



## Case report

# A case report of small round cell tumor of palm: A difficult code to decipher on cytology

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## ABSTRACT

**Introduction:** Small round cell tumors (SRCT) are difficult to sub categorise on fine-needle aspiration cytology (FNAC) samples as they are rare and it is difficult for cytopathologists to obtain enough experience for rendering reliable diagnoses. Various sub categories of SRCTs are morphologically very similar. Many SRCTs do not have specific antigens which could be demonstrated with immunocytochemistry (ICC) or they lose them when poorly differentiated. Besides, cross-reactivity exists between some SRCTs. Suboptimal FNAC sampling from a heterologous component and unstandardized performance of ICC contributes to the pitfalls.

**Presentation of the case:** A 40-year-old male presented with a swelling measuring 3 cm in diameter on palmar aspect of right-hand. Magnetic resonance imaging suggested cyst of tendon sheath. However, on cytology in combination with ICC, a diagnosis of non-lymphoid small round cells tumor was suggested, with confirmatory diagnosis on histopathology.

**Conclusion:** FNAC assisted with ICC can be a rapid and economical diagnostic tool in cases of high-grade malignant tumors for which early diagnosis is extremely important.

## 1. Introduction

Malignant small round cell tumor includes tumor with similar cytomorphology comprising of round cells which are large and twice the size of red blood cells on the air-dried smears [1]. This group of neoplasms is characterized by small, round, relatively undifferentiated cells. They generally include Ewing sarcoma, peripheral neuroectodermal tumor (PNET), rhabdomyosarcoma, synovial sarcoma, non-Hodgkin's lymphoma, retinoblastoma, neuroblastoma, hepatoblastoma, and nephroblastoma. Other differential diagnoses of small round cell tumors include small cell osteogenic sarcoma, granulocytic sarcoma, and intraabdominal desmoplastic small round cell tumor. Well differentiated tumors are generally easy to diagnose, but for poorly differentiated tumor definitive diagnosis may be difficult [2].

Ewing sarcoma is a tumor of bone classically described under small round cell tumors [3]. It is the third commonest primary malignant bone tumor in all age-groups. Among children and young adults, it is the second most frequently occurring bone malignancy. The median age at presentation is 15 years. Males are affected more frequently than females with a ratio of 1.5:1. Extremities are the most common sites of

presentation. The disease was less common in the axial region, extraosseous sites, chest wall, skull, and pelvic bones. Metastasis at presentation is most commonly seen in lungs. Ewing sarcoma arises within the bone, but can also be extraosseous. It mainly affects the pelvis and the femur region, mostly occurring in second decade of life [4].

Rhabdomyosarcoma is the most common soft tissue tumor in children. Botryoid and spindle cell type have the best prognosis but accounts together for 9% of all cases. The most common subtype is embryonal which have an intermediate prognosis. Alveolar type (31%) has poor prognosis [1].

We present a case of a round cell tumor of palm, diagnosed with application of a multimodal approach combining FNAC along with ancillary techniques for immunophenotyping. Present case is reported in line with the SCARE guideline 2020 [5].

## 2. Case report

A 40-year-old male presented with swelling in the palmar aspect of the right hand for 2 months. The swelling had rapidly increased in size. On clinical examination swelling measured 3 cm in maximum diameter.

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It was firm, tender, and had restricted mobility. The overlying skin was tense and the patient had difficulty in making a fist (Fig. 1). Patient was sent for radiological examination and fine needle aspiration from the swelling.

### 2.1. Radiological examination

On Magnetic resonance imaging (MRI) of the hand a well-defined lobulated T2/STIR hyperintense cystic lesion with T1 hypointensity around flexor tendons in the palmar space of the hand was identified. The lesion was extending from the distal end of the carpal row up to the heads of metacarpals and up to the metacarpophalangeal joint of the fourth digit. It was encasing the flexor tendons and measured  $28 \times 44 \times 69$  mm in size with thin internal septations. There was no significant edema in the adjacent fat. MRI suggested a diagnosis of tendon sheath cyst/synovial cyst (Fig. 2).

### 2.2. Cytological examination

Fine needle aspiration cytology of the swelling was done and multiple smears were prepared. Cell block was prepared from the material left inside in the needle hub. May Grunwald Giemsa stained cytosmears showed a dual population of cells, one was of larger cells having vacuolated cytoplasm with vesicular nuclei and other population was of smaller cells with scant cytoplasm and hyperchromatic nuclei. These cells were arranged in clusters and at places also forming rosettes (Fig. 3). Similar findings were identified on cell block preparation (Fig. 4). Based on these cytomorphological features a provisional cytological diagnosis of small round cell tumor was considered. Special stains and immunocytochemistry was done on remaining smears and cell blocks.

The large cells were positive for periodic Schiff (Fig. 5a). On immunocytochemistry, the cells were positive for vimentin (Fig. 5b) and negative for CD45, S-100 and epithelial membrane antigen. Based on these findings a cytological diagnosis of a small round cell tumor with possibilities being Primitive neuroectodermal tumor/Ewing sarcoma and rhabdomyosarcoma was rendered and biopsy was advised.

### 2.3. Histopathological examination

Histopathological examination of core biopsy showed a tumor comprising of diffuse sheets of small round cells having a high nucleocytoplasmic ratio, vesicular chromatin, indistinct nucleoli, and scant amount of pale to clear cytoplasm. Stroma showed rich vascularity. Mitotic figures were 6–8 per high power field. Immunohistochemical analysis showed a CD99 immunoreactivity score of 2+ in round neoplastic cells. Cells were positive for desmin and myogenin, but negative for FLI1. A final diagnosis of Ewing sarcoma was rendered.

### 2.4. Treatment and follow-up

The patient was started on radiotherapy and adjuvant chemotherapy. A whole-body Positron emission tomography (PET) scan was performed after 1 month, which was found to be normal. The hand lesion completely resolved after fifth cycle of chemotherapy (Fig. 6).

During the follow-up, whole-body PET scan with contrast was repeated after 1 year of initial diagnosis. There was no metabolically active area identified. During this period patient was asymptomatic and his normal functional hand movements were regained.

However, during further follow-up, contrast enhanced computed tomography (CECT) scan after about one year and six months from initial diagnosis, a subtle lytic lesion was found in the lateral epicondyle of the right humerus along with ill-defined sclerosis in the upper metaphyseal region of the right humerus suggesting an old healed metastasis.

A follow-up, whole-body PET-scan and MRI scan of thorax was done further after six months. PET-scan revealed few soft tissue thickenings in the lower lobe of the right lung, which was abutting the pleura posterolaterally and measured  $3.4 \times 1.0$  cm in size. MRI of the lumbar spine showed heterogeneous T1 and T2 signal intensities in the L4 vertebral body with heterogeneous contrast enhancement. A lytic lesion with surrounding soft tissue component and heterogeneous enhancement in the right transverse process of L2 vertebra was seen extending to the right side of the vertebral body. Mild diffuse disc bulges causing mild spinal canal was seen from L3-L4 vertebrae. A small posterior epidural enhancing soft tissue component indenting over the anterior thecal sac was found.



Fig. 1. Left hand palmar and dorsal aspect shows firm swelling with tensed skin.

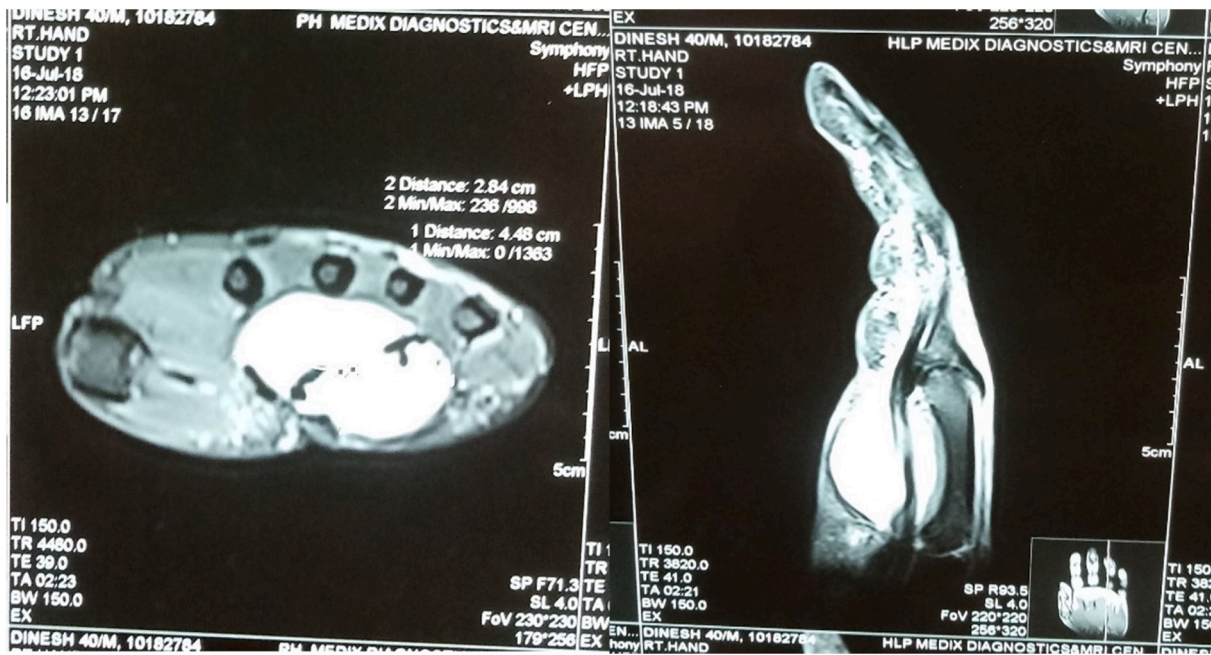


Fig. 2. MRI show lesion involving second to fourth metacarpal bones.

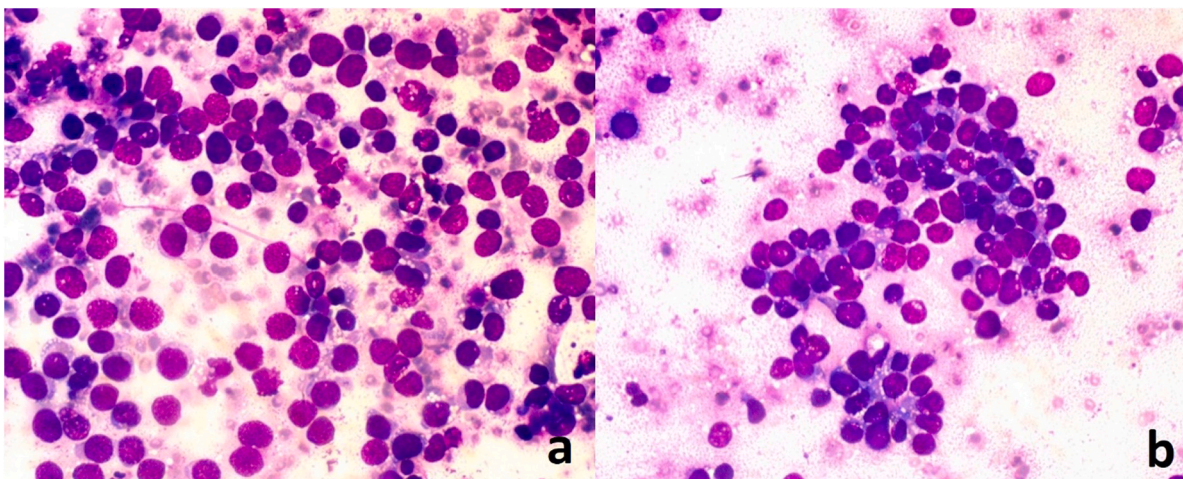


Fig. 3. Cytosmears show high cellularity, dual population of cells, large cells with vacuolated cytoplasm and vesicular nuclei; and smaller cells with scant cytoplasm and hyperchromatic nuclei (a, 400×, May Grunwald Giemsa) and focal rosettes (b, 400×, May Grunwald Giemsa).

These findings suggested occurrence of florid skeletal metastasis in this case. Radiotherapy and chemotherapy were started for metastatic disease. However, during the treatment patient got COVID-19 and died due to its complications.

### 3. Discussion

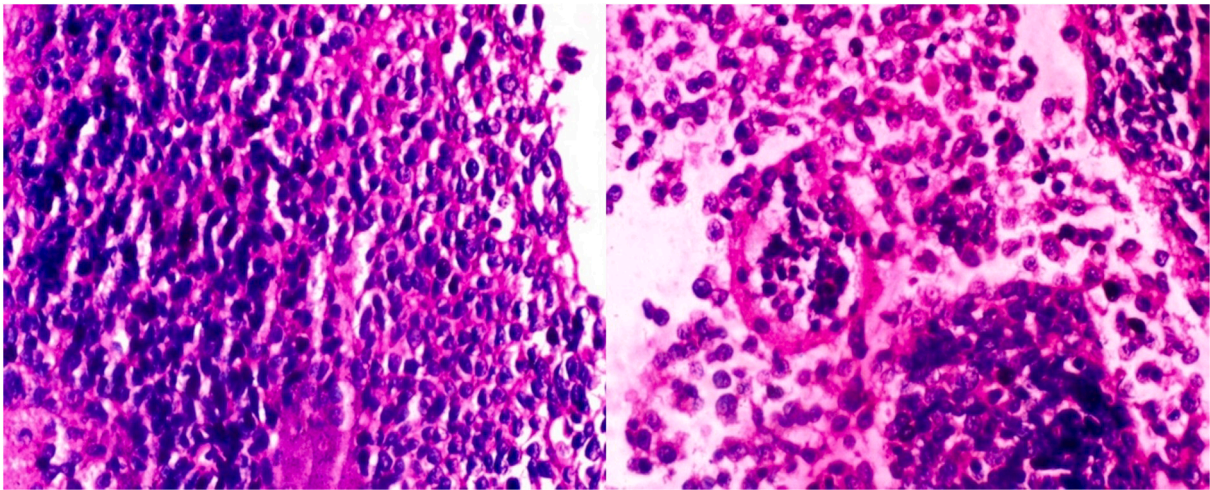
Ewing sarcoma of the hand bones is extremely rare. The hand and wrist account for less than 1% of all diagnosed cases. The most common locations in the hand are the metacarpal and proximal phalanges. The thumb (28%) and the middle finger (28%) are most commonly affected.

Pain and swelling are the most common complaints of the affected finger [6]. Clinically it presents with fever and increased ESR. It usually arises within the bone, but can also occur within the soft tissue (extraosseous variant) and PNET arises within soft tissues. Clinical differential includes local infection, metastasis, and hematological malignancy [7]. This neoplasm mainly affects the pelvis and the femur region and

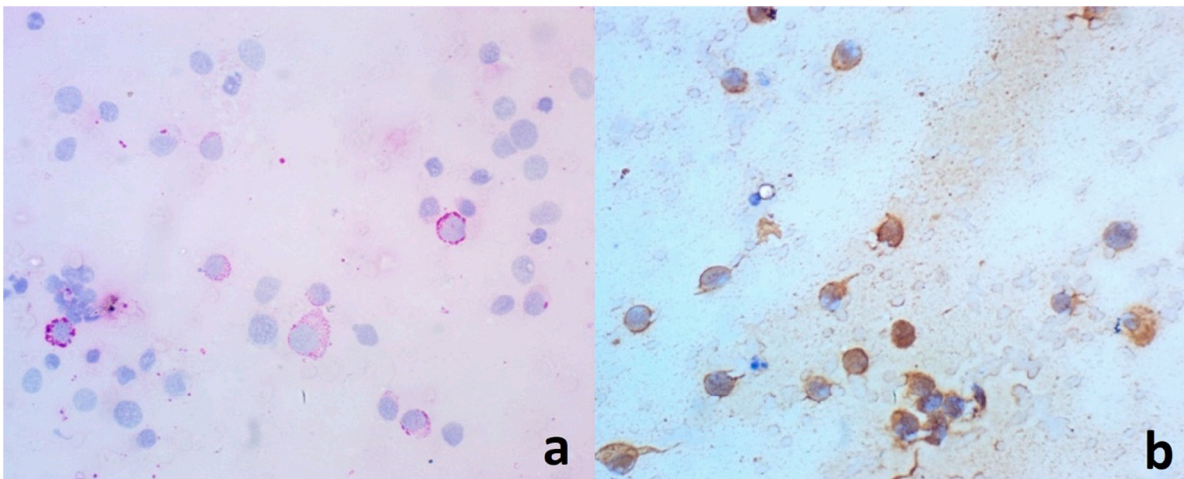
predominates in the second decade of life. Radiologically, it may be seen as bone destruction and expansile lesion. Bone expansion, cystic or honeycomb appearance, periosteal reaction, and cortical thickening of the bone are less seen in the lesion on the hand or the foot. Regardless of the treatment method, the localization of the tumor on the hand is an important prognostic factor. When the distal parts of the extremities are affected, the survival rate is much higher [6].

The present case is unique for several reasons. Firstly, this tumor rarely involves hands and wrists and patients usually present in the second decade of life. However, this patient presented very late at the age of 40-years. The cytological, as well as histological differentials, include various round cell tumors like metastatic neuroblastoma, rhabdomyosarcoma, and NHL in children and metastatic small anaplastic carcinoma and Non-Hodgkin's lymphoma in adults [8].

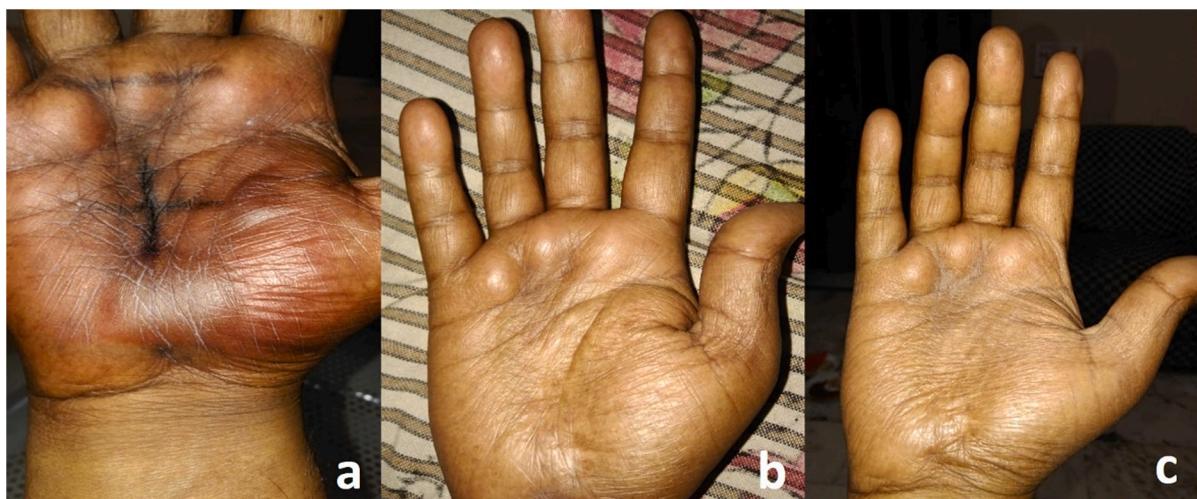
Similar to the present case Joseph Sanjay A. et al. published a case report of a 56-year-old male with enlarging Ewing sarcoma of size 3.0 cm in the palm of the right hand which was associated with pain,



**Fig. 4.** Cellblock shows a dual population of cells, one having hyperchromatic nuclei with scant cytoplasm and other having vesicular nucleus with eosinophilic cytoplasm (1000 $\times$ , hematoxylin and eosin).



**Fig. 5.** Large cells show positivity for periodic acid Schiff (a, 400 $\times$ , PAS). Immunocytochemistry shows large cells positive for Vimentin expression (b, 400 $\times$ , DAB).



**Fig. 6.** Hand after the first (a), third (b) and fifth (c) cycle of chemotherapy.

numbness, and tingling down his fingers. The tumor led to functional impairment with the patient's ability to work on a farm. Ewing sarcoma breakpoint region 1 (EWSR1) gene translocation was present [9].

Gökalp M et al. presented a case of a 27-year-old female patient who presented swelling on the proximal phalanx of her right-hand middle finger for 3 years. However, the mass was excised as it was rapidly increasing in size leading to pain. The pathological diagnosis was Ewing sarcoma. The patient received postoperative chemotherapy consisting of VAC + IE (cyclophosphamide, actinomycin, vincristine, ifosfamide, and etoposide). On follow-up after 1 year, no postoperative local recurrence or metastasis was detected [6].

It is evident from the present and the previous case reports that the site and size of a primary tumor are crucial for optimal treatment. X-ray and MRI of the primary site, chest CT, and bone scintigraphy should be performed for staging.

X-ray findings included a typical destructive pattern with indistinct margins, onion-skin-type periosteal reaction, and soft tissue masses in the diaphysis or, more rarely, in the metaphyseal/diaphyseal region. On X-ray, it may be confused with osteomyelitis due to bone destruction. Furthermore, tuberculous dactylitis is characterized by expansile lesions of the hand and the absence of periosteal reaction [6].

MRI is an ideal method for evaluating soft tissues, the intramedullary involvement of the disease, and the involvement of the primary tumor in the surrounding soft tissues. Bone scintigraphy assists in detecting the bone involvement and, to an extent, the amount of intramedullary involvement. Conventional Tc99 bone scintigraphy is ideal for metastatic disease scanning [6].

In case report by Rajappa S, et.al an 18-years boy, presented with pain and swelling of his left-hand fingers. This case was initially misdiagnosed as tuberculous dactylitis. However, further histopathological and immunohistochemical analysis (positive for CD99 and negative for CD45, CD117, and SMA.) confirmed the diagnosis of Ewing sarcoma. Local therapy is achieved by surgery and radiation and systemic control is achieved by combination chemotherapy which includes vincristine, doxorubicin, cyclophosphamide, etoposide, ifosfamide and actinomycin D [7].

Chemotherapy is the mainstay in the treatment of the Ewing Sarcoma and it is also essential for control of localized disease [10]. Chemotherapy has drastically improved the survival in patients with localized disease. However, there role of chemotherapy is limited in the metastatic disease. In review by Kridis et al. [11] the overall 5-year survival in localized Ewing tumor was 70% while it was 30% in metastatic disease. In the present case, even after complete chemotherapy, relapse and metastasis was seen, suggesting a suboptimal response to the chemotherapy.

#### 4. Conclusion

Most of the previous studies have used on surgically resected material or biopsy for diagnosis of SRCT. However, FNAC assisted with ancillary diagnostic techniques like immunocytochemistry, flow cytometric immunophenotyping, and even reverse-transcriptase polymerase chain reaction can be extremely useful for diagnosis of these undifferentiated tumors. This can be of help in rapid diagnosis and deciding appropriate treatment protocols.

#### Provenance and peer review

Not commissioned, externally peer-reviewed.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Ethical approval

N/a.

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#### Guarantor

Corresponding author is the Guarantor for this study.

#### Research registration number

N/a.

#### CRedit authorship contribution statement

AY for study concept and design. SKP for data collection. SS and NS for analysis and interpretation. AY and SKY for writing the manuscript.

#### Declaration of competing interest

None declared.

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