

# Subperiosteal bone proliferation at the tibia in neurofibromatosis - a case report

S. INOKUCHI AND N. USAMI

Department of Orthopaedic Surgery, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo 160, Japan

## Summary

A very rare case of subperiosteal bone proliferation described as 'a bone cyst' on the distal end of the tibia in association with neurofibromatosis is reported in a 9-year-old girl. The pathological finding progressed within 6 months from 'a cyst-like bone lesion' filled with haematoma to 'a bony protuberance' and is documented with plain X-rays, CT and MRI, and subperiosteal haemorrhage on the tibia was strongly suspected. Clinical findings met the NIH criteria for neurofibromatosis, and the histopathological features were consistent with neurofibromatosis. To our knowledge, only 21 cases of this lesion have been reported in the literature. The cause of this lesion is the subperiosteal haemorrhage caused by periosteal abnormalities due to inversion by neurofibromatosis or mesodermal dysplasia. In spite of their frequent recurrences these lesions become huge and cause deformity and they should be resected before functional and cosmetic problems occur.

**Keywords:** tibia; bone proliferation; cyst; neurofibromatosis; subperiosteal

## Introduction

Neurofibromatosis or von Recklinghausen's disease, is a systemic disease characterized by café au lait skin lesions, intertriginous freckling, iris hamartomas, and multiple skin neurofibromas. It may be associated with spinal and peripheral nerve neurofibromas and bone abnormalities. Five to ten per cent of patients who have neurofibromatosis also have a congenital pseudarthrosis of the tibia [1].

Subperiosteal bone proliferation in neurofibromatosis is very rare. Only 21 cases have been reported in literature since the initial report of two cases in 1924 [2]. The cause of this lesion most likely

is a subperiosteal haematoma which may lead to the formation of large bone cysts and to gross deformity [3]. In the present paper a case of neurofibromatosis with excessive osteogenesis under the periosteum of the distal end of the tibia in a child in the absence of any clear history of fracture or other injury is reported. To our knowledge, MRI features of bone proliferation in neurofibromatosis have not yet been documented in the literature.

## Case report

A 9-year-old girl was first examined in 1991, because of pain on walking and increasing swelling of the distal left leg and heel over a period of 5 months. On the first visit, a 7×5 cm bony protuberance was

Correspondence: Suguru Inokuchi, MD, 6-6-7 Honkomagome, Bunkyo-ku, Tokyo 113, Japan.



Figure 1

Xeroradiographs with hemispheric ossification at the distal tibia and protuberance of the overlying soft-tissue shadow. (A) anteroposterior view; (B) lateral view.

palpated 3–10 cm proximal to the medial malleolus, and a soft trabecular mass was palpated at its surface. The skin on the medial aspect of the left heel had an elephantiasis appearance, and a soft 3×4 cm mass with ill-defined borders was palpated beneath the skin. The affected extremity was 1.5 cm longer than the normal side. Numerous café au lait spots were noted, predominantly on the patient's trunk. Small brown spots were scattered in the left axilla, so-called 'axillary freckling', and thus the patient met the diagnostic criteria [4] for neurofibromatosis. There were neither a history of injury nor a family history of neurofibromatosis. Serologic laboratory data were within normal limits. No abnormalities were detected on plain radiographs at the first examination. However, xeroradiography 7 days after the initial examination showed hemispheric ossification (Figure 1A,B), MRI 9 days after the initial examination (Figure 2A,B) and CT scan 1 month after the examination

(Figure 3) showed a cystic lesion at the posterior aspect of the tibia.

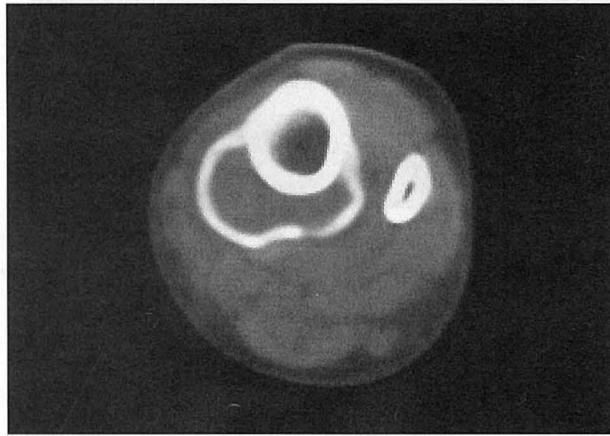
The soft tissue mass on the surface of the bony protuberance at the distal tibia was biopsied, and subsequently resected as extensively as possible. The resected soft tissue specimen revealed cells with deeply stained nuclei and cytoplasm with indistinct boundaries, adipose tissue associated with severe mucous degeneration and fibrous tissue proliferation. The pathologic diagnosis was neurofibroma (Figure 4).

Based on these findings a diagnosis of a bone cyst-like lesion secondary to neurofibromatosis was made and the patient's course was observed; 6 months after initial examination the patient was admitted for surgery, because the bony protuberance failed to regress and the mass in the heel region had increased in size. A bony protuberance and posterior and medial bowing of the tibia were observed on plain



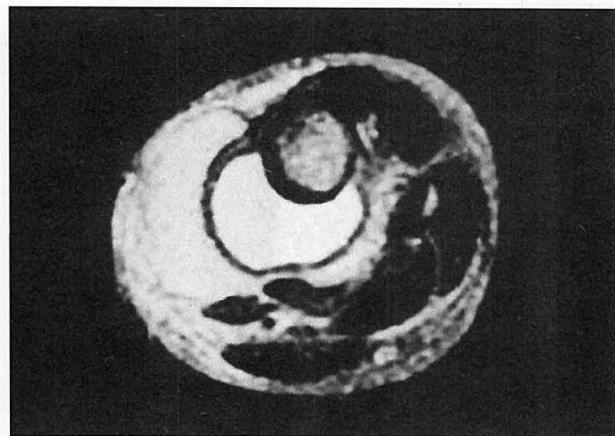
**Figure 2**

MRI with a cystic lesion in contact with the posterior cortex of the tibia. Almost perfectly homogenous internal signal, low signal on T<sub>1</sub>-weighted MRI image (A) and high signal on T<sub>2</sub>-weighted MRI image (B), surrounded by a single-layer low signal region peripherally on (A) and (B) in continuity with the bone cortex. An area with indistinct borders seen as low signal on (A) and high signal on (B) coincided with the soft tissue mass overlying the bone lesion.



**Figure 3**

CT scan with cystic lesion surrounded by a bony capsule on the posterior surface of the tibia.



**Figure 4**

Pathology of the soft tissue mass specimen obtained during the initial biopsy (H-E stain  $\times 80$ ).

radiographs (Figure 5A,B). The bony protuberance of the tibia was marginally resected, with periosteum attached, and the soft-tissue mass in the heel region was removed. A clearly defined boundary was observed between the tibial cortical bone and the bony protuberance, but the surface of the protuberance was covered by the same periosteum as the surrounding tibia. The resected hemispherical specimen contained a bone cyst-like cavity (Figure 6). The remainder of the specimen consisted of normal mature bone, and no invasion by neurofibroma was detected. The soft-tissue mass in the heel region

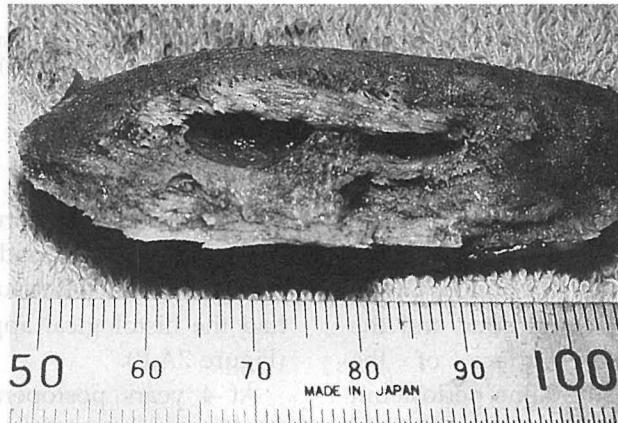
macroscopically appeared to be lipoma with poorly defined boundaries, and was removed as extensively as possible. The soft tissue specimen of the heel region had the histological appearance of a neurofibroma (Figure 7A,B).

At 4 years postoperatively, the patient has no swelling and no pain on walking, but the mass in the heel area has again increased in size. There is no evidence of recurrence on plain radiographs, but posterior bowing of the tibia has persisted (Figure 8A,B).



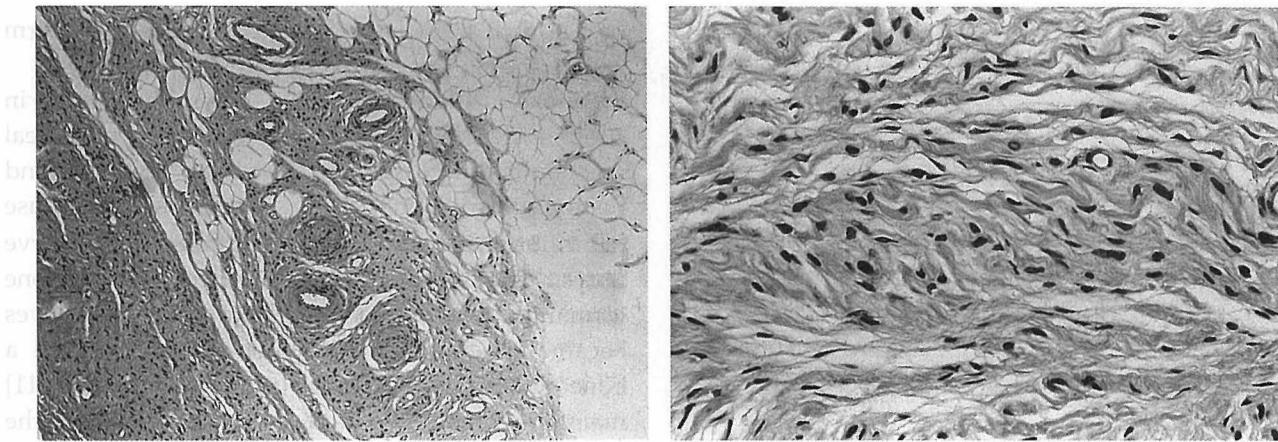
**Figure 5**

Radiographs 6 months after initial examination. (A) Anteroposterior view with bony protuberance at the posteromedial aspect of the tibia. (B) Lateral view with posterior bowing of the tibia.



**Figure 6**

The resected hemispherical specimen ( $7 \times 5$  cm) contained a bone cyst-like cavity.



**Figure 7**

Histopathological appearance of resected soft tissue specimen from the heel (H-E stain). (A) Proliferation of fibrous tissue and nerve tissue between mature adipose tissue ( $\times 80$ ). (B) Proliferation of cells containing oval or spindle-shaped deeply stained nuclei. The boundaries of the cytoplasm were indistinct and cell transition into an undulating fibrous component was observed ( $\times 400$ ).



**Figure 8**

Radiographs 4 years after the resection without evidence of recurrence. (A) Anteroposterior view without bony protuberance at the tibia. (B) Lateral view with slight posterior bowing of the tibia.

**Table 1**

Bone cyst-like lesions due to neurofibromatosis

Author	Year	Age (years)	Sex	Site
1 Brook	1924	12	Male	Tibia
2 Brook	1924	22	Female	Clavicle
3 Lehman	1926	30	Female	Femur
4 Weber	1930	47	Female	Tibia
5 Holt	1948	43	Male	Fibula
6 McCarrol	1950			Radius
7 Hensley	1953	13	Male	Tibia
8 Sane	1971	6	Male	Tibia
9 Kullman	1972	11	Male	Femur
10 Kullman	1972	12	Male	Tibia
11 Pitt	1972	13	Male	Tibia
12 Pitt	1972	20	Female	Femur
13 Pitt	1972	24	Male	Femur
14 Klatte	1976	12		Tibia
15 Yaghmai	1976	11	Male	Femur
16 Yaghmai	1976	9	Female	Tibia
17 Holt	1978	9	Female	Femur
18 Hooper	1979	4	Female	Tibia
19 Locht	1981	12	Female	Tibia
20 Mandell	1985	6	Male	Tibia
21 Huk	1991	22	Female	Femur
22 Inokuchi	1997	9	Female	Tibia

## Discussion

It is rare to find a bone cyst-like lesion or excessive bone formation underneath the periosteum of the tibia in the absence of an identifiable cause such as a fracture, consequently an underlying disease was suspected in the present case. This patient met the diagnostic criteria for neurofibromatosis clinically [4], and a neurofibroma was identified histopathologically at the site of the soft tissue mass. Thus, the diagnosis of subperiosteal bone proliferation associated with neurofibromatosis was made.

In 1924 Brooks [2] first reported two cases of subperiosteal bone cyst-like lesions due to neurofibromatosis in the tibia and clavicle. To our knowledge, only 21 cases have been reported, until present none in Japan (Table 1) [2, 3, 5–18].

The diagnosis 'subperiosteal bone cyst' for this lesion derives from the fact that new bone develops as a result of the high osteogenic potential of the periosteum, which detaches from the cortical bone and produces bone cyst-like changes on its surface. However, if the ossification proceeds to the centre of the cyst-like lesion, it produces an arc-like bony protuberance, as observed on the radiographs of our

own patient at the second surgery. Therefore the term 'subperiosteal bone proliferation' is more logical.

Brooks [2] observed neurofibromas in subperiosteal tissue and reported that a periosteal reaction had occurred and new bone formation and bone destruction had developed because neurofibromas had arisen from intraperiosteal nerve fibres. The author proposed that if new bone formation was predominant, the tumours themselves became covered with new bone and exhibited a bone cyst-like morphology. In 1972, Kullmann [11] maintained that the bond between the bone and the periosteum was weakened as a result of invasion by neurofibroma, and that the periosteum itself ossified. However, in 1972, Pitt [12] failed to find any invasion of the periosteum by neurofibroma and reported that subperiosteal haematoma was due to the fragility of the junction between bone and periosteum secondary to mesodermal dysplasia in neurofibromatosis. At present it is generally accepted that the subperiosteal haemorrhage occurs because of periosteal abnormalities, and that haematomas form and gradually ossify. Opinion is divided, however, as to whether these periosteal abnormalities are due to invasion by neurofibroma [11, 16, 17] or due to mesodermal dysplasia [3, 12, 14].

In the present case, we did not find any evidence of invasion by neurofibroma in either the periosteum or subperiosteal tissue. A MRI showed a homogenous low signal area on the T1-weighted image and a high signal on the T2-weighted image that was consistent with haematoma. The resected bone specimen demonstrated new bone that had formed between the cortical bone of the tibia and its periosteum. It was hemispherical, containing a bone cyst-like cavity at its centre, and strong bone formation by the periosteum.

There have also been reports that one of the causes for new bone formation was vascular abnormality due to mesodermal dysplasia, contributing to haemorrhage under the periosteum, increasing local blood flow and resulting in hyperplasia of the affected extremity [12, 14]. No vascular lesions were demonstrated in our patient histologically.

The greater ease with which the periosteum detaches in children may be the reason why these bone changes tend to occur in children [11], because the strength of the junction to bone is weaker than

in adults, in whom this junction is reinforced by Sharpey's fibres.

We believe that under conditions that facilitate detachment of the periosteum, relatively mild external forces, such as blows, sports, everyday microtrauma, contraction force of attached muscles, etc., may cause bleeding under the periosteum, a rapid increase of the periosteal detachment, and subsequent ossification of the haematoma.

The important differential diagnoses include sclerotic osteosarcoma, sclerotic osteomyelitis, and paraosseous osteosarcoma. However, the radiograph of subperiosteal bone proliferation in Recklinghausen's disease, is usually diagnostic. The diagnosis is confirmed by bone cyst-like lesions on CT and MRI, by absence of serologic inflammatory response or ALP elevation, by histologic demonstration of a neurofibroma and by exclusion of a tumorous lesion.

Due to repeated recurrences after resection, some authors have taken a negative view of operative treatment of subperiosteal bone proliferation in neurofibromatosis [17]. Fortunately, there are no signs of recurrence in our patient 4 years postoperatively, and there appears to be a number of patients who do not experience recurrences. Moreover, there are patients in whom the lesions become very large and cause deformity when left untreated. Therefore, we believe that these lesions should be resected before they create mechanical or cosmetic problems [3].

## References

- 1 McElhannon FM Jr. Congenital pseudarthrosis of the tibia. *Southern Med J* 1975; **68**: 824-827.
- 2 Brooks B, Lehman EP. The bone changes in Recklinghausen's neurofibromatosis. *Surg Gynec Obstet* 1924; **38**: 587-595.
- 3 Huk O, Newman N, Fowles JV. Recurrent massive subperiosteal hemorrhage in a patient with neurofibromatosis. *Can J Surg* 1991; **34**: 259-262.
- 4 National institute of health consensus development conference. Neurofibromatosis, conference statement. *Arch Neurol* 1988; **45**: 575-578.
- 5 Lehman EP. Recklinghausen's neurofibromatosis and skulltton. A plea for complete study of the disease.. *Arch Dermatol Syphilol* 1926; **16**: 178-187.
- 6 Weber FP. Periosteal neurofibromatosis with a short consideration of the whole subject of neurofibromatosis. *Qurt J Med* 1930; **23**: 151-165.
- 7 Holt JF, Wright EM. The radiologic features of neurofibromatosis. *Radiology* 1948; **51**: 647-663.
- 8 McCarroll HR. Soft tissue neoplasmas associated with congenital neurofibromatosis. *J Bone Joint Surg* 1956; **38-A**: 717-731.
- 9 Hensley CD. The rapid development of a 'subperiosteal bone cyst' in multiple neurofibromatosis. *J Bone Joint Surg* 1953; **35-A**: 197-203.
- 10 Sane S, Yunis E, Greer R. Subperiosteal or cortical cyst and intramedullary neurofibromatosis—uncommon manifestations of neurofibromatosis. A case report.. *J Bone Joint Surg* 1971; **53-A**: 1194-2000.
- 11 Kullman L, Wouters HW. Neurofibromatosis, gigantism and subperiosteal haematoma. *J Bone Joint Surg* 1972; **54-B**: 130-138.
- 12 Pitt MJ, Mosher JF, Edeiken J. Abnormal periosteum and bone in neurofibromatosis. *Pediatr Radiol* 1972; **103**: 143-146.
- 13 Klatte EC, Franken EA, Smith JA. The radiographic spectrum in neurofibromatosis. *Semin Roentgenol* 1976; **11**: 17-33.
- 14 Yaghmai I, Tafazoli M. Massive subperiosteal hemorrhage in neurofibromatosis. *Pediatr Radiol* 1977; **122**: 439-441.
- 15 Holt JF. Neurofibromatosis in children. *Am J Roentgenol* 1978; **130**: 615-639.
- 16 Hooper G, McMaster MJ. Neurofibromatosis with tibial cyst caused by recurrent hemorrhage. *J Bone Joint Surg* 1979; **61-A**: 274-275.
- 17 Locht RC, Huebert HT, McFarland DF. Subperiosteal hemorrhage and cyst formation in neurofibromatosis. *Clin Orthop* 1981; **155**: 141-146.
- 18 Mandell GA, Harcke HT. Subperiosteal hematoma. Another scintigraphic 'doughnut'. *Clin Nucl Med* 1986; **11**: 35-37.