Appendices of the Nipple and Areola of the Breast in Neurofibromatosis Type 1 Patients Are Neurofibromas

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Abstract. In NF1-patients, tumours arising in the areola region of the breast often appear similar to the nipple. The aim of this study was to analyse tumours of this region. Eighty-three specimens from 55 patients with NF1 were analysed [females: 42, males: 13, mean age of the total group: 41.6 years, range: 4–62 years]. NF1 patients with apparent extensive affections of the breast who received debulking procedures for disfiguring invasive or superficial plexiform neurofibroma were excluded. All specimens were found to be composed entirely from neurofibromas with no residues resembling segments of glandular structures. Following ablative surgery, no local recurrence was noted within a follow-up period of 10 years. Tumours arising in the areola and nipple area and mimicking an accessory nipple were all neurofibromas. Local excision of neurofibromas was adequate to relief patients from an often unsightly appearance.

Neurofibromatosis type 1 (NF1) is an autosomal dominant inherited disease (1). The disease is assigned to the heterogeneous group of phacomatoses being defined by pigmentary disorders of the integument. In NF1 multiple café-au-lait spots are characteristic affections of the skin. However, NF1 is a complex disease affecting several organs such as bone, endocrine glands or vessels. The hallmark of the disease is cutaneous or subcutaneous tumours that are derived from the peripheral nerve sheath. These tumours are individually variable in number and size and usually appear during or after puberty. The tumour can develop at almost any site. Tumours arising in patients with the genetic background of NF1 in the areola region of the breast often appear similar to the nipple. In some cases the tumours are even appendices of the nipple (2, 3). In order to elucidate the nature of these organoid structures, a systematic analysis was performed in NF1 patients with tumours of the areola and nipple.

Patients and Methods

Eighty-three specimens from 55 patients with NF1 were analysed (females: 42, males: 13, mean age of the total group: 41.6, range: 4–62 years, mean age of females: 40.9, range: 4–62 years, mean age of males: 43.5, range: 12–61 years). All patients were surgically treated for tumour reduction of neurofibromas affecting the skin, including tumours of the areola and nipple. All patients fulfilled the current diagnostic criteria of NF1 [NIH, USA, (4)]. Tissues were excluded from the analysis if there were apparent extensive affections of the breast and the patients had received debulking procedures for disfiguring invasive or superficial plexiform neurofibromas. The analyses included all surgically treated patients who had macroscopically defined small tumours, often of a fungoid or nipple-like shape, that originated inside the areola (Figure 1). Histological description was performed according to the World Health Organisation (WHO) criteria for nerve sheath tumours (5, 6, 8). The histological methods are described elsewhere in detail (6-8).

Results

All specimens were found to be composed entirely from neurofibromas with no residues resembling segments of glandular structures (Figure 2). Histological tumour types in females were: dermal (n = 23), diffuse (n = 13), dermal-diffuse (n = 2), with high or low cellularity (1 each) and plexiform-diffuse (n = 2). In males, 6 cases proved to be either of diffuse or dermal type. In one case the tumour showed a plexiform-diffuse growth pattern. Following ablative surgery, no local recurrence was noted within a period of 10 years). Multiple tumours of an individual arising in this region showed the same differentiation. No tumour showed signs of malignant degeneration.

Discussion

This study revealed that tumours arising in the areola and nipple area of NF1 patients and mimicking an accessory nipple were all neurofibromas. They occurred in both men...
and women, and occasionally in children. However, there was an obvious predominance for females to develop cutaneous neurofibromas in this location. Local excision of neurofibromas combined with minor plastic surgery to maintain a symmetrical areola region was adequate to relieve patients from an often unsightly appearance. Neurofibromas of the breast are extremely rare. Up to 1991 about 21 cases seemed to have appeared in the English literature (2); these authors added a further 24 cases with Schwann cell tumors. Nineteen proved to be neurofibromas and of these, 5 had a history of neurofibromatosis (26.3% of neurofibromas, 20.8% of all cases). One of these 5 cases presented with a malignant peripheral nerve sheath tumor at an advanced stage of the disease and died with evidence of tumor progression (2).

NF1 is a tumor-predisposition syndrome (9, 10). NF1 patients have a slightly higher risk of developing breast cancer (11). In this series, none of the patients had yet developed breast cancer. Patients sought surgical therapy in order to reduce the numbers of cutaneous tumours at various body sites, including the breast region. The higher number of females compared to males in this study may have been due to bias, since females have usually stronger motivation to improve the aspect of their skin than males. Indeed, scar formation due to removal of numerous cutaneous tumours was well tolerated by NF1 patients, even after ablative surgery of large areas. This report supports previous results emphasizing that tumors of the nipple and areola area show no glandular structures but are all neurofibroma (2, 12). Tumours of this site are probably more frequent than calculated in earlier studies (2), if NF1 patients are investigated (12). Our results support the earlier clinical reports about the prevalence of neurofibromas of the nipple and areola area of NF1 patients in up to 21% (13).

References


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