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Case Report

Giant Neurofibroma in the Right Lower Limb of a 26-Year-Old Woman: Report of a Case

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Neurofibromatosis (NF) is a genetically inherited, autosomal-dominant disease with an incidence of 1 in 3000 live births. There are two types of NF, NF 1 and NF 2, and NF 1 is the most common. This study reports on the diagnosis, treatment, and related family medical history of a rare case with NF-1 in the right lower limb.

Key words: Neurofibromatosis – von Recklinghausen's disease – Surgery

Neurofibromatosis (NF), first described by Von Recklinghausen in 1882, is an autosomal-dominant genetic disorder.[1] An affected individual has a 50% chance of passing it on with each pregnancy. NF often first appears in infants or during early childhood. The distinct features include the presence of light brown spots on the skin, as well as solitary or multiple hemispherical, or pedicled, neurofibromas on the trunk or extremities. Complicated Lisch nodules (iris hamartomas), skeletal lesions, and central nervous system abnormalities appear in some patients, and these lead to epileptic seizures and cognitive deficits. Neurofibromas can also become cancerous in a minority of patients.[2] The present study reports a case with primary manifestations of multiple neurofibromas and light brown spots on the trunk. However, the right lower limb was also affected by this rare giant neurofibroma.

Case Report

A 26-year-old woman from Nanxian County of Hunan Province complained of a lump in the right lower limb for 10 years, with symptoms worsening for 3 years. She was admitted to the hospital on March 17, 2009. She explained that a thumb tip-sized lump appeared on the dorsum of the right foot in 1999. The lump increased gradually and developed toward the limb, thigh, buttocks, and perineal region. The patient was ambulant, but with occasional distending pains. At the same time, a dark brown pigment formed on the skin of the right lower limb, perineal region, buttocks, waist, and abdomen. Several years later, multiple nodules were observed on the forehead, back of the ear, neck, chest, back, both arms, and left lower limb. At the beginning of 2006, the lump in the right lower limb began to grow rapidly, eventually presented as elephantiasis. From June 2006, the patient was no

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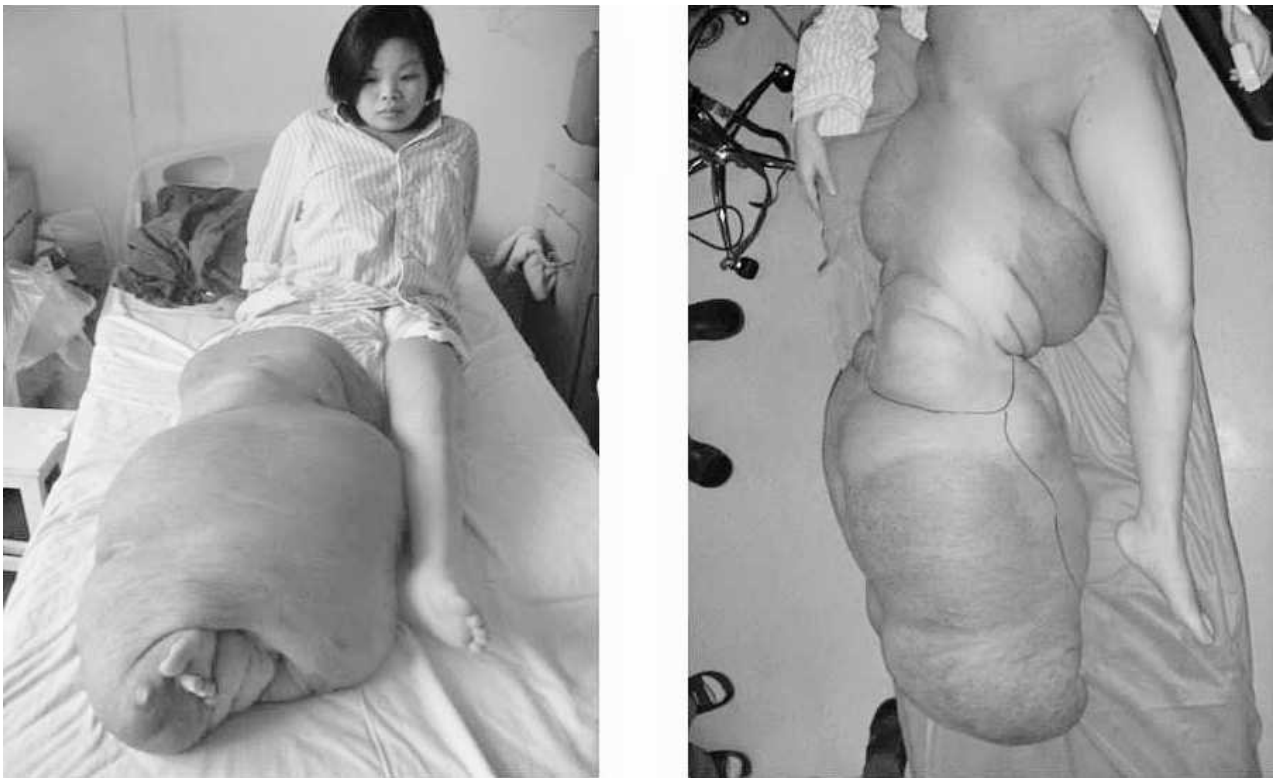


Fig. 1 The patient before surgery.

longer ambulant, and experienced nocturnal and exacerbating pain during the night. The physical examination revealed as follows: body height, 156 cm; body weight, 103 kg; right lower extremity, buttocks, perineal region, and waist presenting as elephantiasis; visible dark brown pigmentation over a large area; multiple soft nodule-like lumps, with a diameter of 3 to 40 mm, on the forehead, postaurem, neck, chest, back, both arms, and left lower limb. Two light brown spots (20 mm × 10 mm and 10 mm × 15 mm, respectively) were observed on the tibial side of the left limb. The lump on the right lower limb was soft. The patient had poor range of motion and elevated skin temperature. The largest circumference of the right thigh was 96 cm and the right limb was 102 cm. The left lower limb was basically normal. The circumference of the left thigh (precisely at 10 cm above the knee joint) was 35 cm, and the largest circumference of the lower left limb was 28 cm (Fig. 1).

Auxiliary examination change for clinical presentations

At admission, laboratory investigation showed a blood cell count in the normal range as well as the liver function tests and glucose level. The patient was O+ positive and tested negative for hepatitis A and B as well as for acquired immune deficiency syndrome.

Radiographic studies revealed soft tissue and skeletal changes in the right lower extremity with growth disturbance at the distal femur, right hip subluxation, deformity and fracture at the distal tibia and medial talus (Fig. 2). In addition, the intramuscular space was observed in cross-sections of the right thigh but not in the lower right limb. Computed tomography (CT) images also showed that the right lower limb exhibited arthrochalasis, widened joint gap, atrophied muscle, and less obvious vascular shadows (Fig. 3).

Color ultrasonography revealed as follow: (1) no obvious abnormalities of the liver, gallbladder, spleen, pancreas, kidneys, ureter, bladder, or perineum; (2) low-echoed nodules were noted in the right adnexal region of the pelvic cavity but pathologic results were undetermined; and (3) bicuspid valve was leaking but the right iliac vein and the vena cava were patent showing a normal flow. B-mode ultrasound imaging of the right lower limb revealed multiple, nonuniform echo lumps, although pathologic results were unconfirmed. In addition, the right tibiofibular periosteum was

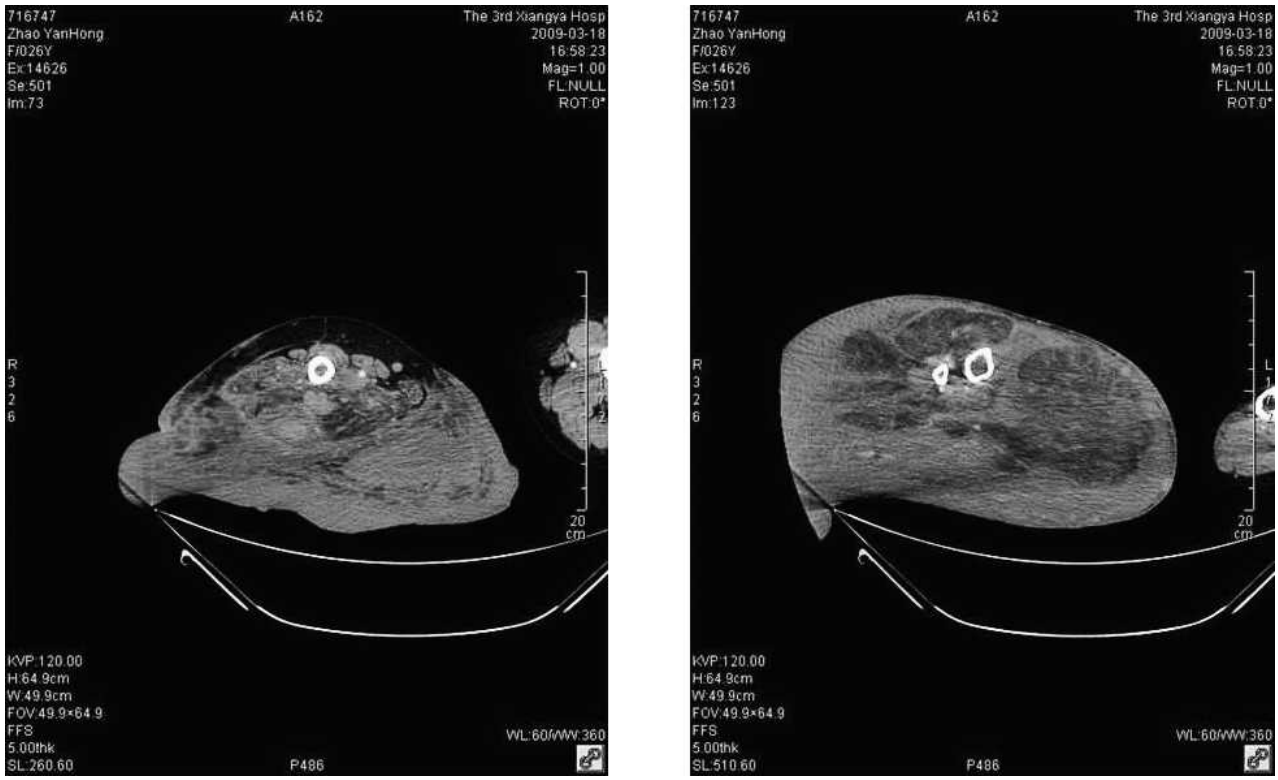


Fig. 2 CT images before surgery.

intermittent, which was consistent with lumps in the lower limb invading the periosteum. Abnormal digital subtraction angiography results were less obvious.

Family medical history

Medical history revealed that other family members suffered from this disease, including the father, paternal brother, and paternal aunt. In the family nine other siblings were found to have symptoms related to NF. They can be traced in the family tree (Table 1).

- Case 1: unknown age of onset, many lumps on body, but the numbers and sizes were unknown; no cause of death given.
- Case 2: unknown age of onset, many lumps with different sizes on trunk; several lumps on the eyelid; no cause of death given.
- Case 3: the patient's father; many soft lumps of various sizes throughout the body, primarily distributed on the face, trunk, both arms, which were clearly distinguishable from adjacent tissue; good range of motion; large area of dark brown pigment on back and neck; suffered from fracture of the left calf due to trauma in his twenties. He also suffered from a right tibia and fibula fracture that was left untreated causing deformity and unabling him to ambulate for a while (Fig. 4).
- Case 4: onset at 18 years of age; many lumps observed on the trunk.
- Case 5: onset at around 20 years of age; lumps presented; no cause of death given.
- Case 6: onset at 20 years of age; many lumps on neck and both hands, with no obvious pigmentation.
- Case 7: 19 years old; large area of pigmentation on trunk since childhood; no obvious lumps.
- Case 8: 21 years old; scattered pigmentation spots on skin; many lumps on trunk.
- Case 9: 18 years old; scattered pigmentation spots on skin; no obvious lumps.

Treatment procedures

In April 2009 the patient underwent partial resection of the neurofibroma under general anesthesia and endotracheal intubation. During surgery, an S-shaped incision was made on the skin above the tumor in the right limb. Along the incision, the skin and subcutaneous tissue were explored. The anatomy of the right lower extremity was distorted. A

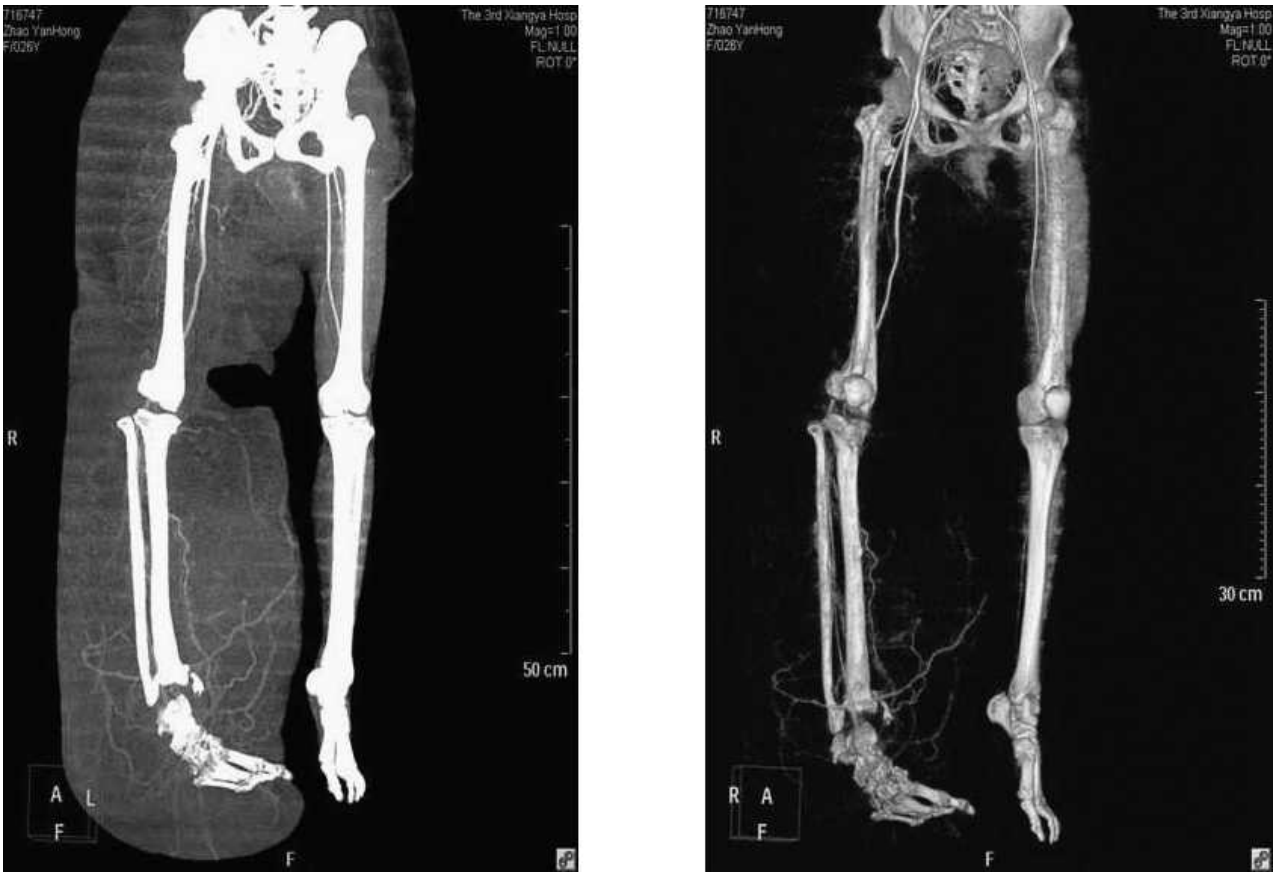
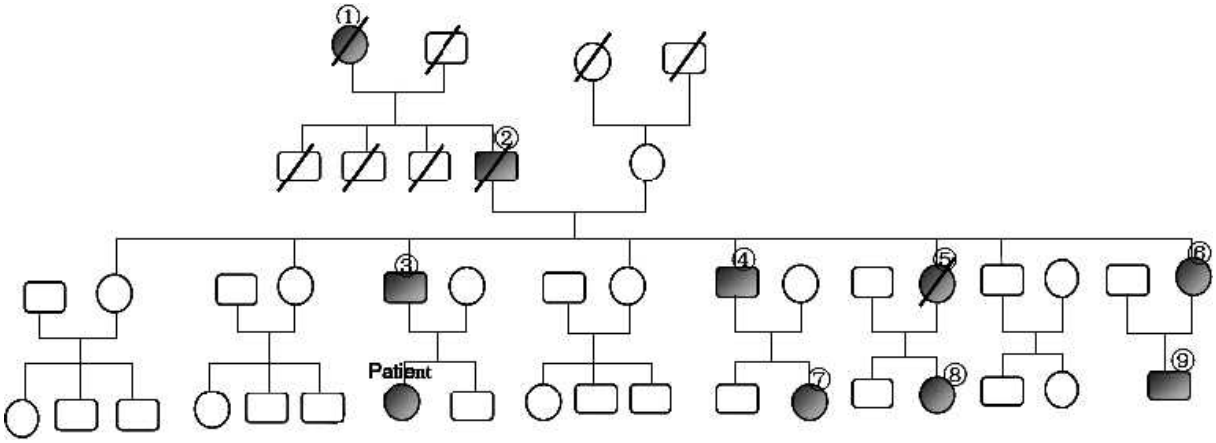


Fig. 3 CT angiography images before surgery.

bulk of the tumor was partially resected over the right lower extremity, as well as part of the tumoral tissue adjacent to the knee joint and the right thigh. Direct skin suture was followed after tumor removal. The resected tumor tissue weighed 21.5 kg. The foot metatarsophalangeal joints were stabilized with K-wires. Of the total of the limb 15% was covered with skin graft and a pressure dressing was used (Fig. 5). The estimated blood loss was 1000 mL and the patient received 600 mL of blood transfusion. The results of the histopathologic examination confirmed the diagnosis of neurofibroma. Hematoxylin and eosin

Table 1 Genealogic tree shows the other family members who have symptoms related to neurofibromatosis



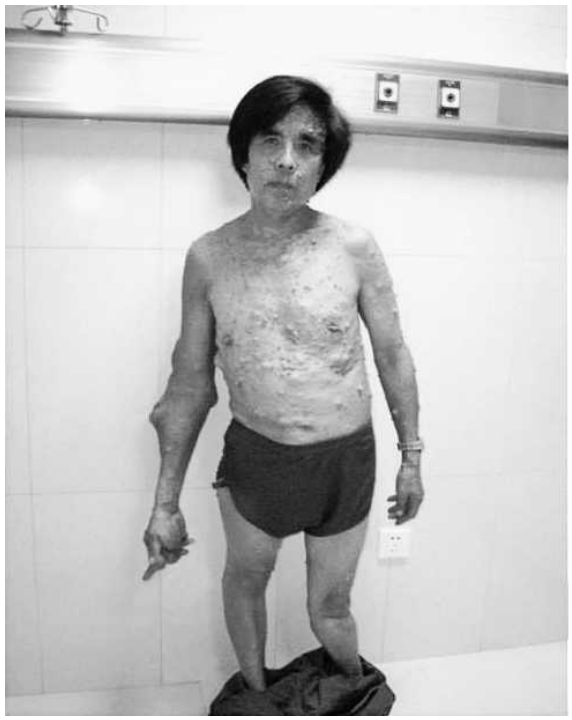


Fig. 4 The patient's father.

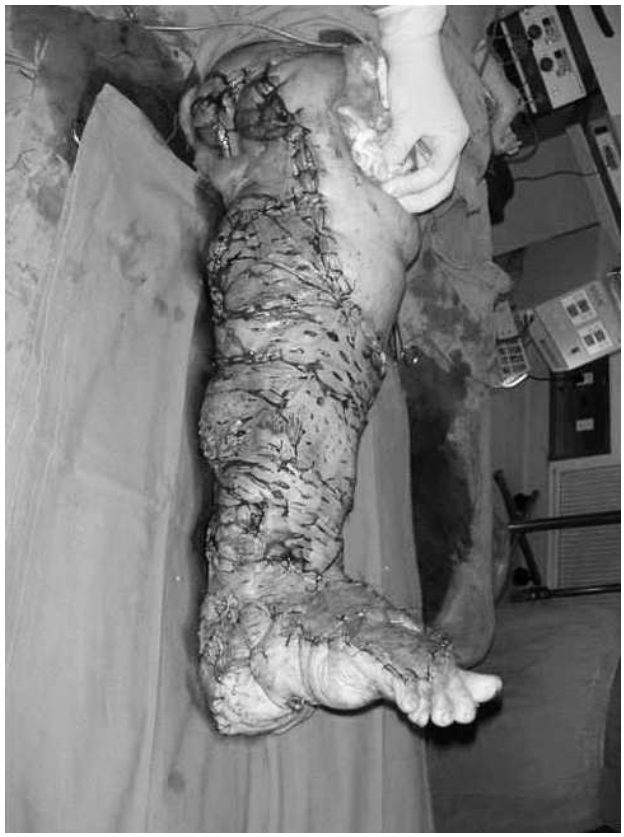


Fig. 5 Patient after the first surgery.

staining revealed spindle-shaped tumoral cells infiltration of the dermis (Fig. 6A). Immunohistochemical study showed that the tumoral cells were positive for S-100 protein (Fig. 6B).

On the first day after surgery, the patient had a fever (39.2°C). Blood examination results demonstrated that the patient suffered from moderate anemia (75 g/L) and hyponatremia (127.7 mmol/L). In addition, leukocytes increased slightly (total number 11.08 $\times$ 10^9/L) and the percentage of neutrophils was 79.5%. Etimicin (Shanhe Ltd., China) and teicoplanin (Sanofi-Aventis, France) were used as anti-inflammatory agents. Fluids and blood infusion, together with wound dressings, were administered. The wound surface released exudate with a strong odor. The patient had intermittent fever. On the sixth day after surgery, antibiotics were replaced by meropenem (Dainippon Sumitomo Pharma Company, Japan), but the fever never ceased, reaching above 39°C. Typically after wound surface dressings, secretions were cultured and were found positive for *Proteus mirabilis.* Neither meropenem nor levofloxacin (Yangzi River Pharma Company, China) were successful in achieving fever control. Most of the transplanted skin graft to the right lower limb survived. However, the skin grafts transplanted

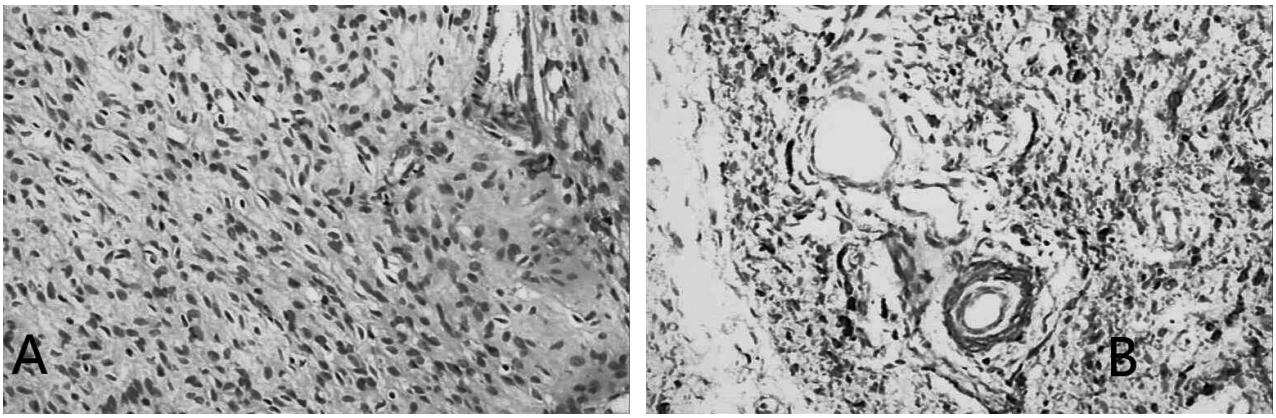


Fig. 6 (A) Histopathologic examination showing spindle-shaped tumor cells infiltration in dermis. H&E staining (×10). (B) Immunohistochemical study showing S-100 protein positive spot in cytoplasm (×10).

into the calcar pedis, dorsum of foot, and limb gradually became black and necrotic, and newly formed jelly-like tumor tissue was observed. At approximately 1 month after surgery, the skin grafts in the thigh become necrotic with bloody exudate from the incision. Necrotic tumoral tissue was also noted. This was accompanied by intense pain and persistent high temperature. It was considered a consequence of necrotic tumor tissue absorption and wound surface infection. The intense limb pain was most likely related to tumor invasion of adjacent tissue. After preoperative preparation, under general anesthesia with tracheal intubation, the right lower limb was amputated through the knee joint, and the resected part weighed 9.8 kg. After surgery, etimicin and meropenem were used to prevent an inflammatory reaction. At the same time, symptomatic treatments, including fluid replacement and 600 mL whole blood infusion, were administered. For wound surface, negative pressure drainage and nanosilver dressing renewals were used. On 16th day, the patient still presented with fever, reaching above 39°C. To address the wound surface infection, antibiotics were replaced by meropenem and levofloxacin. However, fever persisted, possibly due to the presence of necrotic tumoral tissue. Antibiotics were ceased, dressing repeated, with nutritional support, allowing the body temperature to gradually return to normal. Finally, the wound gradually healed (Fig. 7). At the request of the patient and her relatives, she was discharged home. The lumps on the thigh, buttocks, and waist were to be resected in a second-stage treatment.

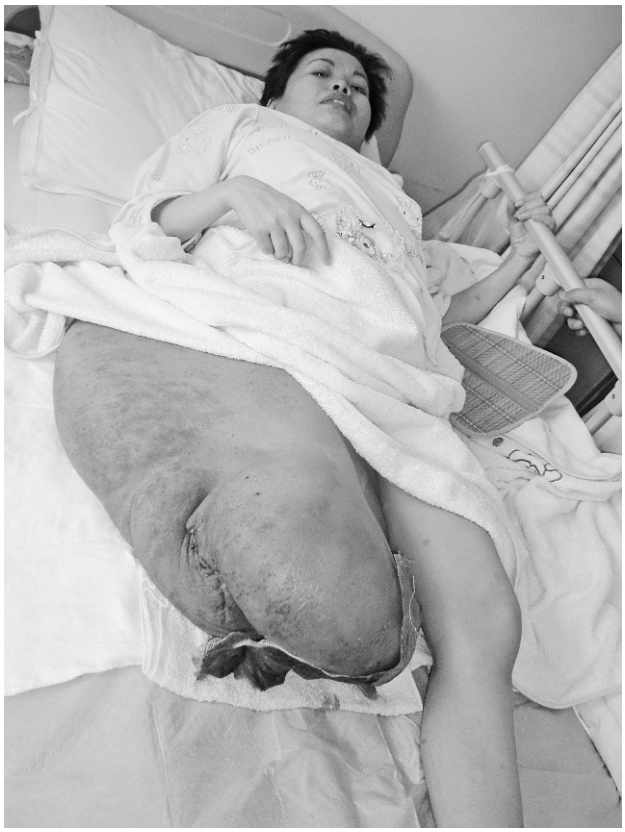


Fig. 7 Patient after the amputation of right lower limb.

Discussion

A neurofibroma is a benign tumor that arises from the epineurium, perineurium, and endoneurium of a nerve in the skin or subcutaneous tissue.[3] It occurs alone or in multiple forms, and often presents with slow-growing painless nodules or lumps. A certain amount of lump expansion often leads to displacement of local or adjacent organs, resulting in surface

malformation, as well as other dysfunctions. When the nodules spread over the entire body, it is called NF.[4] The present patient fit well the diagnostic criteria for NF (*i.e.*, many neurofibromas of varying sizes throughout the body, skin pigmentation, many light brown spots, and several family members showing similar symptoms).[5] In addition, the lumps appear primarily among young and middle-aged people. Auxiliary examination results from the present study revealed a completely diseased right lower limb, joint arthrochalasis, widened joint gap, muscular tissue degeneration, and weakened vascular shadow. In addition, the heart was expanded and the bicuspid valve was slightly back-streamed.

NF surgical treatment is performed for large-sized tumors that result in pain or dysfunction, or are suspected to worsen. In the present study, the giant tumor in the right lower limb caused severe dysfunction and pain, and exhibited cancerous potential, thus warranting surgical treatment.[6] The surgery aimed at improving function and cosmesis. As much tumor tissue as possible should be excised during surgery, and the skin tissue could be left in place.[7] In the present patient, the postoperative wound surface was too large. Therefore, the tumor surface skin was dissected and used to cover the wound surface. However, after surgery, the patient presented with persistent high fever, pain in the affected limb, and skin graft necrosis. In addition, there was the risk of uncontrollable infection or tumor tissue invasion into adjacent tissue. Therefore, amputation was performed to ensure the life of the patient. After surgery, body temperature returned to normal, and the wound surface of the amputated limb gradually healed. The remaining tumor tissue is to be excised in a second-stage surgery.

Results from the present case study demonstrate that it is difficult to preserve joint function when tumoral tissue remains present and continues to proliferate. After the second surgery, the patient took rehabilitation exercise, but no motional improvement of the right lower limb was observed.

It remains to be determined whether the skin over the surface of the tumor, which presented with a normal appearance, is healthy and tumor cell-free. Histopathologic, immunohistochemical, and molecular biological analyses should be performed.

Intraoperative hemorrhage cannot be easily controlled because the neurofibroma tissue contains many blood sinuses with thin and poorly contractible sinus cavities.[8] Therefore, when planning surgical procedures, sufficient blood should be available. Angiographic examination should be considered to determine vascular involvement, and one should contemplate vascular embolization or electrochemical improvisation to control hemorrhage during surgery. The patient in the present study received a total of 1700 mL of blood during her hospitalization.

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