**Pleomorphic Adenoma of Salivary Glands Does Not Appear to Be a BRCA-1-dependent Tumour in a Polish Cohort**

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**Abstract.** Background: The aim of the study was to examine whether pleomorphic adenoma of salivary glands can occur on the basis of constitutional BRCA-1 mutations. Materials and Methods: Two hundred and sixty-eight patients affected by mixed tumour of salivary glands were examined for occurrence of three BRCA-1 mutations dominating in Poland. Results: BRCA-1 mutation was detected in only one of the patients, a female affected by breast cancer and pleomorphic adenoma of parotid gland. Parotid gland tumour showed clinical and histopathological features of typical pleomorphic adenoma with no morphological features of high-grade malignancy, which are characteristic of BRCA-1-dependent tumours. Conclusion: Considering the low frequency of BRCA-1 mutation in the examined group and also the absence of features characterizing BRCA-1-dependent tumours in the only BRCA-1-positive case, pleomorphic adenoma of salivary glands should not be recognized as a BRCA-1 dependent tumour.

**Materials and Methods**

The group of cases consisted of 268 unselected, consecutive patients operated on due to pleomorphic adenoma of salivary glands in Departments of: Otolaryngology with Laryngological Oncology and Maxillofacial Surgery, Pomeranian Medical University, Szczecin, Poland (76 and 114 patients respectively) and Department of Otolaryngology – Head and Neck Surgery, Holy Cross Cancer Center, Kielce, Poland (78 patients) during the period 1999-2006. Clinical data collected on each patient included: sex, age at diagnosis, age at operation, rate of tumour growth, tumour size and localization, tumour-associated ailments, clinical staging, operation outcome – especially preservation of facial nerve function, and postoperative histopathological results.

From all of the patients, DNA was obtained from peripheral blood. Patient DNA was studied at the International Hereditary Cancer Center, Department of Genetics and Pathology, Pomeranian Medical University, Szczecin, Poland for the occurrence of three BRCA-1 mutations namely, C61G, 4153delA and 5382insC using techniques as described by Górski et al. (6, 7). Mutation analysis for mutations 4153delA and 5382insC was carried out by a multiplex specific polymerase chain reaction (PCR) assay. The third mutation (C61G) generates a novel restriction enzyme site in exon 5. This mutation is detected after digesting amplified DNA with Ava II (MBI Fermentas). To visualize the different BRCA-1 alleles, the PCR products were subjected to electrophoresis in a 1.5% agarose gel, stained with ethidium bromide. Each sample run included a positive and a negative control.

The control group included 1,000 adults unaffected by pleomorphic adenoma of salivary glands nor by any malignancy. Data about controls were obtained from the registry of International Hereditary Cancer Center.

**Key Words:** Pleomorphic adenoma, salivary glands, BRCA-1, mutation.
Results

BRCA-1 mutation was detected in only one of the patients affected by the pleomorphic adenoma of salivary gland. The identified mutation was 5382insC, which is the most frequent BRCA-1 mutation in Polish populations (6). This patient was a female with a mixed tumour of the right parotid gland diagnosed at the age of 38 years. The tumour was noticed by the patient herself within a month before the fine-needle biopsy diagnosis. It was a 20 mm, trouble-free tumour, localized posteriorly to the right mandibular angle. Two months after initial diagnosis, superficial parotidectomy was performed at the Department of Otolaryngology – Head and Neck Surgery, Holy Cross Cancer Center, Kielce, with a good outcome. The tumour was removed with a margin of healthy tissue and facial nerve function was preserved. Histopathologically, the tumour showed typical features of pleomorphic adenoma of the parotid gland. Morphological features of malignancy of high-grade were not found. The same patient was affected by breast cancer at the age of 36 years. She was treated with surgery and postoperative chemo- and radiotherapy. Histologically, the breast tumour showed features characteristic of BRCA-1-dependent tumours: it was ductal, of high grade and estrogen receptor negative (8).

Among 1,000 controls, BRCA-1 mutation was detected in 5 cases, namely, a 74-year-old male (4153delA), a 62-year-old female (5382insC), a 58-year-old male (5382insC), a 57-year-old male (C61G) and 45 year old female (5382insC). The frequency of BRCA-1 mutations among controls (0.5%) showed no statistically significant difference as compared to that of the patient group.

Discussion

Knowledge of the spectrum of tumours associated with BRCA-1 constitutional mutation seems to be very important clinically. It has been well proven that BRCA-1 mutation carriers need special programmes of prevention, surveillance and treatment of breast and ovarian cancer (9-13). The latest findings suggest that tumours of other sites in BRCA-1 mutation carriers also show clinically important features such as high morphological grade and high clinical stage at the time of diagnosis (14, 15). Since chemotherapy schemes for BRCA-1-dependent cancers of the breast and ovaries should probably be distinct, the modification of treatment of BRCA-1-dependent tumours of other sites probably should also be considered (16-18). However, according to our data, it appears that pleomorphic adenoma of salivary glands should not be recognized as a BRCA-1-dependent tumour. Firstly, the frequency of BRCA-1 mutation in our series of consecutive, unselected pleomorphic adenoma of salivary glands patients was not different from that of the controls. Additionally, pathological features of pleomorphic adenoma in the only BRCA-1-positive case detected in our study were not those characterizing BRCA-1-dependent tumours.

Conclusion

Since mixed tuomour of salivary glands does not appear to be a BRCA-1-dependent-tumour, in some rare cases of patients from families with breast and ovarian cancer aggregations related to BRCA-1 constitutional mutations, clinical management of patients with pleomorphic adenoma of salivary glands should not be different from that of standard protocols.

References


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