# Case Report Melanotic neuroectodermal tumor of infancy in the soft tissue of the forearm: report of a case

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**Abstract:** Melanotic neuroectodermal tumor of infancy is rare. Only 3 cases have been reported in the soft tissue of the extremities up to date. It has a typically biphasic feature in morphology. Epithelial and melanotic markers are positive in the epitheliod cells and neuron-specific enolase or synaptophysin is positive in the small blue round cells in immunohistochemistry. Radical resection and close follow-up is the treatment strategy in general situation. Here we report one case of MNTI in the upper extremity with review of the literature. This is the first case of MNTI in the forearm.

Keywords: Melanotic neuroectodermal tumor of infancy, soft tissue, forearm

#### Introduction

Melanotic neuroectodermal tumor of infancy (MNTI) is an uncommon, rapidly expanding and pigmented tumor in infancy. Krompecher described the initial case in 1918 [1]. Borello and Gorlin first designated the tumor as melanotic neuroectodermal tumor of infancy in 1966 for the case they reported had high urinary excretion of vanillylmandelic acid (VMA) which suggested the tumor might be an origin of neural crest [2]. 486 cases of MNTI have been reported since 1918 [3-9]. It is widely accepted that MNTI is a benign tumor, though sometimes it can recur and occasionally can metastasize. It usually presents as a painless, firm, and pigmented mass without any discomfort for the patients. Most of the cases are identified in the maxilla. The tumors of MNTI located in the extremities are very rare and only 7 cases have been reported up to now (4 cases in the femur and 3 cases in the soft tissue) [10-16]. Herein, we describe the first case of MNTI in the forearm and review the literature.

## Case report

A 10-month-old girl presented to our hospital for a soft tissue mass near the right elbow for six months. The mass was first detected to be 2.5×2×1 cm by her parents and was stable without any change in size since then. Physical examination revealed the mass was hard and firm. MRI scan showed there was a mass in the subcutaneous fat layer of the right proximal forearm (**Figure 1**).

The mass was completely resected. It was found located in the adipose layer just near the muscle during the operation. No adjuvant treatments such as chemotherapy and radiation therapy were given after surgery. The child recovered very well without evidence of tumor recurrence and metastasis 3 months after surgery and was still in follow-up. Written informed consent was got from the child's parents.

## Pathological findings

Macroscopically, the specimen was a gray mass measuring 2×1.8×1.5 cm. The mass was welldemarcated but without a capsule. The cut surface exhibited a black appearance and the texture was tough.

Microscopically, the tumor was biphasic in composition and had a lot of fibrocollagenous stroma (**Figure 2A**). The epitheliod cells had a predominance and they had plenty of cytoplasm and abundant melanin pigments in the cyto-



**Figure 1.** Magnetic resonance imaging scan showed a mass in the subcutaneous fat layer of the right proximal forearm (arrow).

plasm. They were arranged in a glandular pattern (**Figure 2B**). Islands of primitive-looking small blue round cells with scant cytoplasm and small round nucleoli were seen focally (**Figure 2C**). And these two components were separated from each other by the collagen. Some small blue round cells were located in the glandular cavity of the epithelioid components and there was a transition between these two populations of cells (**Figure 2D**). The tumor invaded the peripheral adipose and striated muscle tissue (**Figure 2E**). Occasionally mitotic figures were found in the small cell component. Necrosis and calcification was not seen in the tumor.

Immunohistochemically, the glandular component was positive for pan-cytokeratin (AE1/ AE3) (**Figure 3A**) and HMB45 (**Figure 3B**). The small blue cell component was positive for synaptophysin (SYN) (**Figure 3C**). All the components were negative for S-100, SMA, DES, GFAP, and CD99. The proliferation index Ki-67 was relatively high at 25% in the small blue cell component, however, negative in the glandular component (**Figure 3D**). The diagnosis was melanotic neuroectodermal tumor of infancy.

# Discussion

Melanotic neuroectodermal tumor of infancy is a very rare benign tumor in infancy derived from the neural crest. A broad nomenclature

has been used for this tumor in the literature: Congenital melanocarcinoma, retinal anlage tumor, pigmented congenital epulis, melanotic progonoma, melanotic neuroectodermal tumor of infancy, pigmented ameloblastoma, pigmented teratoma, atypical melanoblastoma, melanotic adamantinoma, retinal choristoma, melanotic epithelial odontoma, and benign melanotic tumor [13, 17, 18]. Most patients are in the first year of life with a peak between the second and the sixth month [19]. The mean age is 4.3 months [20]. MNTI has a male predilection [19]. 92.8% of MNTIs occur in craniofacial region, mostly in maxilla (68-80%), skull (10.8%), mandible (5.8%), and brain (4.3%). Some other uncommon location includes epididymis, paratesticular region, testis, ovary, mediastinum, uterus and extremities [19]. Only 8 cases of MNTI were reported in the extremities including our case. Half of the 8 cases were located in the soft tissue. Clinicopathologic features of all the 4 cases in the soft tissue of extremites were summarized in Table 1. They were all girls. The age interval was between 5 months and 10 months and all the patients were less than 1 year which was the common age range. Of the 4 cases, two were in the thigh, one in the upper arm and one in the forearm. Our case was the only one in the forearm. The tumors were 2.0-4.0 cm in maximum diameter. Grossly, the tumors were firm, solid and welldefined. The cut surface was gray-black. Histologically, all the 4 cases showed a biphasic feature and had two populations of cells. One population of cells was the epithelioid cells. They were cuboid and had plenty of eosinophilic cytoplasm and abundant intracellular melanin granules. These cells arranged in a glandular pattern. The other population of cells was the small blue round cells which just looked like the neuroblasts and had scanty cytoplasm. This kind of cells was aggregated in islands. These two components were embedded by a dense fibrocollargenous stroma. Occasional mitotic figures were found in the small cell component. 3 of the 4 tumors infiltrated the adjacent soft tissue. Immunohistochemically, the two kinds of cells had different immunoprofiles (Table 2). The epithelioid cells were positive for cytokeratin (4/4) and HMB45 (3/4). Neuronspecific enolase or synaptophysin was positive in the small blue round cells in all the cases. Ultrastructual study was conducted in 2 of the 4 cases and confirmed the presence of a bipha-

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sic cell population [14, 16]. Primitive junctions and premelanosomes were identified in the epithelioid components. There were intracytoplasmic dense-core granules in the small blue round cells. The genetic study of MNTI was rarely reported. Gomes et al reported that MNTI might harbor the oncogenic BRAFV600E mutation which first provided the insights to the targeted therapy of MNTI [4].

Our case shared the same clinicopathological features with the previous 3 cases: infants,

tumor size, the grey-black cut surface, classic biphasic pattern in morphology, and similar immunohistochemical phenotype. The diagnosis of MNTI was definitive. However, the location of our case was still uncommon for MNTI although 3 cases had been reported in the soft tissue of the extremities.

The differential diagnosis for MNTI includes metastatic neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma/peripheral primitive neuroectodermal tumor, desmoplastic round cell



**Figure 3.** Immunohistochemical features of MNTI. A. Pancytokeratin was diffusely positive in the epithelioid components, however, negative in the small blue cell components (×100). B. The glandular components were positive for HMB45 (×200). C. The small blue cell components were positive for SYN (×200). D. Ki-67 index was about 25% in the small blue cell components (×100).

Case	Sex/Age (Mo)	Location	Chief complaint	Maximum tumor diameter (cm)	Management	Follow-up
Scheck et al [14]	F/6	Left thigh	mass	2.0	Operation	AWRM 15 m after surgery
Al-Marzooq et al [15]	F/6	Right upper arm	mass	4.0	Operation	Unknown
Lacy et al [16]	F/5	Right thigh	mass	2.5	Operation for twice	AWRM 40 m after the initial surgery
Present case	F/10	Right forearm	mass	2.0	Operation	AWRM 3 m after surgery

Mo, months old; m, months; cm, centimeters; F, female; AWRM, alive without recurrences and metastases.

tumor (DSRCT), malignant melanoma, myeloid sarcoma and lymphoma. Metastatic neuroblastoma does not have the biphasic feature in morphology and epithelial markers are negative for this tumor. Rhabdomyosarcoma would have immunoreactivity for myogenic markers such as desmin, myogenin and myoD1. Ewing's sarcoma/peripheral primitive neuroectodermal tumor usually has strong membranous CD99 expression and EWS-FLI1 fusion also can be detected. DSRCT does not have the epithelial component and melanin pigments are absent in the tumor. Malignant melanoma is very rare in infants and does not have the small round cell component. Myeloid sarcoma and lymphoma expresses a panel of hematopoietic markers which are negative for MNTI.

The treatment guidelines have not been established for MNTI for their scarcity. Early diagnosis, total resection and regular follow-up are optimal. Radical excision should be emphasized and is the core of the treatment strategy. Chemotherapy may be effective for the cases

	Scheck et al [14]		Al-Marzooq et al [15]		Lacy et al [16]		Our case	
	Epitheloid	Small blue	Epitheloid	Small blue	Epitheloid	Small blue	Epitheloid	Small blue
	cells	cells	cells	cells	cells	cells	cells	cells
Pancytokeratin	+	-	+	-	+	-	+	-
HMB45			+	-	+	-	+	-
Vimentin	+	+			+	-	-	-
NSE	+	+	-	+	+	+		
SYN					-	+	-	+
Leu-7	-	-					-	+
S-100	-	-			-	-	-	-
GFAP	-						-	-
DESMIN	-	-			-	-	-	-
CD99					-	-	-	-

Table 2. Immunohistochemical features	of MNTI in the soft tissue of the extremities
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+, positive; -, negative. Abbreviations: NSE, neuron-specific enolase; SYN, synaptophysin; GFAP, glial fibrillary acidic protein. Blank: the result unclear or not performed.

that have difficulties in surgery, tumor residue or metastases. Reported chemotherapy was effectively used in 3 cases of facial MNTI [21]. Willi Woessmann presented a case of MNTI in the right maxilla who was primarily cured with chemotherapy without operation [22]. Radiation therapy was restrictedly used for it might cause severe late side effects in infants. All the data suggest the prognoses of MNTI are good. All the 4 cases just received extensive tumor resection without any adjuvant therapy including 1 case received surgery for twice for the initial positive surgical margins. The follow-up was between 3 and 40 months except the follow-up of 1 case was unstated in the report. 3 cases were all uneventful in the reported follow-up time. Occasionally recurrences and metastases can happen in some MNTI cases. The local recurrence rate after resection was between 10% and 15% [19]. Kruse-Lösler et al made an analysis of 140 MNTI cases reported between 1990 and 2004 and found that the overall recurrence rate was 20% [19]. 5-10% of MNTI cases had metastases [15]. Metastases appeared in 23 MNTI cases which accounted for 6.5% of total 355 cases [19]. Some experts had suggested that aneuploidy in MNTI was a useful prognostic marker for predicting tumor recurrence or metastases, but it was still controversial [17, 20, 23]. Comprehensive therapy may be helpful for these intractable cases.

In conclusion, we presented a rare case of MNTI in the soft tissue of the extremities. This is the first case in the forearm. Although this tumor has specific histological, immunohistochemical, and ultrastructural features, MNTI still must be remembered to enter into the differential diagnosis of small round cell tumors or pigmented tumors in the soft tissue of the extremities. More data are needed to understand the behaviour of this kind of tumor in the extremities.

# Disclosure of conflict of interest

None.

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