

## CASE REPORT

## Sudden multiple fractures in a patient with sarcoidosis in multiple organs

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**SUMMARY**

A 30-year-old man who incidentally fractured his right olecranon and other multiple phalanges was admitted to our hospital. He had a 2-year history of uveitis and bilateral hilar lymphadenopathy (BHL), and pulmonary sarcoidosis was diagnosed from transbronchial lung biopsy. Right elbow arthrodesis was performed, and biopsied specimens showed non-caseating epithelioid cell granuloma, suggesting osseous sarcoidosis. He was discharged uneventfully without further treatment, but BHL had progressed with the appearance of lung parenchymal lesions 3 months later. At that time, involvement of other organs was also noted on Gallium-67 scintigraphy, showing accumulations in BHL, axillary and inguinal lymph nodes, enlarged liver and spleen and subcutaneous areas. After initiation of steroid therapy, multiple organ involvement improved, and no further bone involvement has been recognised to date. Osseous sarcoidosis complicated by bone fracture is an extremely rare presentation, but should be considered in patients with sarcoidosis, especially when multiple organs are involved.

**BACKGROUND**

Sarcoidosis is a systemic disease, and the frequency of osseous sarcoidosis is 1–13%, but bone fracture is extremely rare. To the best of our knowledge, only 23 cases have been reported so far. We describe a case of osseous sarcoidosis with multiple organ involvement and review the literature for this pathology associated with bone fracture.

**CASE PRESENTATION**

A 30-year-old man was admitted to our orthopaedics ward because of sudden fracture of the right olecranon when he turned to speak to his friends. Two years previously, he had been diagnosed with pulmonary sarcoidosis based on findings of non-caseating epithelioid cell granuloma on transbronchial lung biopsy. He had uveitis and bilateral hilar lymphadenopathy (BHL) on chest X-ray, but had been in good health until then without any treatments during his regular visits to our hospital.

Vital signs and physical examination were normal except for swelling in the area of the right olecranon. Lateral radiography of the right elbow showed the fracture line at the right olecranon (figure 1A; white arrowhead) with cystic lesions, suggesting osteolytic changes. Furthermore, radiography showed multiple osseous erosions (figure 1B, C; arrow) with osteolytic lesions, and fractures of the middle phalanx of the left digitus minimus manus (figure 1B; white arrowhead) and base of

the left metacarpal bone of digitus annularis (figure 1B; black arrowhead).

Axial T1-weighted imaging (T1WI) demonstrated a low-intensity intramedullary mass measuring 2 cm in the right olecranon (figure 1D), which appeared hyperintense on axial T2WI (figure 1E) and heterogeneously enhancing on fat-suppressed enhanced T1WI (figure 1F). Tc-99m methylene diphosphonate bone scintigraphy showed multiple hot spots on the left parietal bone, middle thoracic spine, bilateral cubital regions, wrists and knees, and below bilateral ankle joints (figure 2).

Right elbow arthrodesis was performed and biopsy specimens showed non-caseating epithelioid cell granuloma on both low-power (figure 3A) or high-power fields (figure 3B). Osseous sarcoidosis with multiple organ involvement was diagnosed and he was discharged uneventfully with no further treatment. Three months later, he presented to our respiratory department with progression of BHL and newly recognised pulmonary involvement with bilateral pleural effusion. Chest X-ray showed BHL with perihilar infiltration and dullness of the left costophrenic angle (figure 4A). Thoracic CT demonstrated consolidation spreading from hilar to peripheral areas showing multiple scattered tiny nodules with bilateral pleural effusions (figure 4B). Gallium-67 scintigraphy showed increased radiotracer accumulation in the lacrimal and parotid glands and normal accumulation in the nasopharynx, creating the mottled appearance of a giant panda, the so-called panda sign. Increased radiotracer accumulation was noted in BHL, axillary and inguinal lymph nodes, subcutaneous nodules, lung parenchyma, enlarged liver and spleen and subcutaneous areas (figure 5). Furthermore, cardiac echography showed interventricular septal thinning and erythema nodosum was noted. Finally, osseous sarcoidosis accompanied by multiple organ involvements (eye, heart, skin, lungs, lymph nodes, liver and spleen) was diagnosed.

**TREATMENT**

Multiple organ involvement including pulmonary lesions was considered to represent sarcoidosis, and the patient was treated with prednisolone at a dose of 0.5 mg/kg/day.

**OUTCOME AND FOLLOW-UP**

After initiation of treatment, multiple subcutaneous nodules and lymphadenopathies disappeared, and almost all lung lesions were improved. No further bone involvement has been recognised to date.



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**Figure 1** Lateral radiograph of the right elbow showing the fracture line at the right olecranon (A; white arrowhead) with cystic lesions, suggesting osteolytic changes. Furthermore, radiographs showing multiple osseous erosions (B and C; arrow) with osteolytic lesions, fractures on the middle phalanx of the left digitus minimus manus (B; white arrowhead) and base of the left metacarpal of digitus annularis (B; black arrowhead). Axial T1-weighted imaging (T1WI) demonstrates a low-intensity intramedullary mass measuring 2 cm in the right olecranon (D), appearing hyperintense on axial T2WI (E) and enhancing heterogeneously on fat-suppressed enhanced T1WI (F).

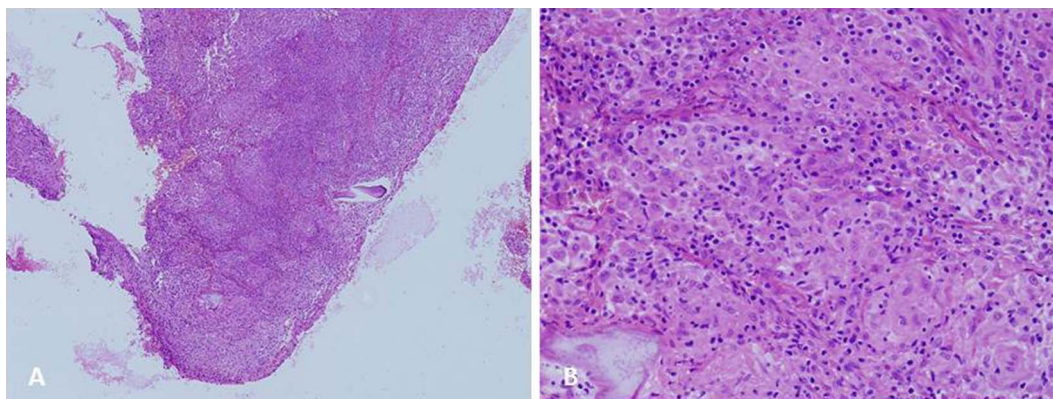


**Figure 2** Tc-99m methylene diphosphonate bone scintigraphy showing multiple hot spots on the left parietal bone, middle thoracic spine, cubital regions, wrists and knees, and below bilateral ankle joints.

## DISCUSSION

Sarcoidosis is a systemic disease, and the frequency of osseous sarcoidosis ranges from 1% to 13%.<sup>1</sup> Radiological features of osseous sarcoidosis include osteolytic lesions, bone erosions, and a lacework pattern, which show a predilection for small bones in the hands and feet,<sup>2</sup> as in the present case.

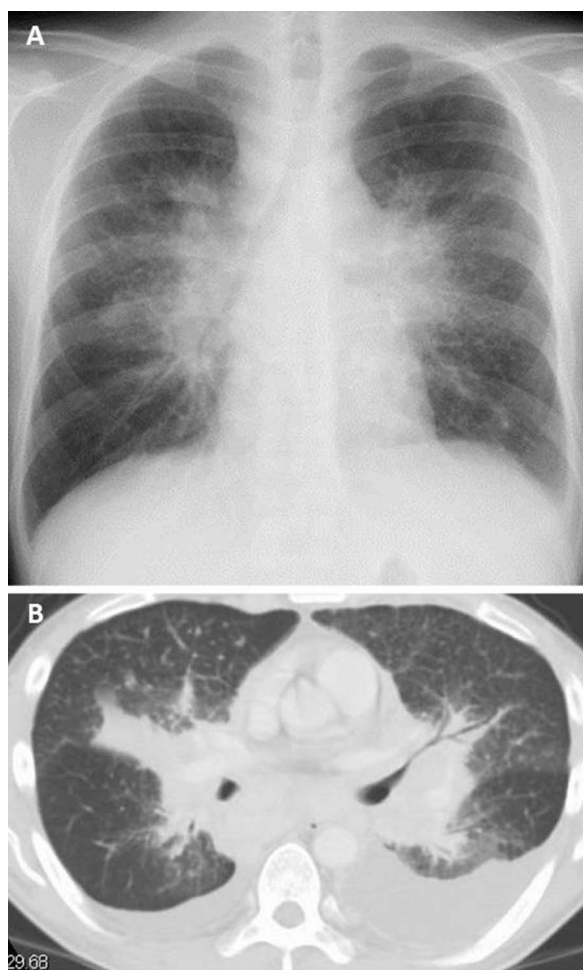
To the best of our knowledge, only 24 cases of bone fracture with sarcoidosis have been reported<sup>2-21</sup> including the present case (table 1). The patients were of the age group ranging from 15 to 59 years old (mean±SD 37.8±12.2 years), with a male-to-female ratio of 9-15. Among these, racial diversity was noted, but people of African descent/origin (n=8) and Asian patients all of whom were Japanese (n=9) appear as prominent populations. Although few reports have described the racial incidence of bone fractures in patients with osseous sarcoidosis, Handa *et al*<sup>3</sup> indicated that people of African descent/origin tended to experience bone fractures, with no mention of Japanese cases. Our results suggest that the number of Japanese cases was equal to that of African descent/origin people. In our review, the areas of bone involvement were the phalanges (n=15), joints (n=5), vertebrae (n=4) and others (n=2), respectively. This means the phalanges were the most affected by bone fracture in osseous sarcoidosis, like our case. O'Daly *et al*<sup>4</sup> described the incidence of osseous involvement as low in patients with early-stage sarcoidosis and absence of cutaneous lesions. Indeed, the present case had sudden bone fractures 2 years after diagnosis of sarcoidosis together with subcutaneous nodules. While, our review showed insidious onset of bone fracture in the clinical course (median: 0.95 years) after diagnosis of sarcoidosis (table 1) with or without skin involvement.



**Figure 3** Biopsied specimens obtained from right elbow arthrodesis showing non-caseating epithelioid cell granuloma on both low-power (A) and high-power fields (B).

Interestingly, new diagnosis of sarcoidosis due to bone fracture was found in 33.3% (n=8) of all cases. The precise mechanism of bone fracture in patients with sarcoidosis is unknown. Importantly, 70% (n=14) of the 20 cases for whom records are available showed bone fracture with no apparent traumatic events and none of them had obvious clinical findings for bone involvement, as was

the present case. Although predicting the possibility for bone fracture is difficult, multiple bone scans might be useful for detecting undiscovered bone involvement in whole body even in patients with asymptomatic osseous sarcoidosis, and accumulation of such cases might lead to evaluate the efficacy of treatments via comparing the two phases (pretreatment and posttreatment). The appropriate treatment for bone fracture in sarcoidosis remains contentious. Furthermore, corticosteroids have not been shown to influence the clinical course of osseous sarcoidosis.<sup>22</sup> The present study showed that 75.0% (n=18) of patients were treated with oral steroids with or without other drugs (methotrexate, n=1; chloroquine, n=1), and orthopaedic operation was performed in 79.2% (n=19) of all patients.



**Figure 4** Chest X-ray showing bilateral hilar lymphadenopathy (BHL) with perihilar infiltration and dullness of the left costophrenic angle (A). Thoracic CT depicts massive consolidation from hilar to peripheral portion with bilateral pleural effusions and multiple scattered tiny nodules (B).



**Figure 5** Gallium-67 scintigraphy showing increased radiotracer accumulation in the lacrimal and parotid glands, the so-called panda sign. Increased radiotracer accumulation was noted in BHL, axillary and inguinal lymph nodes, subcutaneous nodules, lung parenchyma, enlarged liver and spleen and subcutaneous areas.

Table 1

Reference	Age (years)	Sex	Race	Bone	Duration (years)	New diagnosis	Atraumatic	Operation	Medication	Multiple organ involvement	Number of organs involved except for bone
<sup>2</sup>	55	M	NA, not applicable	Vertebra	NA, not applicable	N	Y	Y	PSL	Y	3
<sup>3</sup>	22	M	Japanese	Phalange	7	N	Y	N	PSL+MTX	Y	2
<sup>4</sup>	39	F	Black	Joint	0.08	N	N	Y	PSL	Y	2
<sup>5</sup>	31	F	Black	Joint	3	N	N	Y	PSL	Y	2
<sup>6</sup>	26	M	Black	Vertebra	2	N	NA, not applicable	Y	PSL	Y	1
<sup>7</sup>	27	F	Black	Rib	0	Y	N	N	PSL	Y	2
<sup>8</sup>	36	F	Black	Phalange	1	N	NA, not applicable	Y	PSL	Y	1
<sup>8</sup>	19	M	Black	Joint	NA, not applicable	N	NA, not applicable	Y	None	NA, not applicable	NA, not applicable
<sup>9</sup>	59	F	NA	Phalange	0	Y	Y	N	PSL	N	0
<sup>10</sup>	29	M	Black	Phalange	0	Y	N	N	None	Y	1
<sup>11</sup>	49	F	Japanese	Phalange	0	Y	Y	Y	PSL	N	0
<sup>11</sup>	35	M	Japanese	Phalange	6	N	N	Y	None	Y	2
<sup>11</sup>	43	F	Japanese	Phalange	32	N	Y	Y	PSL	Y	3
<sup>12</sup>	48	F	NA	Phalange	0	Y	Y	Y	PSL	N	0
<sup>13</sup>	25	F	Moroccan	Phalange	2	N	Y	Y	None	Y	2
<sup>14</sup>	59	F	Japanese	Phalange	0.5	N	Y	Y	None	Y	1
<sup>15</sup>	38	F	Black	Phalange	12	N	Y	Y	PSL	Y	2
<sup>16</sup>	45	F	Portugese	Femur, Ulna	0	Y	NA, not applicable	Y	None	N	0
<sup>17</sup>	55	M	Japanese	Vertebra	3	N	Y	Y	PSL	Y	2
<sup>18</sup>	34	M	Japanese	Phalange	0	Y	N	Y	PSL	Y	6
<sup>19</sup>	36	F	NA, not applicable	Vertebra	0.9	N	Y	N	PSL+CQ	Y	3
<sup>20</sup>	52	F	NA, not applicable	Phalange	0	Y	Y	Y	PSL	Y	4
<sup>21</sup>	15	F	Japanese	Phalange	2	N	Y	Y	PSL	Y	2
Present case	30	M	Japanese	Joint, Phalange	2	N	Y	Y	PSL	Y	5

In our review, multiple organ involvement was noted in 79.2% (n=19) of all cases, potentially representing a risk factor for bone fracture in sarcoidosis, as reported by a previous study.<sup>3</sup>

Given these findings, the possibility of bone fracture should always be considered in sarcoidosis patients with various clinical findings via multiple organ involvement. Our case and review of the literatures demonstrated that the incidence of osseous sarcoidosis among Japanese patients seemed to be greater than that of previous recognition.

### Learning points

- ▶ Frequency of osseous sarcoidosis is 1–13%, but bone fracture is rare.
- ▶ Bone fracture can be an initial presentation of sarcoidosis.
- ▶ The phalanges are the part most affected by bone fracture in osseous sarcoidosis.
- ▶ The precise mechanisms of bone fracture in patients with sarcoidosis are unclear, and appropriate treatments are still under debate.
- ▶ Multiple organ involvement might be one risk factor for bone fracture.

**Contributors** MS and TS wrote the manuscript and managed the patient in a hospital setting; HI and HG managed the patient in the outpatient department.

**Competing interests** None.

**Patient consent** Obtained.

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