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Exploring unconventional sites of bone metastasis: a comprehensive exploration of common and uncommon tumors in the Lesser-Known realms

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Abstract

Introduction Bone metastases rank third in prevalence among metastatic afflictions, following lung and liver. Historically linked to breast, prostate, and lung cancers, evolving cancer therapies now reveal skeletal metastasis in diverse cancer types previously not associated with it. This study delves into unique cases of bone metastasis received over a year in a specialized lab dealing with soft tissue and bone specimens. It explores the challenges associated with diagnosing such atypical occurrences.

Materials and Methods Examining 1230 bone biopsies received between January 1, 2023, and December 31, 2023, we focused on rare secondary bone malignancies, excluding benign pathologies and primary bone malignancies.

Results Following meticulous adherence to the predefined inclusion and exclusion criteria, a comprehensive cohort of 14 cases became the focal point of this study. Within this cohort, the gender distribution revealed 9 female and 5 male participants. Notably, among the subjects, 4 were aged above 60 years, while the remaining 10 were below this age threshold. The predominant bone metastasis originated from Follicular Thyroid Carcinoma, reported in 3 cases (21.4%). 7 (50%) cases had bone metastasis as an initial presentation of occult primaries. Metastasis manifested in 9 cases within the appendicular skeleton and 5 cases within the axial skeleton. Further granularity within the appendicular skeleton revealed the humerus as the most prevalent site of metastasis, closely trailed by the femur in frequency.

Conclusion This study highlights the diagnostic challenges of rare secondary bone malignancies, with half of the cases presenting as the first sign of occult cancers. Bone metastases were most common in the humerus and femur, emphasizing the need for thorough evaluation of unexplained bone lesions.

Keywords Bone and bones, Neoplasm metastasis, Solitary fibrous tumors, Phyllodes tumor, Humerus

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Introduction

The skeletal system is the third most common site for metastatic disease, after the lungs and liver, with both bone and bone marrow frequently involved in cancer metastasis. Such occurrences typically signify advanced stages and correlate with poor prognosis, heightened morbidity, and limited treatment options.

Predominantly, bone metastases originate from breast, prostate, or lung cancers, although kidney and thyroid tumors may also metastasize to bone. Referred to as secondary bone cancer, this condition denotes tumors originating in other tissues and spreading to the bone [1].

While not all cancers have a propensity for bone metastasis, certain skeletal regions exhibit varying susceptibility. Advances in cancer treatment have improved overall survival rates, leading to an increased incidence of cancers not traditionally associated with skeletal metastasis. This necessitates a continual awareness of the potential for bone involvement in cancer management.

In this context, we present 14 cases highlighting usual and unusual sites of bone metastasis from primary tumors elsewhere in the body. The significance of such studies lies in continually expanding our understanding, emphasizing the need to consider bone metastasis in the management of cancer patients for enhanced outcomes and survival.

Materials and methods

In the period from January 1, 2023, to December 31, 2023, our laboratory received 1230 bone biopsies. All the biopsies that were diagnosed as metastasis to bone were retrieved and reviewed for availability of imaging findings, follow-up data, clinical features, etc. The cases without sufficient information/ Imaging findings were excluded and the rest of the metastatic tumors to bone were included irrespective of age, gender, or outcome.

The study focused on rare and unusual secondary bone malignancies, while also considering common tumors that metastasize to bone. Benign pathologies, primary bone malignancies, and metastatic tumors of unknown primary origin were excluded.

Following stringent inclusion and exclusion criteria, 14 cases were selected for the study. Comprehensive demographic information, clinical history, and pertinent radiology reports were collected and analyzed to determine the final diagnosis.

Results

Following the predefined inclusion and exclusion criteria, our study encompassed a total of 14 cases. Among these, 9 (64.3%) were identified as female, while 5 were male. Notably, 4 (28.6%) cases were aged 60 years or older, with the remaining 10 (71.4%) cases falling below this age threshold.

Distribution of metastases revealed that 9 (64.3%) cases exhibited metastasis to the appendicular skeleton, while 5 (35.7%) cases demonstrated metastasis to the axial skeleton. Within the appendicular skeleton, the humerus emerged as the most prevalent site of metastasis, closely followed by the femur. The predominant bone metastasis in this study originated from Follicular Thyroid Carcinoma, reported in 3 cases (21.4%). Two instances involved the humerus, while the third manifested in the posterior 4th rib. Seven cases (50%) presented with primary manifestations of bony metastasis from occult sources, whereas the remaining cases were diagnosed in patients already under the care of oncology services.

These findings contribute to a nuanced understanding of the demographic and anatomical characteristics of bone metastases in our study cohort. The individual cases and their presentation are explained below.

Case 1

A 65-year-old female presented with bilateral thyroid swelling and right-sided chest pain. CT scan revealed an expansile destructive lesion in the right 4th posterior rib, likely neoplastic. Core needle biopsy confirmed metastatic follicular thyroid carcinoma. Subsequent thyroid evaluation showed a TIRADS 5 lesion involving both lobes (Fig. 1A–C)

Case 2

A 28-year-old male, post-operative for rectal carcinoma, presented with pelvic pain. CT scan revealed a lesion in the right ischial bone, suspected to be metastatic. Core needle biopsy confirmed mucin-secreting adenocarcinoma, indicative of metastasis as shown in Fig. 1D.

Case 3

A 30-year-old male, previously treated for a nasal cavity neuroendocrine tumor, presented with left shoulder pain. MRI revealed multiple cystic lesions in the left humerus, suggestive of osteomyelitis. Biopsy from the cyst wall confirmed metastasis, showing tumor cells having high nuclear-cytoplasmic ratio, round hyperchromatic nucleus, inconspicuous nucleoli, and scant amount of cytoplasm.

Immunohistochemistry, positive for CD99 and negative for CD45, NKX2.2, and synaptophysin, supported the diagnosis of metastatic neuroendocrine tumor from the nasal cavity as shown in Fig. 1E.

Case 4

A 45-year-old female, previously treated for a phyllodes tumor in the right breast in 2021, presented with a pathological fracture of the right femur. Intramedullary curettings from the fracture site confirmed metastatic phyllodes tumor, characterized by spindle-shaped cells

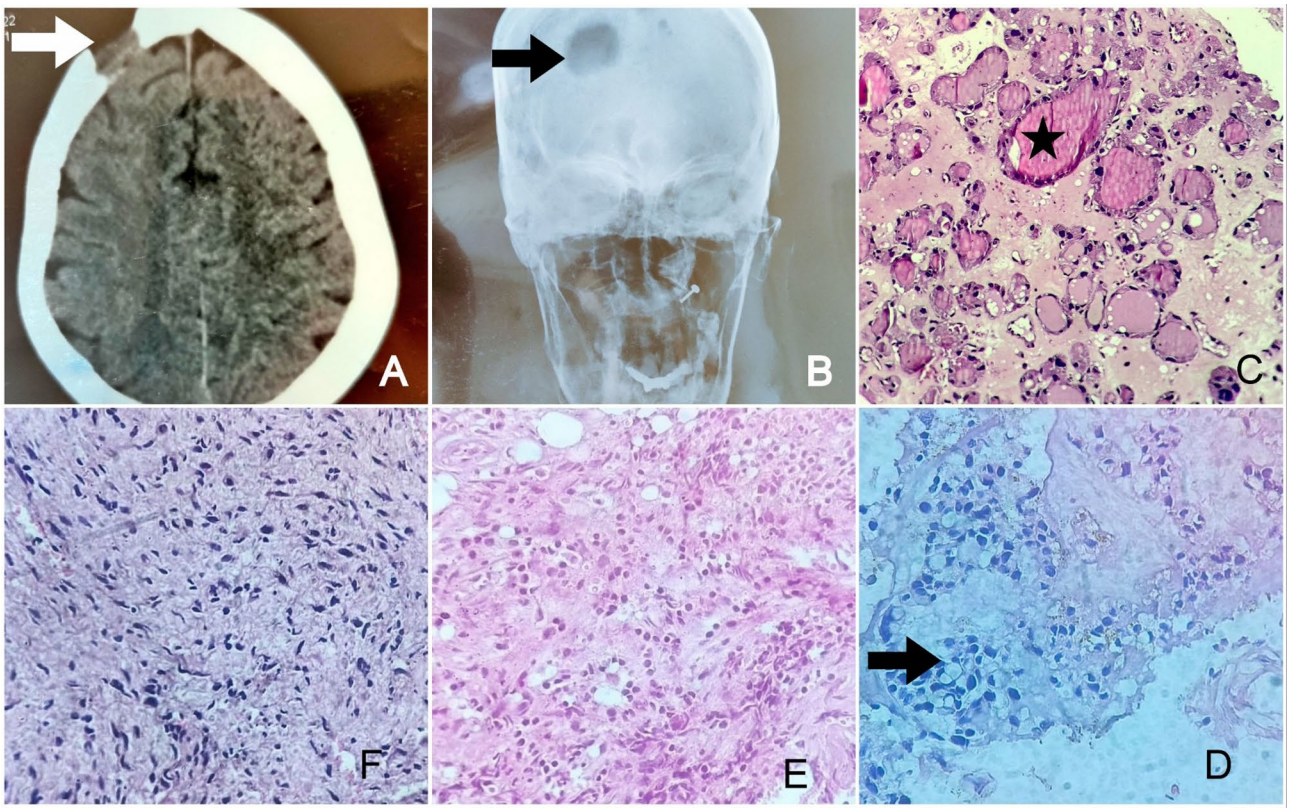

Fig. 1 **A** & **B**- CT scan and X-ray showing involvement by tumor (Case 1); **C**- colloid filled Follicles lined by malignant cells having high Nuclear- cytoplasmic (N: C) ratio embedded in a Cartilaginous and bony matrix suggestive of a Metastatic deposit of follicular thyroid carcinoma (H & E, 40 X); **D**- Signet ring cells (Case 2) -Mucinous adenocarcinoma metastasis from carcinoma colon (H & E, 10 X); **E**- Section Shows small round blue cells having Scant cytoplasm, vesicular- Salt & Pepper nucleus infiltrating into fibromuscular and fibrofatty tissue (Case 3) suggestive of a Neuroendocrine tumor (H & E, 10 X); **F**: Section from right femur shows atypical wavy- spindled cells in a known case of Borderline Phyllodes tumor (Case 4) suggestive of metastasis (H & E, 40 X)

with moderate pleomorphism, hyperchromatic irregular nuclei, inconspicuous nucleoli, and a scant amount of eosinophilic cytoplasm as shown in the Fig. 1F. Mitotic figures were 5–6/10 high power field and showed positive immunohistochemistry for vimentin and PR (10%).

Case 5

A 66-year-old female, with a history of smoking and hypertension, presented with left femur fracture, hemoptysis, and cough. Biopsies from the left femur during correction surgery confirmed metastatic malignant melanoma, characterized by tumor cells with brown-black pigment, vesicular nuclei with prominent eosinophilic macro nucleoli, a moderate amount of eosinophilic cytoplasm, few cells showed intra nuclear inclusion and positive HMB45 immunohistochemistry.

A further workup was prompted. CT chest revealed a neoplastic mass in the right lung with bilateral axillary and mediastinal lymphadenopathy. Subsequently, the patient experienced a right lung collapse mandating a lung Biopsy which also showed features of malignant melanoma. (Fig. 3A and B)

Case 6

A 23-year-old male, previously treated for malignant solitary Fibrous tumor of the brain (STAT 6 Positive) with chemotherapy and radiotherapy, presented with left shoulder swelling and pain. MRI indicated a heterogeneous mass in the metaphyseal location of the left humerus, suggestive of parosteal osteosarcoma or juxtacortical chondrosarcoma. Ultrasound-guided biopsy revealed a poorly differentiated round cell tumor with stag-horn vasculature, positive for MDM2 and negative for SATB2, S100, CD99, CD45, FLI1, NKX2.2, osteonectin., CD31, CD34, vimentin, Pan Ck, GFAP, Myogenin, ERG and NSE. Given the histomorphology, immunohistochemistry, radiological findings, and the patient's history of brain tumor, a diagnosis of metastatic malignant Solitary Fibrous Tumour of the humerus was suggested (Fig. 2A–F).

Case 7

A 47-year-old female presented with a left humerus pathological fracture. Ultrasound-guided biopsy revealed tumor cells forming variably sized follicles with colloid-like fluid, positive for Thyroglobulin, CK7, vimentin, and

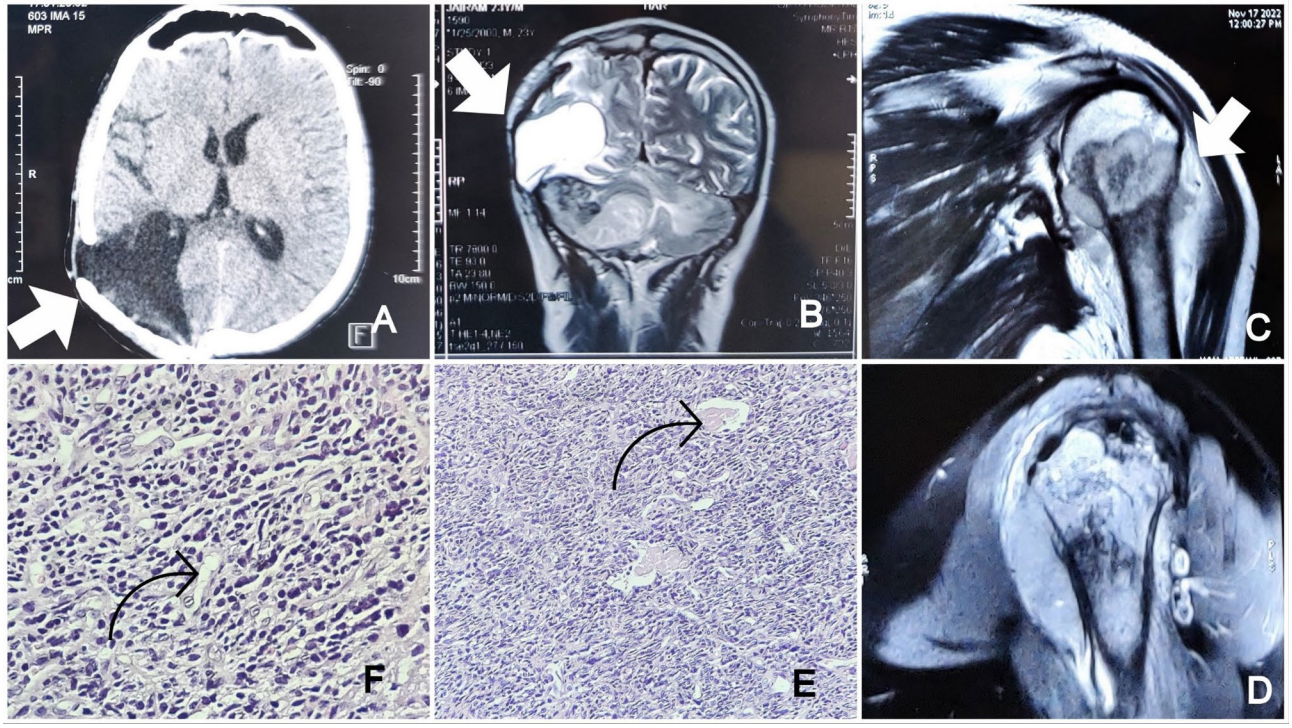

Fig. 2 **A** & **B**- CT and MRI showing a space-occupying lesion in the right hemisphere causing midline shift and fracture of skull bones; **C** & **D**- MRI of left humerus shows a heterogenous mass lesion with onion peel periosteal reaction; **E** & **F**- Section from humerus shows small round to oval tumor cells with intervening stag horn vessels (H & E, 10X and 40 X) (Case 6)

NSE, and negative for ER, TTF1, CK20, MUM1, CD38, inhibin and Ki67. Histomorphology and immunohistochemistry suggested a potential occult primary in the thyroid, prompting further investigation for thyroid involvement. USG thyroid confirmed a thyroid malignant tumor.

Case 8

A 59-year-old patient presented with a left scapular mass, revealing a large enhancing lytic soft tissue lesion in the CEMRI, indicative of malignancy/metastasis. Ultrasound-guided biopsy confirmed metastatic squamous cell carcinoma. A subsequent PET CT scan was done to look for primary and disclosed metabolically active lesions in the right lung, left frontal lobe, right cerebellar hemisphere, and extensive soft tissue involvement in the left scapula. The diagnosis was established as non-keratinizing poorly differentiated squamous cell carcinoma through endobronchial biopsy, suggesting a primary origin in the right lung (Fig. 3C).

Case 9

A 23-year-old female presented to the orthopedics department with right thigh pain and difficulty walking for 8 months. The X-ray revealed a lytic lesion in the supra-acetabular region of the right ilium and upper half of the right femoral shaft. A biopsy indicated a malignant mesenchymal tumor, and a subsequent immunohistochemistry (IHC) workup was initiated. History revealed a previous right shoulder swelling and nodular lesions in the right humerus in 2019, consistent with a high-grade mesenchymal tumor. Suspecting metastasis, a PET scan was suggested which showed hypermetabolic lesions in various locations, including the liver (Segment IV A & VII), lymph nodes (Intraparotid, bilateral cervical, axillary, and pelvic lymph nodes), lungs, and multiple bones (right humerus, left 8 th ribs, D7 vertebra, sternum and left iliac bone). IHC demonstrated positivity for NSE, ALK, and TFE3 (nuclear) and negative Myogenin, Myo D1, HMB 45, Melan A, Pan CK, EMA, Desmin, SMA, CD 10, CD 30, CD 15 and CD 31, leading to a diagnosis of Metastatic Alveolar Soft Part Sarcoma (Fig. 4A–H).

Case 10

A 60-year-old female presented with back pain for several months. CEMRI revealed D2 vertebral body collapse with retropulsion, suggesting compressive myelopathic changes, possibly Pott's spine or neoplastic collapse (metastasis). Further investigation led to the diagnosis of lung adenocarcinoma. A biopsy of the D2 vertebral bone ruled out tuberculosis and confirmed metastatic adenocarcinoma from the lung. Gene Xpert was negative for TB (Fig 3D–E).

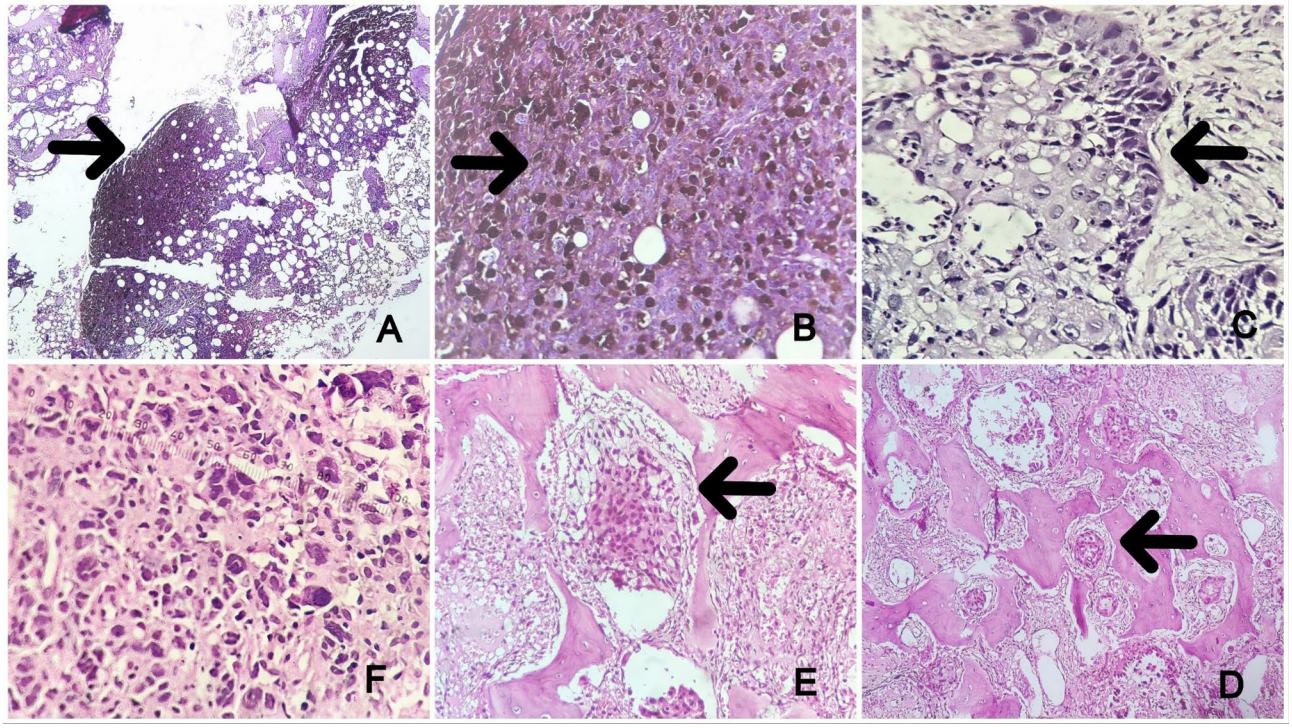

Fig. 3 **A** & **B**– Section from the left femur (Case 5) shows bone marrow infiltrated with pigmented (pigmented) tumor cells. Occasional tumor cells show prominent nucleoli (H & E, 4 X, 40X); **C**- Section from the scapula (Case 8) shows infiltration with Atypical Squamous cells having high N: C ratio, moderate cytoplasm, vesicular to hyperchromatic nucleus; **D** & **E**- Section from D2 lytic lesion (Case 10) shows Adenocarcinoma deposits in bone (H & E, 10X, 40X); **F**- Section from Sacrum shows malignant cells having moderate pleomorphism, high N: C ratio, moderate eosinophilic cytoplasm, hyperchromatic irregular nucleus and occasional prominent macro nucleoli (H & E, 40X) (Case 14)

Case 11

A 62-year-old female presented with right shoulder pain after a recent fall, jaundice, itching, and appetite loss. X-ray revealed a fractured humerus (right), leading to corrective surgery. Bone biopsy confirmed metastatic carcinomatous deposit. Abdominal ultrasound and triple-phase CT indicated an ill-defined mass in the distal CBD causing IHBR dilatation, GB sludge, multiple hepatic lesions, and abdominal lymphadenopathy. Diagnosis: Gall bladder metastasis to the right humerus.

Case 12

A 40-year-old female presented with a left humerus fracture. MRI revealed a pathological fracture with altered signal intensity and marrow infiltration, suggestive of metastasis. NCCT showed a lytic lesion in the left proximal humerus, possibly metastatic. Additionally, multiple well-defined rounded lesions in both lungs were indicative of metastasis. Biopsy from the humerus fracture site confirmed metastatic follicular thyroid carcinoma.

Case 13

A 56-year-old female presented with 7 months of low back pain. Imaging revealed L4-L5 spondylodiscitis, likely tuberculosis, with prevertebral and right iliopsoas abscess, and grade IV right hydronephrosis with proximal hydroureter possibly due to abscess involvement. MRI showed a large collection in the right iliopsoas muscle extending to L3-L5, causing right lytic destruction of L4 and L5, severe compression of the right mid-ureter, and significant hydronephrosis with renal parenchyma thinning. Multiple necrotic retroperitoneal lymph nodes were noted. Biopsy from L4-L5 intervertebral tissue revealed metastatic papillary adenocarcinoma, with immunohistochemistry positive for CK7 and CEA, and negative for PR, CD20, and TTF, consistent with metastatic urothelial carcinoma (Fig. 5A–F).

Case 14

A 48-year-old male, undergoing treatment for nodular lymphocyte-predominant Hodgkin lymphoma (NLP-HL), presented with widespread nodal and extranodal lesions, including brain involvement and suspected sacral involvement on a routine PET scan. Histopathological examination of a sacral bone biopsy confirmed the presence of metastatic NLP-HL deposits with CD 20 positivity and CD 30, CD 15, Pan CK, PAX 5, CD 34, Vimentin, and CD 45 negativity. However, the simultaneous biopsy from the nodes showed the RS cells to be positive for

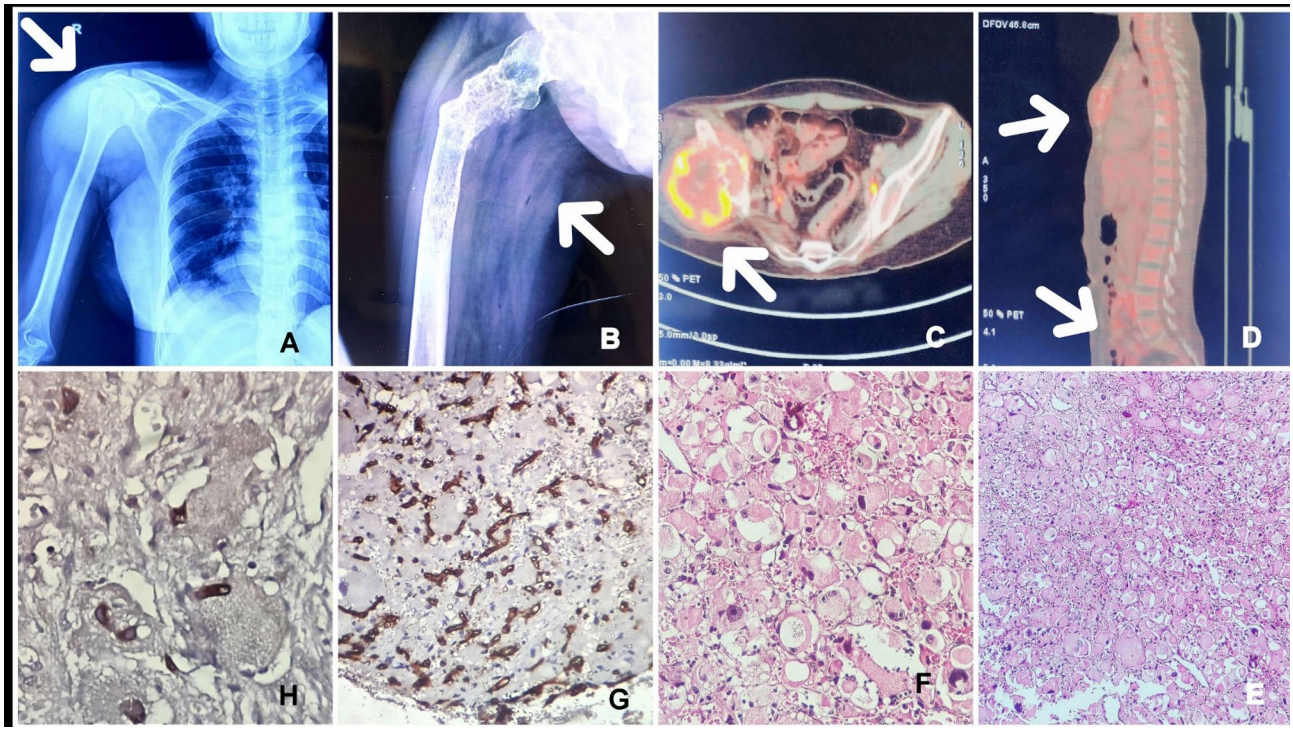

Fig. 4 **A** X-ray AP view of Chest and Right shoulder showing a soft tissue lesion in the deltoid region; **B**- X-ray AP view of right Hip shows a Lytic lesion in the supra acetabular region of the right ileum and right femoral shaft with thinning of the cortex; **C**- PET scan showing FDG Avid lytic lesion in Acetabulum, Ischium and head of the right femur; **D**- PET Scan sagittal section shows multiple FDG Avid lesions in Sternum, L 3 Vertebra, and iliac bones; **E** & **F**- Shows large, round to polygonal cells with well-defined cell borders and abundant granular cytoplasm, round– vesicular nucleus with prominent nucleoli arranged in sheets (H & E, 10 X & 40 X respectively); **G**- Immunohistochemistry with CD 34, showing positivity in the capillaries amidst the tumor cells (40X); **H**- Immunohistochemistry showing strong diffuse Nuclear positivity with TFE3 in the Tumor cells (100X) (Case 9)

LCA, CD 20, and PAX 5 and negative for CD 15 & CD 30 (Fig. 3F).

Discussion

Bone metastasis, surpassing primary bone tumors, ranks as the third most frequent site for metastatic occurrences. The prevailing sites of metastasis include the lung and liver, with prostate and breast cancers being predominant contributors. The incidence of overall bone metastasis remains elusive, but the relative distribution across primary tumors reveals notable figures: Breast cancer (65–75%), Prostate (65–75%), Thyroid (60%), Lung (30–40%), Bladder (40%), Renal cell carcinoma (20–25%), and Melanoma (14–45%) [1].

Recognizing the incidence and maintaining a high index of suspicion for bone involvement symptoms is imperative, given its potential as an initial indicator of an occult primary malignancy elsewhere. Evaluating an occult primary presenting with bone primary has its challenges. While decalcification is necessary for bone tumor samples, it causes irreversible alterations to proteins and nucleic acids, leading to potential false-negative results. Antigenicity is altered post-decalcification with hydrochloric acid, contrasting with preserved integrity using EDTA or formic acid. False-negative results, particularly for nuclear antigens, highlight the resistance of membranous and cytoplasmic antigens to strong acid-based decalcification. Protein and nucleic acid integrity depend on decalcification duration; EDTA preserves protein and morphology but requires a longer processing time. EDTA or short-term formic acid-based decalcification is recommended for ancillary techniques and molecular analyses without prejudicial effects [2].

The expression of classical immunohistochemistry markers in primary tumors may differ in metastatic regions, posing challenges in diagnosing occult primaries with bone metastasis. Factors such as increased tumor mutation burden (TMB), including single-base substitutions (SBSs), double-base substitutions (DBSs), and indels (IDs), can contribute to these differences [3]. Additionally, chemotherapy-induced changes in antigen expression, as observed in malignant solitary fibrous tumors, can further complicate diagnoses. Instances, like NLP-HL case in this study, where simultaneous biopsies from lymph nodes and bone show distinct expression patterns, highlight the complexity of metastatic disease. The malignant Solitary Fibrous tumor also showed negative STAT 6 in the bone biopsy contrary to the brain biopsy (Primary– 3 years ago).

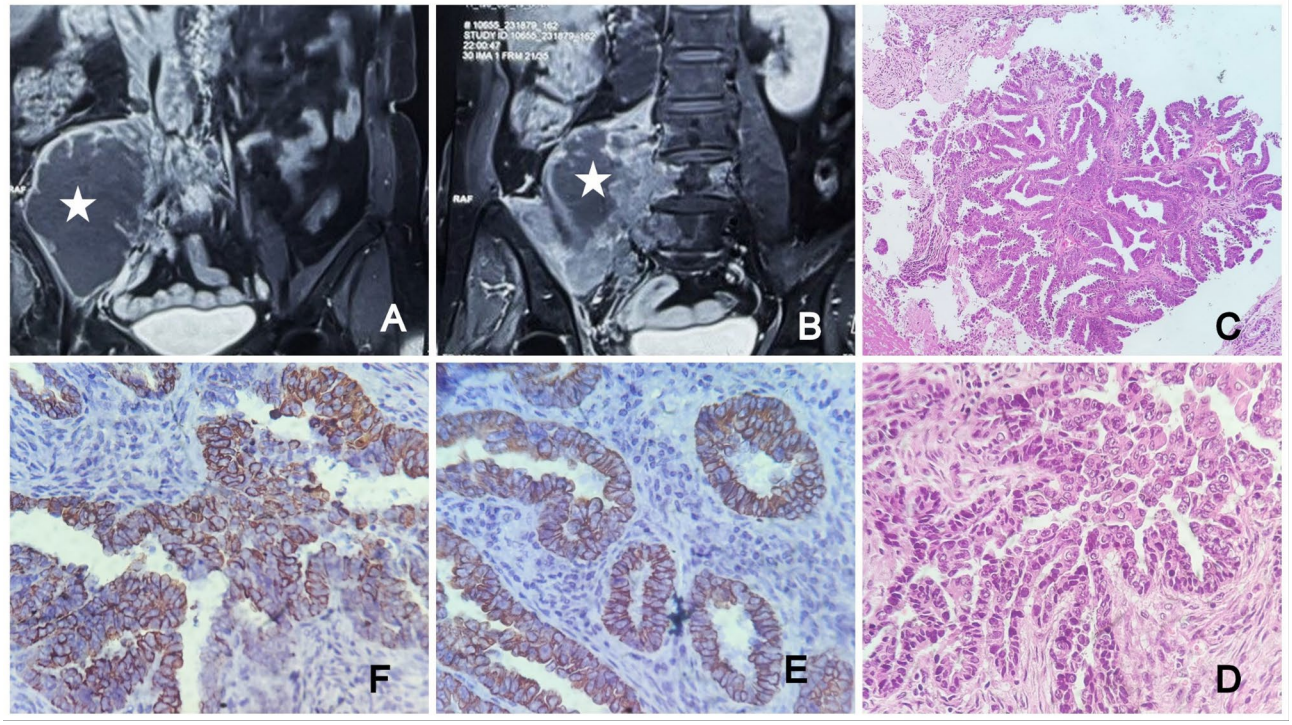

Fig. 5 **A** & **B**- shows coronal section Contrast Enhanced Computed Tomography (CECT) Lumbar Spine showing a 10 × 8.6 cm right iliopsoas abscess with peripheral enhancement; **C** & **D**- Section from L4- L5 vertebra shows Papillary Adenocarcinoma deposits (H & E, 20X and 40X respectively); **E** & **F**- CK 7 & CK 20 showing membranous and Cytoplasmic positivity in the tumor cells (40X) (Case 13)

Table 1 Demographic details with diagnosis

Case	Primary tumor	Metastasised to	Age	Sex
1	Bilateral thyroid swelling- Follicular thyroid carcinoma	4th posterior rib	65	F
2	Carcinoma rectum-treated	Right ischial bone	28	M
3	Neuroendocrine tumor- nasal cavity	Left proximal humerus	30	M
4	Right breast- Borderline phyllodes	Right femur	45	F
5	Right lung-Malignant melanoma	Left femur	66	F
6	Hemangiopericytoma (Malignant Solitary Fibrous Tumor) brain	Left humerus	23	M
7	Follicular thyroid carcinoma	Left humerus	47	F
8	Right lung-squamous cell carcinoma	Glenoid and body of scapula	59	M
9	Alveolar soft Part Sarcoma	Right humerus	23	F
10	Lung adenocarcinoma	D2 vertebrae	60	F
11	Gall bladder adenocarcinoma	Right shoulder	62	F
12	Follicular thyroid carcinoma	Left proximal humerus	40	F
13	High-grade urothelial papillary adenocarcinoma	L3-L5 vertebral body	56	F
14	Nodular Lymphocyte Predominant- Hodgkin Lymphoma	Sacrum	48	M

In our study, among the total biopsies, 14 unusual metastatic cases were identified. Bone metastasis manifests clinically through pathologic fractures (most common), reduced mobility, spinal cord compression, or metabolic complications like bone marrow aplasia or hypercalcemia.

The prognosis associated with bone metastasis is generally poor, with limited curative prospects once metastasis occurs. The median survival following the diagnosis of bone metastasis varies among primary tumors: Lung (6 months), Bladder (6–7 months), Renal cell carcinoma (12 months), Prostate (12–53 months), Breast cancer (19–25 months), and Thyroid (48 months) [1]. A delay in identifying rare metastatic sites can lead to a loss of crucial time in managing patients with unknown primary malignancies [1]. In our study encompassing 14 cases, a gender distribution of 9 females and 5 males was observed. Additionally, 4 cases were aged > 60 years, while the rest were < 60 years. Metastasis patterns showed involvement in the appendicular skeleton in 9 cases and axial skeleton in 5 cases. Notably, the humerus emerged as the primary site of appendicular metastasis, followed by the femur (Table 1).

Thyroid

Thyroid carcinoma's propensity for bone metastasis is well-documented, with reported incidences ranging

from 7 to 23% as of 2022. Among distant metastatic sites, lungs and bones are the most frequently affected. Follicular thyroid carcinoma exhibits the highest rate of bone metastasis. The predominant factor influencing the site of metastasis is the average blood flow by thyroid carcinoma. Notable sites involved in thyroid carcinoma metastasis to bone include Vertebrae (29–47%), Pelvis (22–38%), Ribs (17–22%), and Femur (11%) [4].

Among the cases detailed earlier, one instance exhibited metastasis to the rib, while two others presented with metastasis to the humerus. Although thyroid carcinoma metastasizing to the ribs is documented in the literature, such occurrences are infrequently encountered in clinical practice [5]. Furthermore, metastasis to the humerus is even more uncommon, with only a limited number of cases reported to date [6].

Colorectal cancer (CRC)

Advancements in colorectal cancer treatment have prolonged patient survival, resulting in an apparent rise in bone metastasis incidence. Kanthan et al., studying colorectal cancer patients from 1970 to 1995, reported a 6.6% incidence of bone metastasis [7]. The liver is the primary site for CRC metastasis, followed by the lungs. Santini et al.'s study on bone metastasis in CRC patients noted involvement rates in various bone sites: Vertebral column (65%), Hip/pelvis (34%), Long bones (26%), and Other sites (17%) [8].

In our case, CRC metastasized to the ischial bone despite the patient being declared tumor-free post-surgery. While CRC has been reported in the pelvic region, instances in treated cases remain unreported. The recurrence of CRC in our case was identified through clinical symptoms related to bone metastasis [8].

Neuroendocrine carcinoma

Neuroendocrine tumors are an exceptionally rare subgroup, constituting less than 0.5% of all tumors. Bone metastasis originating from a primary neuroendocrine tumor is a recognized but infrequent complication, reported at 20% and 6.4% in two separate studies [9, 10]. Typically, the axial skeleton is more commonly involved, followed by the pelvis and femur.

In the case presented in our series, the patient initially had a neuroendocrine tumor of the nasal cavity, which subsequently metastasized to the humerus despite undergoing multiple cycles of chemotherapy and radiotherapy. While neuroendocrine tumors are commonly reported in the axial skeleton, our case stands as the first documented instance of metastasis to the appendicular skeleton.

Malignant melanoma

Malignant melanoma, known for recurrence and metastasis, primarily targets the lung, liver, and brain. Skeletal metastasis is the fourth most common occurrence, usually affecting the skull, vertebrae, pelvis, and ribs. Femur metastasis is exceptionally rare [11]. Our patient, initially presenting with a femur fracture and lung mass, was later diagnosed with metastatic malignant melanoma, revealing the severity after spreading to the lung and causing a pathological fracture, emphasizing the poor prognosis associated with bone involvement.

Malignant phyllodes

Phyllodes tumor, constituting less than 1% of all breast tumors, is a rare entity. Malignant phyllodes is uncommon, and the occurrence of bone metastasis is an exceedingly rare complication, with only a handful of cases reported in the literature. To date, only two instances have been documented of malignant phyllodes metastasizing to the femur [12]. Our case represents the third documented occurrence.

Similar to the CRC case, in this instance, the discovery of bone metastasis to the femur occurred after the patient had been declared tumor-free post-mastectomy. This emphasizes the critical importance of considering metastasis from both common and uncommon cancers to both familiar and unfamiliar bony sites.

Squamous cell carcinoma

Skeletal metastasis is a recognized complication of long-standing lung cancer, with small-cell carcinoma and large-cell carcinoma commonly associated with bone metastasis. However, it is infrequent for a clinically quiescent squamous cell carcinoma of the lung to lead to bone metastasis. Sudipta et al. reported such a case in 2014, detailing a clinically silent squamous cell carcinoma of the lung with metastasis to the humerus [13]. In our report, we present an occult squamous cell carcinoma of the lung metastasizing to the scapula, with the diagnosis of lung carcinoma emerging subsequently. To the best of our knowledge, this represents the first documented case of this entity metastasizing to the scapula.

Malignant solitary fibrous tumor

Intracranial Malignant Solitary Fibrous Tumors are uncommon mesenchymal brain tumors, typically occurring in young adults. While most cases remain localized to the brain and spine, instances of extracranial metastasis are well-documented. Although bone is frequently involved, specific sites with a predilection for bone metastasis remain unidentified [14]. Our patient, a 23-year-old previously treated for intracranial solitary fibrous tumor, developed humeral metastasis following the completion of therapy.

Alveolar soft part sarcoma

Alveolar soft part sarcoma, a rare malignancy with a high metastatic potential, commonly metastasizes to the lung, with bone involvement being infrequent. The literature lacks specific sites in the skeleton for bone metastasis. Diagnosis at the time of metastasis significantly impacts disease-specific survival [15]. It is crucial to actively search for metastasis at both diagnosis and during treatment to improve prognostic assessment.

Lung adenocarcinoma

Lung carcinomas typically exhibit a predilection for spreading to the brain, bones, and adrenal glands, with involvement of other organs often observed in advanced disease stages. Among the various types of lung carcinomas, specific metastatic sites can be preferential, such as liver metastasis in small-cell lung carcinoma (SCLC) and brain metastasis in both SCLC and adenocarcinoma [16]. While existing literature doesn't explicitly outline the preferences for various bone sites by lung cancer, our patient presented with vertebral metastasis initially misdiagnosed as Pott's spine clinically. Subsequent histopathological examination revealed a metastatic deposit, leading to the identification of the primary tumor in the lung. It is crucial to consider metastasis as a differential diagnosis when encountering spinal lesions that present with vertebral collapse in radiological images, as metastatic spread to the spine can mimic Pott's spine both symptomatically and clinically.

Gall bladder adenocarcinoma

Gallbladder cancer stands as the most prevalent biliary tract malignancy, often characterized by the presence of metastases at the time of presentation. The most common sites for metastasis in gall bladder cancer include the liver, regional lymph nodes, and peritoneum, with less common involvement of the lung and brain. Skeletal metastasis in gall bladder malignancy is considered rare [17].

The literature lacks documentation regarding specific sites in the skeleton prone to metastasis in gall bladder malignancy. In our case, the patient presented with a pathological fracture, prompting further investigation that unveiled a primary tumor in the gall bladder with a confirmed metastatic deposit in the right humerus at the fracture site, as verified by histopathology.

Urothelial carcinoma

Urothelial carcinoma typically remains localized, but when metastasis occurs, it can spread to various organs including the lungs, liver, prostate, uterus, and bones. Pelvic bones are commonly affected, although the incidence of involvement of the vertebral column by this cancer is not well-documented [18]. In our case, the patient presented with low back pain, initially diagnosed as tuberculosis. Subsequent biopsy for confirmation revealed a metastatic deposit, prompting further investigation to identify the primary tumor. The patient was eventually diagnosed with metastatic urothelial carcinoma.

NLP-HL (Nodular lymphocyte predominant Hodgkin Lymphoma)

Extranodal lymphoma affecting the spine is a late manifestation of Hodgkin Lymphoma (HL) and can manifest with pain and neurological symptoms. The sacrum, containing hematopoietically active bone marrow, is prone to metastasis, especially in hematolymphoid malignancies like lymphoma. However, the true incidence of sacral involvement remains unknown. Spinal lesions are found in approximately 5.8% of Hodgkin Lymphoma cases and 6.5% of Non-Hodgkin Lymphoma cases [19].

A study conducted by Shamsudini Hashi et al. in 2018 on the management of extranodal lymphoma of the spine in 30 patients did not report any cases involving the sacrum in NHL-HL. Only the cervical, thoracic, and lumbar regions were involved in NHL-HL cases [19]. Our patient, a known case of NHL-HL, developed metastasis to the spine while undergoing treatment.

Limitation

Due to the small sample size, the study's findings may not reflect the general population. Being a referral center for bone and soft tissue pathology may inflate the incidence of these cases. Larger studies over longer periods are needed for accurate demographic data and more meaningful conclusions.

Conclusion

Bone metastasis can indicate poor prognosis. Advances in treatment and imaging reveal more skeletal sites involved, sometimes as symptoms of occult tumors. Early identification and management are vital for improving outcomes. This study emphasizes the diagnostic challenges of atypical bone metastases, particularly with occult primaries. It highlights the need for a thorough evaluation of unexplained bone lesions, especially in older adults.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s42047-025-00179-3.

Supplementary Material 1

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Data availability
The data for the current study is available from the corresponding author at reasonable request.

Declarations

Ethics approval and consent to participate
Written informed consent and verbal consent taken from the patient. The Institute ethics committee was informed regarding the case report. They have approved of the writing of the manuscript and provided an ethical waiver.

Consent for publication
Written informed consent was taken from the patient included in the study.

Competing interests
None.

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