods included the application of digoxigenin labelled probes for calcitonin (0.lng/ml) and thyroglobulin (0.2ng/ml). ret, met and p53 oncogene expression was also investigated by immunohistochemistry. Anti-bodies to ret and met (1:100 dilution) were followed by indirect peroxidase technique and p53 (1:200 dilution), followed by the avidin-biotin technique. All antibodies were from Santa Cruz Biotechnology.
Morphological verification of diagnosis was carried out in accordance with the criteria of the WHO classification of thyroid tumours [6].

3. Results

Among 10 patients 6 were male and 4 female. The age of the patients was 8, 9, 10 (2 cases), 11, 12 (2 cases), 13 and 14 years (2 cases). Papillary carcinomas were verified in 9 cases. In one case the material available unfortunately showed the surrounding thyroid tissue only. Five tumours showed the solid follicular pattern of papillary carcinoma. Two were predominantly oxyphil carcinomas. They were classified with papillary carcinomas on both architectural and cytological grounds. Two tumours showed the features of the classic type of papillary carcinoma; in one of these cases the histological feature of papillary microcarcinoma was found. The diameter of this tumour was less than 1 cm. Lymph node metastases were found in 7 cases. Histological conclusions were confirmed by immunohistochemistry and in situ hybridisation in all cases of papillary carcinomas. All 9 tumours showed follicular cell differentiation, with irregular accumulation of thyroglobulin in different parts of the tumour and irregular distribution of cells which show thyroglobulin synthesis in different tumour areas. Focal collections of C-cells were found in the surrounding thyroid tissue of 4 cases. Oncogene investigation showed expression of met oncogene by single and groups of carcinoma cells in 5 primary and 3 metastatic thyroid tumours. Only tumours with cells showing membrane staining for met were considered to be positive. Four tumours were positive by immunohistochemistry for ret protein. These tumours showed cells with either cytoplasmic or membrane positivity. No tumour showed positivity on immunohistochemistry for p53 protein.

4. Discussion

We have performed histological verification of cases of thyroid cancer that have occurred in children in the contaminated areas of Russian Federation after Chernobyl and confirmed the diagnosis of papillary thyroid carcinoma in 9 cases. In one case material available were presented only by surrounding thyroid tissue. The solid follicular pattern of thyroid carcinoma is predominant in younger children in the UK and in the great majority of the recent childhood cases in both Belarus and the Ukraine. This variant formed 55% of our cases. In two cases tumours were predominantly oxyphil cell in type. They were classified as papillary carcinomas on both architectural and cytological grounds which included intranuclear cytoplasmic invaginations, nuclear grooves and ground glass nuclei. Two cases showed the features of the classic type of papillary carcinoma, predominant among the older children in the UK. The age of the Russian children in these cases was 12. In one of these cases papillary microcarcinoma of thyroid was diagnosed. Its maximal size was less than 1 cm. The tumour was revealed by screening ultrasound examination.

Analysis of met oncogene expression showed positivity in more than half of all primary tumours and in one third of metastatic tumours. It is known [7], that the c-met proto-oncogene encodes a transmembrane tyrosine kinase, identified as the receptor for a Hepatocyte Growth Factor (HGF). HGF is a potent mitogen for epithelial cells and promotes cell motility and invasion. It is suggested [7], that the overexpression of c-met oncogene may play a role in the pathogenesis and progression of thyroid tumours derived from the follicular epithelium. Four tumours showed positivity for the ret oncogene. Translocation of this protooncogene has only been demonstrated in papillary thyroid carcinomas [8]. Further studies are needed to determine the frequency and type of ret translocation in these tumours.

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