Histologic Evidence of Neurofibroma in Congenital Pseudarthrosis of Tibia - A Report of Two Cases

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ABSTRACT

Congenital pseudarthrosis of tibia is one of the most mysterious entities in terms of pathogenesis. This is because about half of these patients have clinical evidence of neurofibromatosis. Intra-osseous neurofibroma has been thought to be one of the causes of this bony abnormality. However, no previous report has identified histologically proven neurofibromatous tissue in the pseudarthrosis site. This study reported two cases, a 21-month old girl and a $3^1/_2$ year-old boy with congenital pseudarthrosis of tibia, both of which were Type V according to Boyd's classification. One case had café-au-lait spots while the other had not. Histologic examination of the pseudarthrosis area by light and electron microscope showed characteristic evidence of a neurofibroma. This report provides the strong evidence that Type V congenital pseudarthrosis of tibia can be directly caused by a neurofibroma.

INTRODUCTION

Congenital pseudarthrosis of tibia, a condition resulting in pathological fracture with congenital anterolateral angulation, is a rare disease with an obscure pathogenesis. A number of theories have been proposed such as mal-development of mesodermal structure in the embryo, lack of blood supply to the bone, failure of ossification centre to fuse and tumor formation such as fibrous dysplasia and neurofibromatosis[1-4]. Because evidence of neurofibromatosis is present in a high proportion (varies from 40-70%) of the patients with congenital pseudarthrosis of the tibia[5-9], pathologic fracture resulting directly from intra-osseous neurofibroma was suspected. However, until now, most authors have reported only dense cellular fibrous tissue resembling fibromatosis at and around the pseudarthrosis site[1,3,11]. Reports with electron microscopic investigation also found no evidence of Schwann cells[2,10-14].

In this study, two cases of congenital pseudarthrosis of tibia were presented with evidence of neurofibroma at the pseudarthrosis site by using routine histologic examination together with electron microscopic study in one case.

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RESULTS

Case 1

A 21-month old girl was born with an antero-lateral deformity of left tibia. She had no family history of neurofibromatosis. She was diagnosed as having congenital pseudarthrosis of tibia and was treated with *in situ* external fixator in a public hospital for 1 year After removing the fixator, the fracture had still remained with non-union. She was referred to our hospital.

Physical examination revealed antero-lateral bowing deformity of the left leg. No café-au-lait spots were found. The radiographs of the tibia showed congenital pseudarthrosis of the distal one-third of tibia and fibula (Boyd Type V) (Fig 1). This patient underwent surgery for excision of the pseudarthrosis in the tibia and fibula followed by rod fixation.

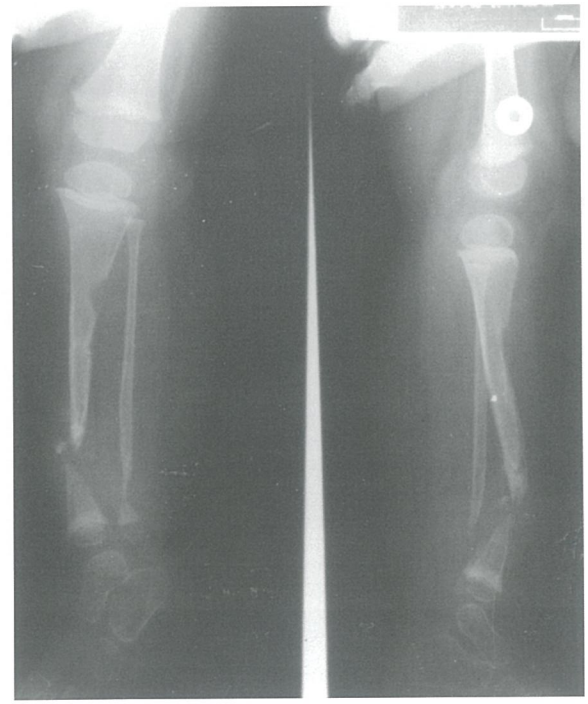

Fig. 1. Radiographs of left leg of Case 1 showing congenital pseudarthrosis at distal tibia and fibula. Both tibia and fibula are severely dysplasia. The osteolytic lesion of the proximal tibia was due to pin tract osteomyelitis from previous external fixation.

Case 2

A 3 1/2-year-old-boy was born with antero-lateral bowing of left leg. The patient was diagnosed as having congenital pseudarthrosis at the age of 1 month and was treated with a brace for 3 months. After 3 months, he was lost to follow up until he returned at the age of 3 1/2 years with inability to walk and more bowing of his leg.

Physical examination showed multiple café-au-lait spots in his trunk and extremities. Neurological exam ination was normal. The left leg was shorter than the right leg by about 2 cm. False motion was noted at the distal one-third of the left leg without pain. The radiograph revealed severe dysplasia of both the tibia and fibula (Boyd Type V) (Fig 2). He was operated for resection of the pseudarthrosis, bone grafting and rod fixation.

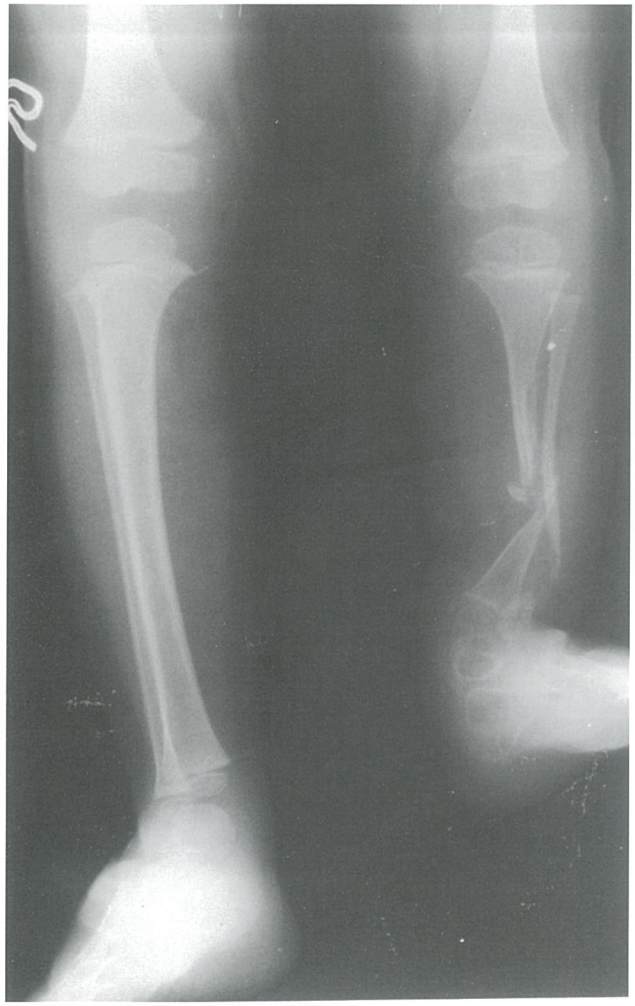

Fig. 2. Radiographs of Case 2 showing congenital pseudarthrosis of left tibia and fibula. The dysplastic area involved middle-third area of the tibia and distal one-third of the fibula. Left leg was 3 cm. shorter than the normal contra-lateral side.

Pathology

Gross examination: Gross examination showed irregular whitish tissue covering the resected bone segment. Cross sections of the bone showed that the medullary cavity was nearly obliterated by whitish tissue. The periosteum was thickened and blended with the surrounding irregular whitish tissue.

Microscopic examination: Histological examination was performed using sections from formalin-fixed and paraffin-embedded tissue stained with haematoxylin and eosin. The sections at the pseudarthrosis site revealed three distinct layers of histological pattern. The centre of the medullary canal showed a cavity containing amorphus material and hyalinized bone fragments. This cavity was rimmed by fibro-granulation tissue with osteoclasts as well as fibro-cartilagenous tissue associated with cancellous bone (Fig 3). These features are characteristic of pseudarthrosis. The outermost lesion was periosteum that blended with the surrounding lesion. This layer composed of interlacing bundles of elongated cells having wavy, dark-staining nuclei intermingled with wire-like strands of collagen and small to moderate amounts of mucoid material, characteristic of neurofibroma (Fig 4). The centre of the lesion was more cellular and had densely packed collagen with smaller amounts of mucoid material compared to the periphery. In some areas of the tumour, vascularity is more prominent and structured resembling specilised receptors were evident (Fig 5). The outer border of the lesion was ill-defined and infiltrated into the surrounding fat tissue.

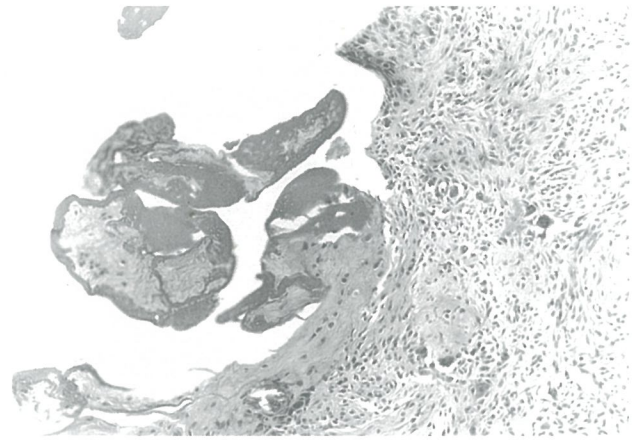

Fig. 3. Histological section showing pseudo-joint cavity. The cavity was rimmed by fibro-cartilagenous tissue.

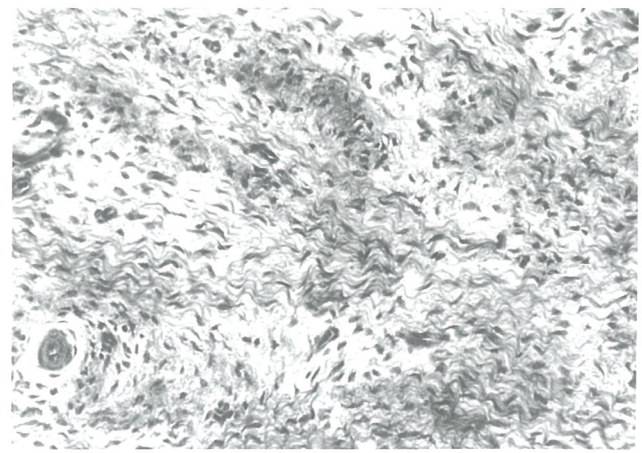

Fig. 4. Histologic section showing characteristic interlacing bundles of wavy elongated cells intermingled with wire-like strands of collagen.

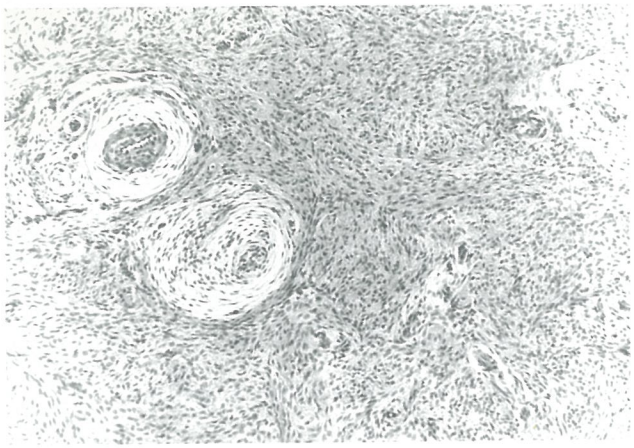

Fig. 5. Histologic section showing a more cellular interlacing bundles. Structures resembling Pacinian corpuscle were seen in the upper left corner. They consisted of a central core of polygonal cells flanked by peripheral zone of concentrically flattened cells.

In case 1, step serial sections from the cut of the pseudo-joint space revealed that the medullary canal was completely obliterated by the neurofibromatous tissue having a more cellular and less mucoid matrix. The formalin-fixed tissue from this area was sectioned for electron microscopic examination. The formalin-fixed tissue of case 2 was not available for electron microscopic study.

Electron microscopy: The electron microscope revealed mixtures of Schwann cells and fibroblasts, which is characteristic of a neurofibroma. The Schwann cell had long attenuated cell processes. Basal lamina consisting of electron-dense material coated the surface of the Schwann cell (Fig 6).

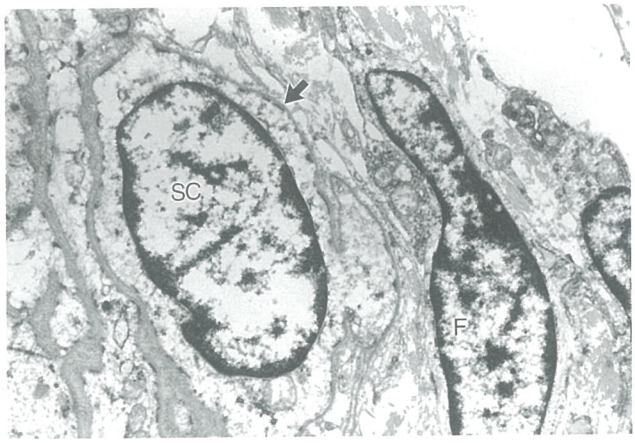

Fig. 6. Electron micrograph showed a Schwann cell (SC) and fibroblast (F). Schwann cell had cell processes and external lamina (arrow), (x10000).

DISCUSSION

We found evidence of neurofibromatous tissue at the pseudarthrosis site in two cases of congenital pseudarthrosis of the tibia. Neurofibroma was confirmed in one case by the presence of Schwann cells on electron microscopy. To our knowledge, this is the first report the literature of Boyd Type V congenital pseudarthrosis of the tibia to have caused by a neuroma in the lesion.

Association of congenital pseudarthrosis of tibia with neurofibromatosis is well recognised. Evidence of neurofibromatosis was reported in approximately 50% of patients with congenital pseudarthrosis and 5-20% of patients with neurofibromatosis have congenital pseudarthrosis[15]. Due to this high co-incidence, the pseudarthrosis might be directly caused by an intra-osseous neurofibroma[1]. However, evidence of neurofibromatosis within the pseudarthrosis itself has not been confirmed. In contrast, most authors found only cellular fibrous tissue resembling fibromatosis either in the medullary cavity or around the periosteum especially in Boyd's Type II congenital pseudarthrosis of the tibia. Reports of Type V congenital pseudarthosis of tibia, which has similar tibial deformity with additional dysplastic fibula are rare[16], but is assumed to have a similar histology.

A number of theories have been developed to explain the development of the deformity. One of the most interesting theories focusses mainly on the pathologic change of periosteum and blood vessels. McElvenny[1] was the first author who stressed the role of a markedly thickened periosteum as a causal factor resulting in pressure atrophy and impairment of blood supply. Our finding also supports this hypothesis. Other than the intra-osseous lesion, the tumour also formed a mass surrounding the periosteum. Actually, the periosteal lesion was more prominent and probably the tumour originated extra-osseously and then extended into the medullary cavity after disruption of the cortex due to fracture.

In this study, the first case did not have any clinical evidence of neurofibromatosis such as café-au-lait spots, freckling, cutaneous neurofibromas or lisch nodules, but neurofibromatosis is still likely because these clinical manifestations may develop later in childhood.

The reason why previous studies reported no evidence of neurofibroma at the pseudarthrosis may be linked with the site of histologic study, the relative paucity of histological sections studied, and the small number of cases investigated by electron microscopy. Most importantly, the lesion may be obscured by replacement of fibrous union tissue or scarring from previous operation. It is also possible that pseudarthrosis associated with neurofibromatosis may be caused by more than one pathogenic process, involving direct and indirect causes.

The finding of a neurofibroma at the pseudarthrosis site has an important clinical implication that all neurofibromas need to be excised to prevent recurrence of the fracture and to enhance healing of the pseudarthrosis.

In conclusion, we have demonstrated two cases of congenital pseudarthrosis of tibia with histologic evidence of neurofibroma at the pseudarthrosis site. It is possible to speculate that pseudarthrosis in neurofibromatosis can be directly caused by neurofibroma.

Acknowledgement

The authors would like to thank Dr Alan Geater for editing the manuscript.

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