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Soft-tissue haemangioma and periosteal new bone formation on the neighbouring bone

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Abstract Deeply situated soft-tissue haemangioma sometimes causes periosteal new bone formation on the neighbouring bone. The purpose of this study was to elucidate the aetiological factors for this phenomenon. We studied 25 patients with soft-tissue haemangioma on whom plain radiographs and computed tomography (CT) and/or magnetic resonance imaging (MRI) examinations were performed. We examined the presence or absence of periosteal new bone formation, haemangioma-bone distance, size of haemangioma and pain. Periosteal new bone formation was seen in 12 of 25 patients. In these 12 patients, the haemangioma was adjacent to the bone in 11 patients, while the haemangioma-bone distance was 4 mm in the other patient. In the remaining 13 patients who had no periosteal new bone formation, the haemangioma-bone distance was 5–27 mm. Pain in the former group was stronger than that in the latter group, the difference being statistically significant. There was no statistically significant difference in size of haemangioma between the two groups. Therefore, the main factor that induces periosteal new bone formation on the neighbouring bone was not the size of haemangioma, but the distance between the haemangioma and the bone.

Keywords Soft-tissue haemangioma · Periosteal reaction · Pain

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Introduction

Although haemangioma is one of the most common soft-tissue tumours (7% of all benign tumours) [19], intramuscular haemangioma is relatively rare (1.8% of all haemangiomata) [8]. Deeply situated, large, intramuscular haemangiomata sometimes cause periosteal new bone formation on the neighbouring bone [5, 9, 14, 15, 17]. Yet even a small haemangioma may occasionally cause periosteal new bone formation [6, 10, 12]. The factors which cause periosteal new bone formation in the neighbouring bone in patients with soft-tissue haemangioma are still unknown. The purpose of this study was to elucidate these factors.

Patients and methods

The subjects of this study were 25 patients who visited us from 1985 onwards because of intramuscular haemangioma and whose plain radiographs and computed tomography (CT) and/or magnetic resonance imaging (MRI) studies were examined. Thirteen were men and 12 were women with an average age of 24.3 years (range 2–57 years). The haemangiomata were located in the lower leg in 10 patients, thigh in 6, forearm in 4, foot in 2, upper arm in 1, hand in 1 and back in 1. The presence or absence of periosteal new bone formation was evaluated by plain radiographs in anteroposterior and lateral projections. CT was performed on 15 patients and MRI on 17 patients. The thickness of each slice in CT and MRI was mostly 5 mm (range 2–10 mm). The patients were divided into two groups: group A, who had periosteal new bone formation on the neighbouring bone, and group B, who had no periosteal new bone formation. For each group, the distance between the haemangioma and the neighbouring bone, the size of the haemangioma and level of pain were examined to find out whether there were any differences between the groups. The distance between the haemangioma and the neighbouring bone was defined as the minimum distance between the two as observed on CT and/or MRI. The size of the haemangioma was calculated by integrating the cross-sectional area of the haemangioma observed in each slice of CT or MRI. Pain was classified into five grades and scored as described in Table 1. Statistical analysis was performed by Mann-Whitney's U-test and Student's *t*-tests, with $p < 0.05$ considered significant.

Table 1 Pain score of haemangioma with five grades

Symptom	Score
No pain	0
Mild pain for which analgesics are not necessary	1
Moderate pain for which analgesics are sometimes necessary	2
Strong pain for which analgesics are always necessary	3
Severe pain for which surgery is necessary	4

Case reports

Two typical cases (cases 5 and 12) are presented below. Case 5 had a tiny haemangioma with a thin, solid, periosteal reaction associated with tremendous pain. Case 12 had a huge haemangioma with prominent periosteal new bone formation on the neighbouring bone.

Case 5

A 51-year-old woman visited us because of pain in the right cubital fossa. The pain was characterized as a constant, severe ache that had persisted for 3 years in spite of conservative therapy with diclofenac (75 mg/day, p.o.), which was partially effective. The pain was so severe that she could not sleep well at night. Her past and family history was not remarkable. Although no mass was palpable at the cubital fossa, the pain on pressure was tremendous. Plain radiographs showed a thin, continuous, periosteal new bone formation on the anterior surface of the ulna distal to the coronoid process, which was more prominent on tomography (Fig. 1A). CT showed a tiny mass measuring $1.5 \times 1 \times 0.7$ cm adjacent to the thickened cortex by periosteal new bone formation (Fig. 1B). MRI revealed a low signal intensity mass on T1-weighted images (Fig. 1C). The pain disappeared immediately after excision of the tumour. The histological diagnosis was cavernous haemangioma.

Case 12

A 23-year-old man visited us because of moderate pain and swelling of the right thigh which had persisted for 4 years. An elastic soft-tumour mass measuring 18×10 cm was palpable on the anterior aspect of the right thigh. Plain radiographs showed periosteal new bone formation on the anteromedial surface of the right femur (Fig. 2A). CT revealed that the medial cortex of the femur was thickened in addition to the periosteal new bone formation (Fig. 2B). MRI showed that the soft-tissue tumour covered two-thirds of the circumference of the femur in axial sections (Fig. 2C–E). Periosteal new bone formation was also seen on MRI. T1-weighted images revealed that the tumour consisted of a high signal intensity area and an iso-signal intensity area intermingled with each other (Fig. 2C). The tumour was strongly enhanced with contrast medium (gadolinium diethylene triamine penta-acetic acid, Gd-DTPA) (Fig. 2D). T2-weighted images with fat suppression signal showed high signal intensity (Fig. 2E). These physical and radiographical findings suggested that the tumour was a haemangioma. Aspiration needle biopsy prior to sclerotherapy demonstrated that the histological diagnosis was cavernous haemangioma.

Results

Clinical and radiographical features

Details of the 25 patients are summarized in Tables 2 and 3. Periosteal new bone formation on the neighbouring bone was seen in 12 patients (group A, Table 2) and not found in 13 patients (group B, Table 3) on the plain radiographs.

Periosteal new bone formations were classified into four types, i.e. lobulated solid periosteal reaction, solid continuous periosteal reaction, elliptical cortical hyperostosis and thin solid periosteal reaction [18]. In group A (n = 12), 5 patients had a thin solid periosteal reaction, 4 had a lobulated solid periosteal reaction, 2 had a solid continuous

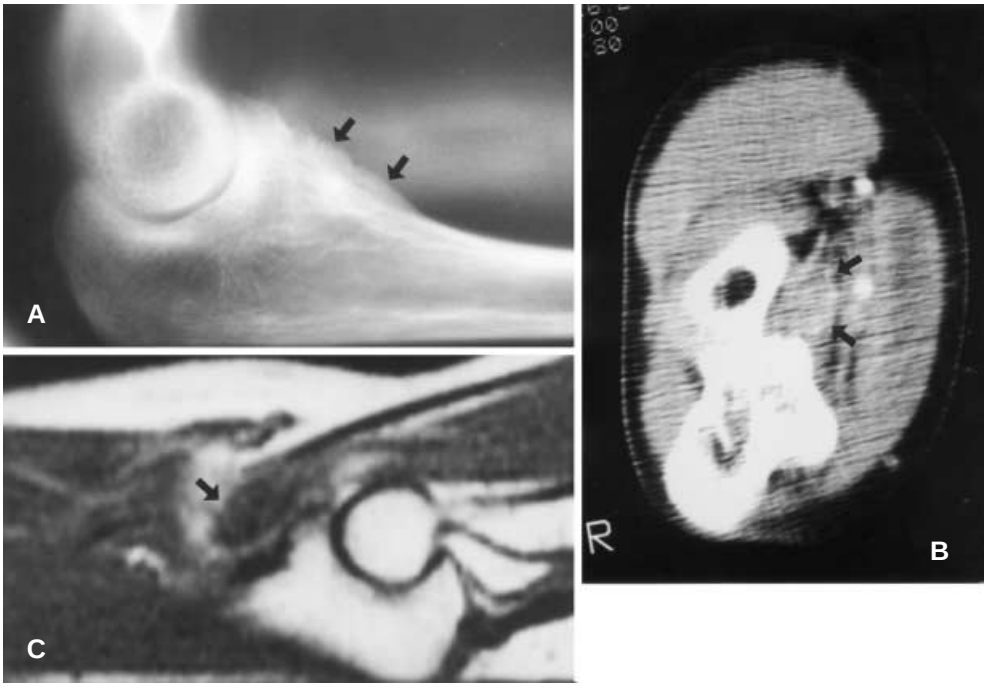

Fig. 1 **A** Tomography of the proximal ulna (case 5). Thin, continuous, periosteal new bone formation is seen on the anterior surface of the ulna distal to the coronoid process (*arrow*). **B** Enhanced CT of the elbow. A tiny mass approximately 1 cm in diameter (*arrow*) is adjacent to the thickened cortex of the ulna. **C** MRI of the tumour shows iso-signal intensity on T1-weighted image (*arrow*)

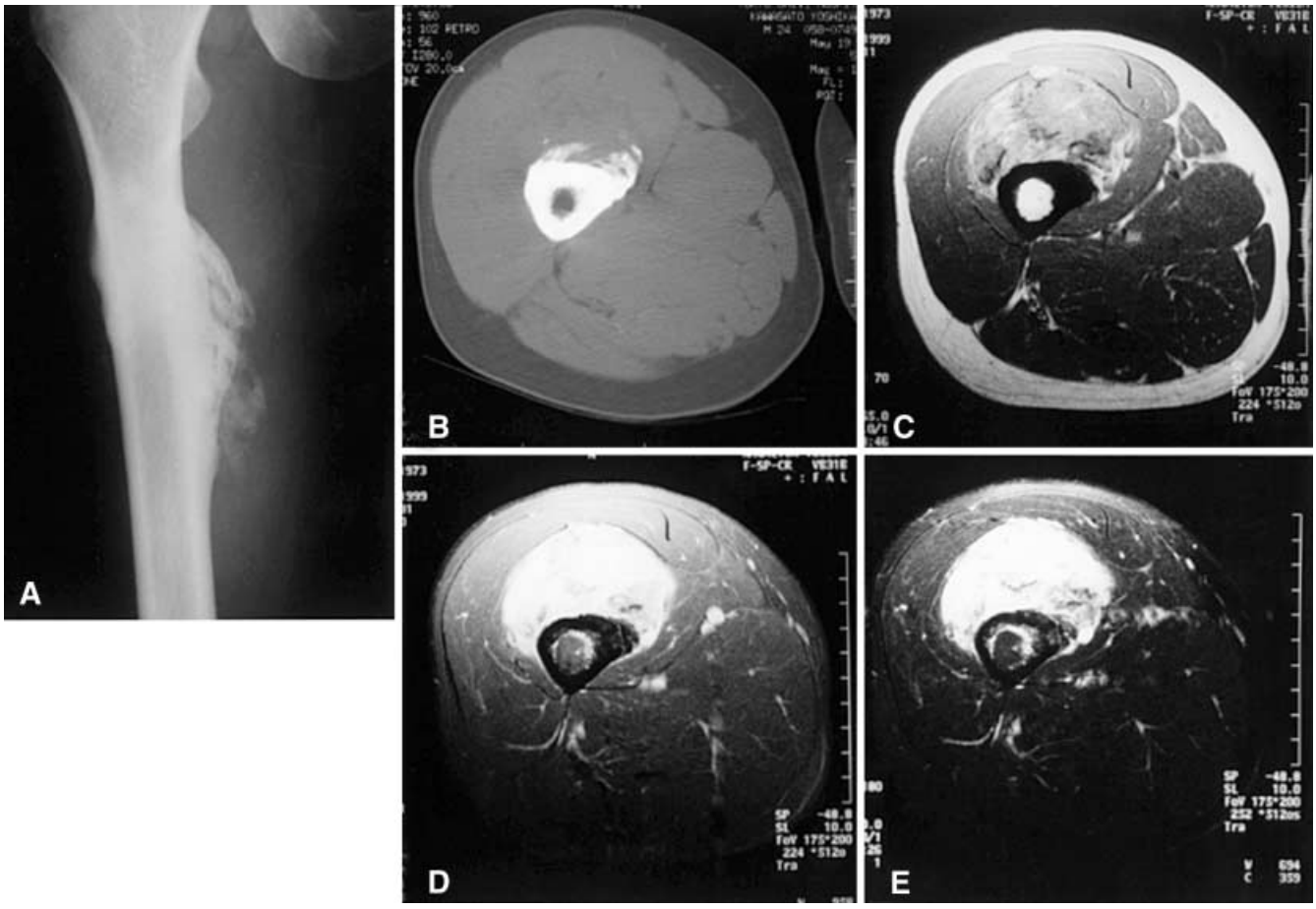

Fig. 2 **A** Plain radiograph shows prominent periosteal new bone formation chiefly on the medial surface of the right femur. Thickening of the lateral cortex is also noted. **B** CT of the right thigh. Extra-osseous bone formation, probably periosteal, is seen in addition to thickening of the medial and lateral cortex. **C** T1-weighted MRI shows that the soft-tissue tumour covered two-thirds of the circumference of the femur. The tumour consists of a high signal intensity area and an iso-signal intensity area intermingled with each other. Thickening of the lateral and medial cortex is seen on this image, although the extra-osseous new bone formation that can be seen on CT (**B**) is not detectable. **D** T1-weighted MRI with gadolinium diethylene triamine penta-acetic acid (Gd-DTPA) enhancement shows that the tumour is strongly enhanced. **E** T2-weighted MRI with fat suppression signal shows some low signal intensity area which reflects the extra-osseous bone formation seen on CT (**B**)

periosteal reaction, and the other one had elliptical cortical hyperostosis (Table 2).

Of the 25 patients 14 underwent excision of the tumour. In addition, 2 other patients underwent biopsy. Histological examination in these 16 patients revealed that the tumour was cavernous haemangioma. The average pain score before excision of the tumour in the 14 patients was 1.7 points (range 0–4). The pain disappeared completely following excision in all patients except one.

Factors influencing periosteal new bone formation

In group A, the haemangioma was directly adjacent to the bone in 11 patients, and the distance between the haemangioma and the neighbouring bone in the remaining patient was 4 mm. In group B, the distance from the haemangioma to the bone was 5–27 mm (average 15 mm). The distance in every case was shorter in group A than in group B, the difference being statistically significant (Mann-Whitney's U-test, $p < 0.0001$).

The mean size of the haemangioma in group A was 88 cm^3 (range 0.42–310 cm^3), whereas it was 45 cm^3 (range 0.13– 230 cm^3) in group B. Although they were larger in group A than in group B, the difference was not statistically significant (Student's *t*-test, $p = 0.13$).

The mean pain score in group A was 2.25 points (range 0–4 points), whereas that in group B was 0.92 points (range 0–2 points). Thus, a haemangioma with periosteal new bone formation in the neighbouring bone was more painful than that without periosteal new bone formation (Mann-Whitney U-test, $p = 0.023$).

Discussion

Though many authors have reported that large haemangiomata sometimes cause a periosteal reaction on the

Table 2 Summary of all patients with periosteal new bone formation on the neighbouring bone (group A). In case 6, the tumour volume could not be calculated because the margin of the haemangioma was unclear in addition to the poor quality of the MRI. However, the fact that the distance between the haemangioma and the bone was 0 mm was apparent from surgical findings (*NSAID* non-steroidal anti-inflammatory drug)

Case	Age (years)/ gender	Location	Neigh bouring bone	Type of periosteal reaction	Dis- tance (mm)	Size (cm^3)	Pain before treatment	Treatment	Pain after treatment	Histological diagnosis
1	13/M	Upper arm	Humerus	Solid continuous	0	13	1	Excision	0	Cavernous
2	13/F	Lower leg	Tibia, fibula	Solid continuous	0	50	4	Excision	0	Cavernous
3	41/M	Foot	2nd metatarsal	Thin solid	0	77	1	Excision	0	Cavernous
4	2/M	Lower leg	Fibula	Thin solid	0	190	0	Observation	0	Unknown
5	51/F	Forearm	Ulna	Thin solid	0	0.55	4	Excision	0	Cavernous
6	23/F	Foot	1st cuneiform	Elliptical	0	Un- known	4	Excision	1	Cavernous
7	33/M	Lower leg	Tibia	Lobulated solid	0	5.3	4	Excision	0	Cavernous
8	26/F	Lower leg	Tibia	Thin solid	0	35	3	NSAID	3	Unknown
9	34/F	Forearm	Radius	Lobulated solid	0	0.42	1	Observation	1	Unknown
10	15/M	Thigh	Femur	Thin solid	4	310	2	NSAID	1	Unknown
11	26/F	Lower leg	Fibula	Lobulated solid	0	5.2	1	Observation	1	Unknown
12	23/M	Thigh	Femur	Lobulated solid	0	280	2	Sclerotherapy	1	Cavernous
Average	25.0				0.3	88	2.25		0.67	

Table 3 Summary of all patients without periosteal new bone formation on the neighbouring bone (group B)

Case	Age (years)/ gender	Location	Neighbouring bone	Distance (mm)	Size (cm^3)	Pain before treatment	Treatment	Pain after treatment	Histological diagnosis
13	13/M	Lower leg	Tibia	20	110	2	NSAID	1	Unknown
14	25/F	Lower leg	Tibia	20	230	1	Excision	0	Cavernous
15	33/F	Back	Scapula	5	50	1	Excision	0	Cavernous
16	26/M	Lower leg	Fibula	20	5.8	2	Excision	0	Cavernous
17	44/M	Thigh	Femur	10	31	0	Excision	0	Cavernous
18	5/F	Thigh	Femur	25	38	1	Observation	1	Cavernous
19	3/M	Forearm	Radius	6	6.3	0	Observation	0	Unknown
20	8/M	Hand	Proximal phalanx	5	0.13	0	Excision	0	Cavernous
21	27/F	Lower leg	Tibia	12	7.9	2	Observation	2	Unknown
22	14/M	Thigh	Femur	5	21	1	Excision	0	Cavernous
23	35/F	Thigh	Femur	24	58	1	Observation	1	Unknown
24	57/M	Forearm	Radius	14	5.3	0	Excision	0	Cavernous
25	18/F	Lower leg	Tibia	27	26	1	Excision	0	Cavernous
Average	23.7			14.8	45	0.92		0.38	

neighbouring bone [5, 9, 14, 15, 17], descriptions of periosteal bone formation in small haemangioma are rare [6, 10, 12]. However, this study suggests that periosteal bone formation in small haemangioma is not rare. The mechanism of reactive bone formation on the neighbouring bone in soft-tissue haemangioma patients remains unknown. Stretching or irritation of the periosteum or passive hyperaemia induced by the tumour may contribute to the periosteal reaction [20]. De Filippo et al. recently described a case in which a periosteal reaction occurred in the ulna adjacent to a haemangioma 3 cm in size and hypothesized that increased regional vascularity adjacent to the tumour caused the periosteal reaction [6]. Recently, Sung et al. studied 115 patients with soft-tissue haemangioma and found changes in the neighbouring bone in 24 [18]. They found that when bone changes were present, the haeman-

giomata were close to the bone cortex, whereas those haemangiomata without reactive bone changes were distant from the bone. However, they did not analyse the distance between the haemangioma and bone precisely. Our quantitative study led us to conclude that the main factor stimulating periosteal bone formation in haemangioma is not the size of the haemangioma, but the distance from the haemangioma to the bone.

There has been no study on the correlation between pain and periosteal new bone formation on the neighbouring bone in soft-tissue haemangiomata. We describe here that haemangiomata accompanied by a periosteal reaction are more painful than those without a periosteal reaction. As described by many authors, soft-tissue haemangiomata are sometimes painful. The pain is due to haemorrhage [4], thrombosis in the blood vessels or thrombophlebitis [1, 4], spasm in smooth muscle elements [1] or distension of the vascular spaces of the tumour [3, 7]. Because non-steroidal anti-inflammatory drugs, e.g. diclofenac and indomethacin, are sometimes effective against pain in haemangioma, prostaglandin E_2 may be the cause of pain. Characteristic strong pain in osteoid osteoma is thought to be caused by prostaglandin E_2 produced by the tumour tissue [11, 16]. Osteosclerosis around the nidus is a feature of osteoid osteoma. Since prostaglandin E_2 has a bone-forming action at low concentrations [2, 13], it may cause osteosclerosis in osteoid osteoma. Analogously, the periosteal new bone formation and pain in haemangioma may be caused by prostaglandin E_2, although we have not yet studied prostaglandins in haemangioma.

It is diagnostically important to know that soft-tissue haemangioma causes periosteal new bone formation on the neighbouring bone, because a periosteal reaction could suggest a misdiagnosis of malignant bone tumour. With a solid or lobulated periosteal reaction of bone on plain radiography, which is very different from that seen in malignant bone tumours, one should consider the possibility of underlying soft-tissue haemangioma adjacent to the bone.

In conclusion, the main factor of periosteal bone formation in haemangioma is not the size of haemangioma, but the distance from the haemangioma to the bone. In addition, pain may have some relationship with the periosteal bone formation.

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