Hiroshima J. Med. Sci.
Vol. 53, No. 3·4, 47~50, December, 2004
HIJM 53–9

Chest Wall Schwannoma Associated with Neurofibromatosis 2 — A case report

Shinji OZAKI*[,1)], Yoshihiro MIYATA[1)], Michinori ARITA[1)], Mamoru TAKAHASHI[1)], Rumi HARUTA[1)], Toshimasa ASAHARA[1)], Mayumi KANEKO[2)], Kaoru KURISU[3)] and Tsuyoshi KATAOKA[4)]

1) Department of Surgery, Division of Frontier Medical Science, Graduate School of Biochemical Sciences, Hiroshima University
2) Department of Pathology, Division of Medical Intelligence and Informatics, Graduate school of Biomedical Sciences, Hiroshima University
3) Department of Neurosurgery, Division of Frontier Medical Science, Graduate School of Biochemical Sciences, Hiroshima University
4) Department of Health Care for Adults, Division of Nursing Science, Graduate School of Health Sciences, Hiroshima University

ABSTRACT

We report a rare case of neurofibromatosis type-2 (NF-2) associated with a chest wall schwannoma that was initially suspected of being a breast tumor. The patient was a 28-year-old female who was diagnosed as having NF-2 at 19 years old. At that time, she noticed a mass in the upper lateral region of her left breast but did not have it examined. The mass grew and became painful, and she was therefore referred to our department. Results of the initial examination indicated the possibility of a breast tumor, but a diagnosis of extramammary tumor of the major pectoralis major muscle was made on the basis of the results of ultrasonography and 3-dimensional computed tomography (3D-CT). An endoscope-assisted extirpation of the tumor was performed. Histologically, the tumor was an Antoni type A and B neurilemoma and was diagnosed as a schwannoma.

Key words: *Chest wall tumor, Schwannoma, Neurofibromatosis 2*

NF-2 is an autosomal hereditary disease characterized by the development of bilateral vestibular schwannomas. Neurogenic tumors, skin tumors and optic disorders may also develop in NF-2 patients. Some cases of NF-2 with a peripheral nerve tumor have been reported. Mutation of the NF-2 gene has also been reported in various cancers, including breast cancer, malignant melanoma and colon cancer, and is thought to be involved in carcinogenesis. Differential diagnosis between a peripheral nerve tumor and cancer in a NF-2 patient is therefore needed. We recently encountered a case of NF-2 associated with a chest wall tumor, initially suspected of being a breast tumor, that developed in the pectoralis major muscle. This case is described herein with a review of the literature.

CASE REPORT

A 28-year-old woman visited our department with the complaint of a left chest mass. She had experienced syrigmus at the age of 18 years, and bilateral acoustic schwannomas, multiple meningiomas and spinal cord tumors were found. She was diagnosed as having NF-2, and radiosurgery (gamma-knife therapy), neurosurgery and orthopaedic surgery were performed. However, she lost hearing in her right ear at 19 years of age and hearing in her left ear at 22 years of age despite radiosurgery, and other neurogenic symptoms gradually advanced. After that she was followed up at a neurosurgery department. At the age of 20 years, she noticed a mass in the upper lateral region of her left breast but did not have it examined. The mass grew and became painful, and she was therefore referred to our department. Physical examination revealed the presence of a hard mass, 6 cm in diameter, in the upper part of the lateral quadrant of her left breast. The movability was poor, suggesting adhesion to the pectoralis major muscle. Mammography (MMG) revealed a round mass, 5 cm in diameter, in the left upper quadrant and the margin was clear. A breast tumor was suspected on the basis of the

*Address: Hiroshima University, 1–2–3 Kasumi, Minami-ku, Hiroshima 734–8551, Japan
TEL:082–257–5222 FAX: 082–257–5224
E-mail: s-ozaki@bf7.so-net.ne.jp

results of the initial examination, but a diagnosis of extramammary tumor was made on the basis of the results of ultrasonography (Fig. 1) and 3D-CT (Fig. 2). A low-echoic lesion or low density area in the periphery of the mass corresponded to neu-

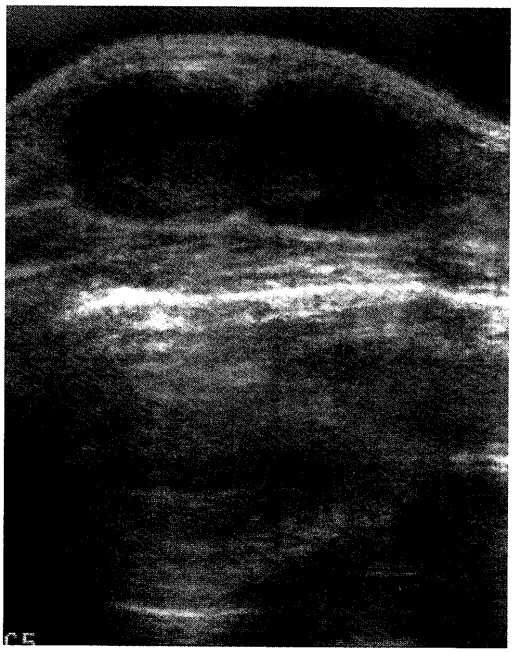

Fig. 1. A mass of round tumors, 2 cm in diameter, on the border of the pectoralis major. Low echoic lesions were noted in the periphery of the mass.

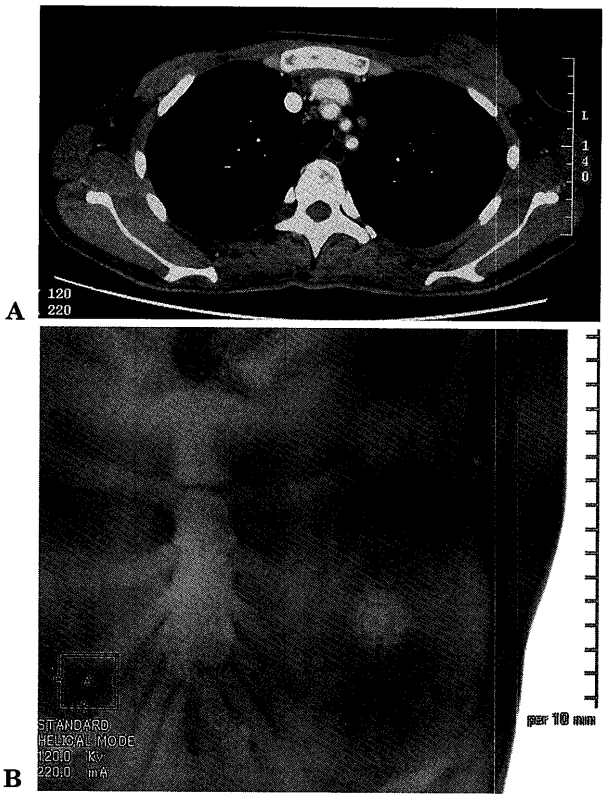

Fig. 2. A: CT showed the same finding as ultrasonography.
B: 3D-CT showed the existence of a mass in the extramammary gland.

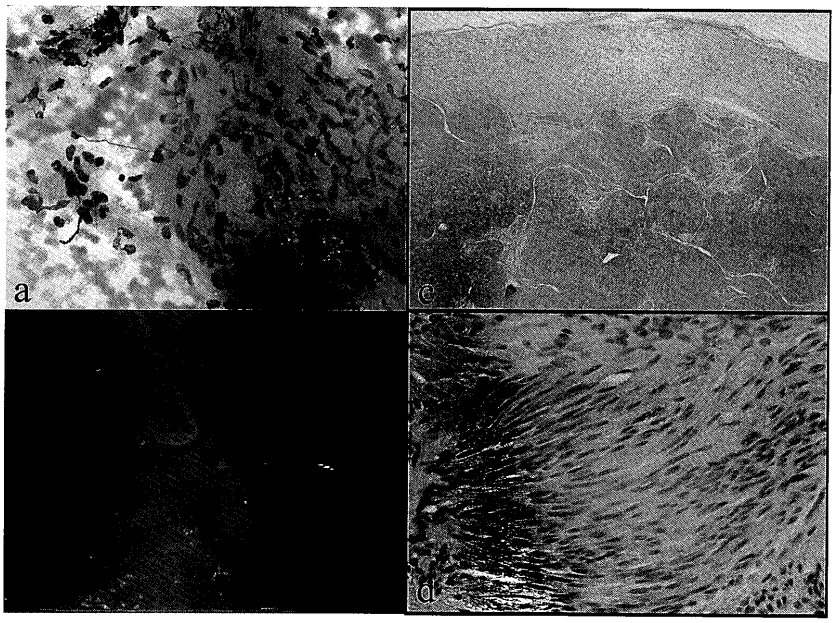

Fig. 3. (a): FNAC revealed some bare nuclear cells derived from interstitial tissue. The nuclei were spindle or rod-shape and constricted, and they were atypical. (Giemsa staining, original magnification × 400)
(b): Separation of the tumor from the pectoralis major.
Results of pathological examination revealed growth of poor atypical spindle cells with a palisade in the center (c) and sparsely distributed tumor cells in the mixomid interstices in the margin (d). These features are in accordance with Antoni type A and B neurilemoma.
(c): HE staining, original magnification × 12.5
(d): HE staining, original magnification × 400

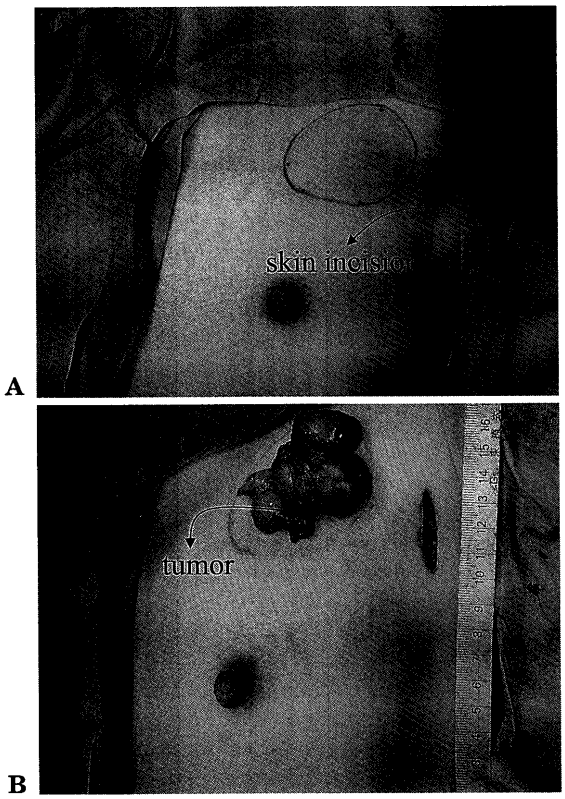

Fig. 4. A: The skin incision was set on the anterior axillary line.
B: Extirpated multilocular solid tumors

rosheath, and these findings are characteristic of schwannoma. Since the tumor was present on the pectoralis major muscle in the extramammary region, we suspected that a schwannoma had grown in the pectoral nerve. Fine needle aspiration cytology (FNAC) revealed a few bare nuclear cells derived from interstitial tissue. The nuclei were spindle-shaped or rod-shaped and constricted, and they were atypical (Fig. 3a). From the imaging findings, we suspected a schwannoma, but the results of cytologic examination indicated the possibility of a phyllodes tumor as a differential diagnosis, and endoscope-assisted extirpation of the tumor was therefore performed for cosmetic considerations. From a skin incision in the left anterior axillary line, a bladeless trocar (ENDOPATH®, ETHICON ENDO-SURGERY) was inserted, and ablation between the subcutaneous tissue and the capsula of the tumor was performed with the assistance of an endoscope. Then separation of the tumor from the pectoralismajor muscle was performed (Fig. 3b), and the tumor was taken out through the skin incision (Fig. 4). Macroscopically, the tumor consisted of four multilocular solid tumors and resembled a schwannoma. It was thought that the tumor had arisen from a peripheral nerve of the pectoral muscle, but a pedicle was not found on the muscle. The pathological findings of the tumor were in accordance with an Antoni type A or B neurilemoma and resulted in schwannoma (Fig. 3c, d). After surgery the left anterior chest pain disappeared, and the patient was satisfied with the results of treatment including the cosmetic results.

DISCUSSION

NF-2 is an autosomal hereditary disease. A National Institutes of Health Consensus Conference formulated clinical criteria for the diagnosis of NF-2 in 1991[7]. The major criterion is the presence of bilateral vestibular schwannomas. Other criteria are a family history of NF-2 plus any one of the following: the presence of a unilateral vestibular schwannoma or the presence of a meningioma, glioma, neurofibroma, schwannoma, juvenile posterior subcapsular lenticular opacities and cataract. Alternative additional criteria are unilateral vestibular schwannoma, multiple meningiomas, or any one of the following: glioma, neurofibroma, schwannoma, juvenile posterior subcapsular lenticular opacities or a cataract.

The NF-2 gene was identified on chromosome 22 by Rouleau and Trofatter in 1993, and the protein product, called schwannomin or merlin, has been characterized as a member of the ERM (ezrin, radixin and moesin) family of proteins that line cell membranes[8,11]. Merlin associates with cell membranous proteins and cytoskeletal elements and plays a role in intracellular and extracellular signaling pathways, such as cytostatic signaling and apoptosis pathways. It is therefore thought to have a tumor growth-suppressing function[1,4,12]. However, about half of NF-2 cases are sporadic, as was the present case. Mutation of the NF-2 gene has also been reported in various cancers, including breast cancers, malignant melanoma and colon cancer, and is thought to be involved in carcinogenesis[9].

The clinical symptoms of NF-2 are various neurogenic symptoms because of the variety of tumors of the central nervous system. These symptoms include syrigmus, deafness and disturbance of static sense, symptoms that are caused by vestibular schwannomas, and facial palsy and quadriplegia, symptoms that are caused by an intracranial tumor or spinal tumor. Most of the tumors are benign, but they can be life-threatening because they grow and increase in number. Moreover, neurosurgical operations can result in various dysfunctions and in deterioration in the patient's quality of life (QOL)[5]. Tumors growing in the peripheral nervous system can also cause functional disorders, and a surgical operation is sometimes needed to improve the patient's QOL. Cases of schwannomas growing in the urinary tract, nervous system, lingual nerve and pudendum have been reported[2,3,11,14]. Extirpation of the tumor was performed in all of those cases. A case of NF-2 associated with a malignant schwannoma in the abdominal wall[6] has also been reported, surgery

should be performed if the tumors are symptomatic or show a tendency to grow due to the possibility of malignancy. Most intracranial tumors in NF-2 patients are benign, but oppression of the surrounding structure can cause various neurogenic symptoms. The mean age of onset of the tumors is 20 years, and the symptoms advance slowly but surely. The prognosis is therefore poor[9].

The optimal therapy for NF-2 is not clear. Observation of the course is common unless severe functional disorders have occurred. However, in juvenile progressive cases with neurogenic symptoms or in cases with rapid tumor growth, neurosurgery is needed. The most important concern is prevention of hearing loss, and a variety of surgical approaches have been employed. Radiosurgical treatment of vestibular or acoustic schwannomas has recently become an established option for patients with sporadic tumors of less than 1 cm in size, and this approach enables preservation of hearing and reduction in the incidence of various complications[5,10]. Since our patient had bilateral and progressive hearing impairment as well as syrigmus caused by acoustic schwannomas, radiosurgical treatment (gamma-knife therapy) of the bilateral acoustic schwannomas and extirpation of the left acoustic schwannoma were performed. However, preservation of hearing was impossible. Extirpation of the spinal cord tumors was also performed because they caused palsy of the right lower limb and neurogenic bladder. After the operation, the patient underwent rehabilitation and became able to walk, and her dysuria was also improved. Extirpation of the left chest tumor was carried out because of the possibility of it being a phyllodes tumor or malignant schwannoma and because it was painful. The skin incision was set on the anterior axillary line and an endoscope-assisted operation was performed for cosmetic considerations.

(Received September 24, 2004)
(Accepted October 27, 2004)

REFERENCES

1. **Araki, N. and Saya, H.** 1999. Cellular signal transduction via the Neurofibromatosis type 2 tumor suppressor gene product: Merlin. Seikagaku **71:** 128–134.
2. **Asano, H., Shibuya, Y., Kodoi, S., Nishimatsu, S., Umeda, M. and Komori, T.** 2000. A case of neurofibromatosis type 2 with glossal neurilemoma (in Japanese with English abstract). Nihon Koukuu Gekagakkaizasshi (Jpn. J. Oral Maxillofac Surg.) **46:** 587–589.
3. **Griebel, M.L., Redman, J.F., Kemp, S.F. and Elders, M.J.** 1991. Hypertrophy of clitoral hood: presenting sign of neurofibromatosis in a female child. Urology **37:** 337–339.
4. **Koga, H., Araki, N., Takeshima, H., Nishi. T., Hirota, T. and Kimura, Y.** 1998. Impairment of cell adhesion by expression of the mutant neurofibromatosis type 2 (NF2) genes which lack exons in the ERM-homology domain. Oncogene **17:** 801–810.
5. **Lieberman, F. and Allan, F.R.** 1999. Clinical aspects of neurofibromatosis 2. Gann Monograph on Cancer Research **46:** 133–139.
6. **Matsuo, K., Tanito, K., Sawada, S., Honda, M., Niimura, M. and Aoki, T.** 2001. A case of neurofibromatosis 2 associated with malignant schwannoma (in Japanese). Rinshou Hihuka (Clinical Dermatology) **55:** 1055–1058.
7. **National institutes of health consensus development conferences statement on acoustic neuroma. Dec.11–13, 1991 The consensus development panel.** 1994. Arch. Neural. **51:** 201–207.
8. **Rouleau, G.A., Merel, P., Lutchman, M., Sanson, M., Zucman, J. and Marineau, C.** 1993. Alteration in a new gene encoding a putative membrane-organizing protein causes nerofibromatosis type 2. Nature **363:** 515–521.
9. **Saya, H., Araki, N. and Nakao, M.** 1999. Neurofibromatosis type 2 (NF2) (in Japanese). Idenshi Igaku **3:** 444–447.
10. **Slattery, W.H., Brackmann, D.E. and Hitselberger, W.E.** 1997. Hearing preservation in neurofibromatosis type 2. Am. J. Otol. **19:** 638–643.
11. **Suenaga, Y., Kihara, S., Ohyama, K., Katabuti, H., Matsuura, K. and Okamura, K.** 2000. A case of neurofibromatosis type 2 associated with schwannoma in the clitoris (in Japanese). Nihon Sankahujinka Gakkai Kumamoto Chihoubukai zasshi (Jpn. J. Kumamoto branch Obstetrics and Gynecology) **44:** 29–33.
12. **Takeshima, H., Izawa, I., Lee, P.S., Safdar, N., Levin, V.A. and Saya, H.** 1994. Detection of cellular proteins that interact with NF2 tumor suppressor gene product. Oncogene **9:** 2135–2144.
13. **Trofatter, J.A., MacCollin, M.M., Rutter, J.L., Murrell, J.R., Duyao, M.P. and Parry, D.M.** 1993. A novel moesin-, ezrin-, radixin-like gene is a candidate for the neurofibromatosis 2 tumor suppressor. Cell **72:** 791–800.
14. **Washimi, O., Washimi, Y., Itou, M., Suzuki, T., Matsumoto, G. and Yamamoto, Y.** 2002. Neurofibromatosis type 2: a case report (in Japanese with English abstract). Seikei · Saigaigeka (Orthopaedic Surgery and Traumatology) **45:** 1207–1211.