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Retrospective Study to find the prevalence of neoplasia in swellings of hand and foot bones

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Abstract

Lesions occurring in them are infrequently reported. In this retrospective study, we analyze all types of lesions affecting bones of the hands or feet, including infections and inflammatory conditions, benign and malignant tumors, and tumor like lesions, correlating clinical, pathologic and biopsy findings. Out of 50 lesions included in the study, infections/ inflammatory lesions constituted 46.0%, benign tumors 32.0%, malignant tumors 12.0%, and tumor like lesions 10.0%. Osteomyelitis was the most common lesion in this series, accounting for 44% of the cases. In other study also it is the commonest lesion. Walking barefoot and Diabetes mellitus constitutes a significant predisposing risk factor for osteomyelitis of the foot. Tuberculosis constitutes the major cause of osteomyelitis in India hence higher incidence of tuberculous osteomyelitis in the small bones of the hands or feet as compared to that in the West. Benign tumors were more common than malignant tumors in our series, GCT constituting 43.8% of benign tumors. This is important in view of the lower recurrence rate in the former compared to the latter. The only other 3 cases of GCR reported during the study period were located in the mandible. In view of overlapping ultrastructural and light microscopic features, as well as similar biologic behavior, aneurysmal bone cyst and giant-cell reparative lesions are thought to represent related responses to intraosseous hemorrhage. Florid reactive periostitis is a reactive process that predominantly involves the bones of the hands or feet, mostly in young women, and a history of minor trauma is seen in less than half of the cases. Similar clinical findings were noted in our patient as well. The importance of this entity lies in the possibility of it being misdiagnosed as a malignant lesion, especially osteosarcoma. Such a lesion was not seen in any other bone in our institution during the study period.

CONCLUSION : Lesions of the bones of the hands or feet are uncommon. Infections/inflammatory lesions are more common in India. Benign tumors were more common than malignant tumors in our series. Giant cell tumor is the commonest neoplastic lesion. . Awareness and correlation of clinical, radiologic, and pathologic features help in making correct diagnoses.

Keywords: Hand Swelling; Foot swelling; Neoplasia in Hand; Neoplasia in foot

1 INTRODUCTION

The bones of the hands and feet constitute more than half of the bones in the human skeleton (106/206), but lesions occurring in them are infrequently reported.^(1,2) If we review the literature of neoplastic swellings there are very few studies regarding this.^(3,4) Although many of the lesions that occur in the rest of the skeletal bones can occur in the bones of the hands or feet, the distribution and frequency differ. Metastatic lesions and myeloma are extremely uncommon, whereas florid reactive periostitis and bizarre periosteal osteochondromatous proliferation are peculiar to the bones of the hands and feet. In this study, we analyze all types of lesions affecting bones of the hands or feet, including infections and inflammatory conditions, benign and malignant tumors, and tumorlike lesions, correlating clinical, pathologic and biopsy findings features so as to calculate the prevalence of neoplasia in these swellings.

2 MATERIALS AND METHODS

This is a retrospective study of lesions involving bones of the hands or feet. The diagnoses were based on patients reported in department of orthopaedics and surgery of a tertiary care teaching hospital and tertiary care district hospital in between January 2018 and September 2019. The demographic data, clinical details, and imaging features were noted in each case. Only those cases were included where the material was processed for routine paraffin sections after fixation in 10% buffered formalin. Decalcification was carried out with 10% nitric acid whenever necessary prior to processing. The diagnoses were based mainly on routine hematoxylin-eosin-stained sections. Immunohistochemistry with an appropriate panel of antibodies was carried out whenever necessary to categorize neoplasms, using routine immunohistochemical analysis as appropriate for the antibodies.

3 RESULTS

During the study period, a total (all sites) of 1014 bone lesions were encountered, 52 (5.2%) of which involved bones of the hands or feet. Two cases were excluded as the biopsy material was insufficient for a definitive opinion. Of the 50 lesions included in the study, infections/ inflammatory lesions constituted 23 (46.0%), benign tumors 16 (32.0%), malignant tumors 6 (12.0%), and tumorlike lesions 5 (10.0%). Table 1 shows the distribution of lesions the involving bones of the hands or feet.

Infections/Inflammatory Lesions

The 23 patients in this category include 15 with nonspecific osteomyelitis, 5 with tuberculous osteomyelitis, 2 with fungal osteomyelitis, and 1 with osseous sarcoidosis.

Among the 15 patients with nonspecific osteomyelitis, ages ranged from 9 to 73 years (median, 40 years), with almost

equal incidence in males and females. Twelve cases involved bones of the feet (phalanges 6 [great toe 5/6], metatarsals 2, cuboid 1, cuneiform 1, calcaneum 2), and the remaining 3 involved the metacarpals. Predisposing factors were noted in 6 patients (diabetes mellitus 3, systemic lupus erythematosus with vasculitis 1, penetrating injury 1, fracture 1).

Of the 5 patients with tuberculous osteomyelitis (mean age, 17.8 years), 1 had spinal involvement and underwent amputation of the fourth toe in another hospital for similar complaints. The phalanges were most commonly involved (Table 2). Three of the patients showed spina ventosa radiologically. Histologically, all cases showed caseating confluent granulomas containing epithelioid cells, Langhans type of giants with a peripheral rim of lymphocytes and plasma cells. Stains for acid-fast bacilli were negative on histologic sections in all cases. However, all patients responded well to antituberculous treatment.

Both patients with fungal osteomyelitis were male; 1 was a known diabetic and the other had a history of penetrating injury. Both had calcaneal involvement, and 1 patient had additional involvement of the ipsilateral cuboid. Radiologic diagnosis was chronic osteomyelitis in both. Histologically, 1 of the cases showed areas of infarction with necrotic bony spicules and marrow elements with frequent narrow septate hyphae branching at acute angles. These hyphae were highlighted by silver methenamine stain. In view of the above morphology, a diagnosis of fungal osteomyelitis due to *Aspergillus* species was made. Culture confirmation was not available in this case. The other case showed mixed granulomatous and suppurative inflammation. Silver methenamine stain showed spherical, oval to elongated yeast and hyphal-shaped organisms. A preliminary diagnosis of fungal osteomyelitis was made. The culture grew *Sporothrix schenckii*.

Osseous sarcoidosis was seen in a known case of sarcoidosis with pulmonary and cutaneous involvement. Computed tomographic scan of the chest showed nodular opacities with conglomeration in the mid zonal distribution involving both lungs with bilateral hilar and mediastinal lymphadenopathy. Bronchial brushings showed granulomas. The patient also had multiple papules on both legs with histologic confirmation of cutaneous sarcoidosis. His skeletal involvement started as a painful swelling of the right little finger. The radiograph showed a lytic lesion with thinned-out cortex and adjacent soft tissue swelling. There was no evidence of calcification/periostitis. His angiotensin-converting enzyme level was 178 U/L (reference range, 14–70 U/L) and serum calcium was 10.1 mg/dL (reference range, 8.5–10.2 mg/dL). Histologically, there were discrete noncaseating granulomas with giant cells. He underwent resection arthrodesis followed by steroid therapy, after which he was asymptomatic for 2 years but later developed swelling of the wrist. Radiographs did not reveal any fresh bony lesion. Synovial biopsy material from the wrist

showed noncaseating granulomas.

Benign Tumors

The demographic data, clinical presentation, site, and imageologic features of all benign tumors involving the bones of hands or feet are given in Table 3.

Giant cell tumor (GCT) was the most common benign tumor encountered in our study, accounting for 7 cases (4 males and 3 females). The patients' age ranged from 17 to 48 years with mean of 32 years. Phalanges were the most commonly involved site, followed by metatarsals. Two of the cases were recurrent lesions. Radiographically, all were lytic with cortical break and the presence of a soft tissue component in 4. Histologically, all showed characteristic morphology, with spatial arrangement of giant cells and mononuclear stromal cells. The stromal cells had oval to spindle morphology. The nuclei of those cells resembled those of regularly interspersed giant cells, which contained up to 40 to 50 nuclei. Mitotic activity (2-4/10 high-power fields) was noted in stromal cells. Osteoid, fibrous spindling or clustering of giant cells was not seen.

Enchondromas constituted the second most common benign tumor with 4 cases. The patients' ages ranged from 3 to 35 years (mean, 19.8 years) with equal sex distribution. One case showed multiple enchondromas (Ollier disease). Radiologically, all were lytic lesions with a narrow zone of transition and internal calcifications. Histologically, all cases showed lobules of hyaline cartilage with chondrocytes located within the lacunae and areas of calcification. No mitotic activity was seen. The case of Ollier disease showed mild anisonucleosis; however, other lesions had bland nuclear morphology.

Chondroblastoma was encountered in 2 male patients in their third decade. Radiologically, both had lytic lesions with sharply defined margins. One of them involved the left calcaneum, and the other was located in the proximal phalanx of the left index finger. Histologically, both showed sheets of relatively uniform polygonal cells. Nuclei were round to oval with indentation and grooving. Reactive giant cells were seen randomly distributed within the lesions. There were islands of pinkish chondroid matrix and foci showing characteristic "chicken wire" calcification. In addition, the calcaneal lesion showed microscopic early aneurysmal bone cyst change with dilated blood-filled spaces lined by spindle cells and giant cells.

Periosteal chondroma was observed in a 50-year-old man. Radiographs showed a periosteal exophytic lesion with well-defined calcifications and cortical irregularity involving the distal phalanx of the right thumb. Histologically, the lesion showed lobules of hyaline cartilage separated by thin fibrous septae. A focal increase in cellularity was noted. There was no pleomorphism or mitotic activity. Areas of calcification were also noted.

A case of osteochondroma involving the neck of the fourth metacarpal of the right hand was seen in an 18-year-old

woman. The lesion was solitary, without any other lesions in the rest of the skeleton. Histologically, there was an outer cover of periosteum with an underlying cartilaginous cap with chondrocytes having bland morphology arranged in columns and clusters. Beneath this, there were bony trabeculae with intervening fatty marrow. The bone-cartilage interface showed enchondral ossification.

Fibroxanthoma was diagnosed in a 32-year-old man, in whom the lesion was located in the left talus. Histologically, the lesion showed an admixture of xanthoma cells, giant cells, cholesterol clefts, and hemosiderin deposits in fibrous areas. There was no hyperlipoproteinemia.

Malignant Tumors

The demographic data, clinical presentation, site, and imageologic features of all malignant tumors involving the bones of the hands or feet are given in Table 4. Both patients with chondrosarcoma were women with metacarpal involvement. The radiologic diagnosis was that of a malignant chondroid lesion. Histologically, one case was a grade 1 lesion, while the other was grade 3 lesion. The patient with the grade 1 lesion had a long history of a slowly growing mass with recent sudden increase and pain. This lesion showed relatively bland morphology resembling chondroma in most areas, with only focal areas showing increased cellularity and mild anisonucleosis. Mitoses were sparse. Correlating with the imageologic and histologic invasive growth pattern, a diagnosis of chondrosarcoma was made. The other case showed obvious malignant histology with increased cellularity, pleomorphism, spindling of tumor cells, giant cells, and mitotic activity.

Of the 2 patients with Ewing sarcoma, one was a middle-aged woman with involvement of the head of the right first metatarsal bone. The radiologic diagnosis in this case was that of a benign tumor, in view of the narrow zone of transition. The computed tomographic scan showed a break in the cortex on the inferomedial aspect with a minimal soft tissue component. The lesion showed intermediate signal intensity with minimal adjacent soft tissue on T1-weighted magnetic resonance images with hyperintense areas on T2-weighted magnetic resonance images. Material from an open biopsy of the lesion showed large areas of coagulative necrosis with focal viable tumor. These areas showed sheets of round cells admixed with dark cells. The nuclei of the round cells showed a dispersed chromatin pattern. Cytoplasm was scant, with indistinct cell borders. The mitotic activity was brisk. The tumor cells were positive for CD99 and negative for CD45 and pancytokeratin. Later, the patient underwent Ray amputation. Her staging workup was negative for any metastasis. She received 6 cycles of chemotherapy and is doing well at 9 months follow-up. The other patient had an obviously destructive lesion involving the metacarpal with similar histologic features. The tumor cells in this case also showed positivity with CD99 and were negative for CD45. The patient

refused any treatment and was lost to follow-up.

Osteosarcoma involving the left talus was diagnosed in a 15-year-old adolescent boy. Histomorphologically, it was a high-grade tumor with spindle to polygonal tumor cells with pleomorphic and hyperchromatic nuclei. Mitotic activity was brisk, including atypical mitoses. Frequent tumor giant cells and areas of chondroid and osteoid matrix formation and necrosis were also noted.

A 50-year-old man who had a history of chronic osteomyelitis was diagnosed with malignant fibrous histiocytoma. The previous radiographs and histologic slides were not available for review. The present radiographs showed a destructive lytic lesion involving the calcaneum with cortical break and soft tissue extension. Histomorphologically, the present tumor showed a mixed population of spindle-shaped cells and polygonal-shaped cells. The spindle cells were arranged in fascicles with a focal storiform pattern. These had oval to elongated nuclei. The polygonal cells showed multinucleation and multilobation of nuclei with abundant eosinophilic cytoplasm. Mitoses were frequent, more so in the polygonal cells, including atypical mitoses. There was no evidence of any matrix formation within the lesion. Following the diagnosis on material from an open biopsy, the patient underwent above-ankle amputation. Even the resected specimen did not show osteoid formation.

Tumorlike Lesions

The demographic data, clinical presentation, site, and imaging features of all tumorlike lesions involving the bones of the hands or feet are given in Table 5.

Giant cell reaction (GCR) was the most common tumorlike lesion noted in the present series, with 3 cases. All patients were male, and their age ranged from 8 to 54 years. Bones of the hand were involved in all 3 cases— phalanges in 2 and metacarpal in 1. Radiologically, all were expansile pure lytic lesions with thinned-out cortex. There was no evidence of cortical break. Histologically, all showed similar morphology with spindled fibrous stroma with scattered osteoclast-like giant cells. Focal clustering of these giant cells was noted, especially around areas of hemorrhage. These giant cells had relatively fewer nuclei compared with those seen in GCT. Hemosiderin deposits and hemosiderin-laden macrophages were also seen. Areas of newly formed osteoid with osteoblastic rimming were also seen within the lesion.

The single case of aneurysmal bone cyst in a 7-year-old boy involved the left calcaneum. The histology showed multiple blood-filled cystic spaces separated by septae of spindled fibrous stroma containing scattered osteoclastic giant cells. These cysts were also lined by spindle cells and giant cells. Areas of newly formed osteoid with osteoblastic rimming and calcified chondromyxoid matrix were also seen within the septae.

The patient with florid reactive periostitis was a 27-year-old woman with involvement of the middle phalanx of the

right middle finger. Radiography showed cortical sclerosis with periosteal reaction and an adjacent soft tissue component involving the middle phalanx of the right middle finger. The biopsy specimen showed fibrous stroma with plump spindle cells with areas of bone and cartilage. Few normal mitotic figures were seen.

4 Discussion

Current study describes the frequency distribution of various lesions of the bones of the hands or feet from two tertiary hospitals of central India. Osteomyelitis was the most common lesion in this series, accounting for 44% of the cases. In other study also it is the commonest lesion.⁽⁵⁾

In the present series, nonspecific osteomyelitis of the small bones of the hands or feet constituted 18.9% of the total cases of osteomyelitis reported during the study period. Of the 275 cases of osteomyelitis reported by Craigen et al,⁽⁶⁾ 55 (20%) involved the bones of the hands or feet, the latter being more commonly involved, similar to the pattern noted in our study. A case of pyogenic osteomyelitis of the small bones of the hands and feet has been reported from India⁽⁷⁾ in a 10-month-old infant with symmetrical involvement of multiple bones of both the hands and the feet. The rest of the skeleton did not show any involvement.

Hands and feet are frequently exposed to trauma, and walking barefoot may increase the risk of trauma and secondary infection. Diabetes mellitus constitutes a significant predisposing risk factor for osteomyelitis of the foot, as seen in our patients.⁽⁸⁾ Factors contributing to bone infection in diabetes include both peripheral neuropathy and vascular insufficiency.

Of the total 110 cases of tuberculous osteomyelitis reported during the study period, 5 (5.3%) involved the bones of the hands or feet, with the majority of the remaining cases involving the spine. Tuberculosis constitutes the major cause of osteomyelitis in India.⁽⁵⁾ This explains the higher incidence of tuberculous osteomyelitis in the small bones of the hands or feet reported here compared to that in the West.⁽¹⁾ Three of the patients with tuberculous osteomyelitis radiologically showed spina ventosa. All cases of tuberculous osteomyelitis histologically showed necrotizing granulomatous inflammation. Though acid-fast bacilli were not seen on special stains, all the patients responded well to antituberculous treatment.

In a large series of 203 lesions of the bones of the hands or feet, Ostrowski and Spuit⁽¹⁾ reported only 5 cases of osteomyelitis and 1 case of tuberculosis.

In both patients with fungal osteomyelitis, predisposing factors were identified. Osseous sporotrichosis, though uncommon, has been reported in the literature.^(9,10)

Diagnosis of specific infections like tuberculosis and fungal osteomyelitis is important for treatment. Submission of curetted material for culture improves the diagnosis and helps guide the choice of appropriate drugs. Use of special stains

for acid-fast bacilli and fungi in all cases of granulomatous inflammation helped us to diagnose fungal osteomyelitis, with culture providing species identification in 1 case.

Reports of bone involvement in sarcoid have ranged between 1% and 13%, with an average of 5%.⁽¹¹⁾ Sarcoidosis preferentially involves the small bones of the hands or feet.⁽¹²⁾ Associated pulmonary and cutaneous lesions with raised angiotensin converting enzyme levels helped in the diagnosis.

Benign tumors were more common than malignant tumors in our series, similar to other reported series where cartilage-forming tumors were the most common.^(1,3,4,13) Benign cartilage-forming tumors (n = 8) including enchondroma, chondroblastoma, periosteal chondroma, and osteochondroma constituted the largest group; however, GCT (n = 7) was the single most common benign tumor, constituting 43.8% of benign tumors involving bones of the hands or feet. In general, GCT stood first among the benign tumors reported in all skeletal sites during the study period. The incidence of GCT is reported to be higher in India^(5,14) and Eastern countries⁽¹⁵⁾ compared with Western countries.^(13,16) In the small bones of the hands or feet, GCT is rare, with the reported incidence in the hand ranging from 1.2% to 4.0% and in the foot from 0.9% to 1.8%.^(17–20) In the present series, the incidence was 3.4% and 2.5%, respectively. Giant cell tumors in these locations affect younger subjects, tend to be multicentric, and have a higher recurrence rate compared with those occurring at other sites.⁽²¹⁾ In the present series, 2 of the lesions were recurrent, and multicentricity was not observed. Histologic findings are critical to differentiate GCT from GCR and aneurysmal bone cyst in view of their overlapping clinical and radiographic findings.⁽²⁰⁾ Ostrowski and Spuit⁽¹⁾ have suggested that most giant cell reparative granulomas are often misinterpreted as GCTs. Though 5 of the 7 lesions reported here were painful, pain was present at initial presentation in only 2 of the cases. In the remaining patients, pain followed the initial presentation of swelling, with 2 patients developing pain following a history of trauma. All patients who had pain radiologically showed cortical break. All the cases showed classic histologic features of giant cells, with spatial arrangement of stromal cells and giant cells. The giant cells showed up to 40 to 50 nuclei, which resembled nuclei of stromal cells. There was no evidence of osteoid formation within the lesion.

All cases of enchondroma (4) and periosteal chondroma (1) showed calcification radiologically and hence could be easily diagnosed before biopsy. Nearly half of all enchondromas in surgical pathology series are known to occur in the hands or feet.^(17,18) In the present series they accounted for 33%, with the majority involving the hand. One of the patients with enchondroma had Ollier disease. Periosteal chondromas account for less than 2% of chondromas and have been commonly reported in small tubular bones.^(17,22–24) The prominent nesting of chondrocytes noted in the present case

may mimic synovial chondromatosis. Synovial chondromatosis has a predilection for large joints, especially the knee, and rarely affects metacarpophalangeal and interphalangeal joints. Preoperatively, the present lesion was a single lobulated mass attached to the cortex of the distal phalanx of the right thumb, with intact overlying periosteum, and hence was diagnosed as periosteal chondroma.

Chondroblastomas involving the bones of the hands or feet are uncommon, with most occurring in the calcaneum and talus. Phalangeal involvement, as noted in one of our cases, is extremely uncommon.⁽²⁵⁾

Although osteochondroma represents the most common benign bone tumor, its occurrence in small bones of the hands or feet is not common.^(1,4) Of the total 50 osteochondromas involving all skeletal sites, only a single case was from the metacarpal.

Fibroxanthoma is an uncommon and somewhat disputed entity. Fechner and Mills⁽²⁶⁾ suggest that xanthoma and fibroxanthoma are within the spectrum of benign fibrous histiocytoma, with a major component of foam cells. This has been infrequently reported in bones of the hands or feet.⁽²⁷⁾ Our patient did not have associated hyperlipoproteinemia.

Chondrosarcoma was the most common malignant tumor in our series, as has also been reported in the literature.^{1,5} Grade 1 chondrosarcoma is difficult to differentiate from enchondroma. The entrapment of nontumoral bony trabeculae and permeation of the tumor through the cortex into soft tissue were helpful in categorizing the tumor as malignant in our case.

Of the total 48 skeletal Ewing sarcomas reported during the study period, 2 (4.2%) involved bones of the hands or feet, which is a higher percentage than that quoted in the literature.⁽²⁸⁾ In our series, Ewing sarcoma paralleled the incidence of chondrosarcoma in bones of the hands or feet, which was comparable to a Mayo Clinic series.⁽¹³⁾ In both of our patients with Ewing sarcoma, the diagnosis was confirmed by immunohistochemistry; this was important as 1 patient was 41 years old.

Biscaglia et al⁽²⁹⁾ reported a 0.6% incidence of osteosarcoma in the bones of the feet, with half being misdiagnosed initially. In the present series, the incidence was 1.5%.

Malignant fibrous histiocytoma is an uncommon tumor, accounting for less than 1% of primary bone tumors in the Mayo Clinic files. Secondary malignant fibrous histiocytoma has been known to complicate various preexisting bone conditions including chronic osteomyelitis,⁽³⁰⁾ as noted in our case. Osteosarcoma may also arise as a secondary tumor in chronic osteomyelitis.

Metastatic bone lesions and hematologic neoplasms were not seen in our study. Bones of the hands and feet are the most common extragnathic sites for GCR.^(31–33) Three such cases with typical histologic features were diagnosed in bones

of the hand. It was difficult to differentiate them clinically and radiologically from GCT. This is important in view of the lower recurrence rate in the former compared to the latter.^(32,34) The only other 3 cases of GCR reported during the study period were located in the mandible. In view of overlapping ultrastructural and light microscopic features, as well as similar biologic behavior, aneurysmal bone cyst and giant-cell reparative lesions are thought to represent related responses to intraosseous hemorrhage.⁽³⁵⁾

Florid reactive periostitis is a reactive process that predominantly involves the bones of the hands or feet,^(36,37) mostly in young women, and a history of minor trauma is seen in less than half of the cases. Similar clinical findings were noted in our patient as well. The importance of this entity lies in the possibility of it being misdiagnosed as a malignant lesion, especially osteosarcoma.⁽³⁸⁾ Such a lesion was not seen in any other bone in our institution during the study period.

5 Conclusion

Lesions of the bones of the hands or feet are uncommon. Infections/inflammatory lesions are more common in India. Benign tumors were more common than malignant tumors in our series. Giant cell tumor is the commonest neoplastic lesion. Awareness and correlation of clinical, radiologic, and pathologic features help in making correct diagnoses.

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