Spontaneous differentiation to ganglioneuroma from neuroblastoma with multiple bone metastases

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Brief running title: Differentiation of NB with multiple bone metastasis

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Abbreviations:

VMA	vanillylmandelic acid
HVA	homovanillic acid
MIBG	metaiodobenzylguanidine

To the Editor

Neuroblastoma with bone metastases is well known to have an extremely poor prognos
however, we experienced a case with spontaneous differentiation of neurob
showed multiple bone metastases.

A 28-month-old boy presented with a subcutaneous mass on his left brow ri
Physical examinations revealed an additional subcutaneous mass of his lef
axillary lymphadenopathy. The urinary vanillylmandelic acid (VMA) and homovanillic acid
(HVA) levels were increased to 18.6 and 46.3 μg/mg creatinine, respective
resonance imaging showed multiple bony tumors (Fig. 1A) and left adrenal tumor (Fig. 1B).
An ^{123}I-metaiodobenzylguanidine (MIBG) scintigram showed accum
adrenal tumor and right humerus (Fig. 1C). Positron emission-computed tomography showed
increased uptakes in the left adrenal tumor and multiple bones (right scapula, right humerus,
bilateral femurs and bilateral tibias) (Fig. 1D). A biopsy from the subcutaneous mass in the
left buttock and axillary lymph node pathologically showed ganglioneuroma (Fig. 1E). Given
the elevated VMA/HVA levels and positive MIBG scintigram findings, the ex
neuroblastoma or ganglioneuroblastoma was suspected in the adrenal gland an
humerus. The left adrenal gland tum
ganglioneuroblastoma mixed (Fig. 1F). The patient then rece
(vincristine 1.5 mg/m^2, cyclophosphamide 800 mg/m^2, and pirarubicin 30 mg/m^2) but the
I^{123}-MIBG scintigram after 3 courses still showed an increased uptake in the right humerus,

with stable VMA and HVA levels. Genetic analyses were perform
differences between ganglioneuroblastoma and ganglioneuroma, showing diploidy and no
MYCN amplification. Array comparative genomic hybridization of these tumors revealed no
chromosomal events in 1p, 10q, 11q, or 17q. The urinary VMA/HVA lev
decreased, although no further chemotherapy was administered. The patient has been healthy
for more than seven years without recurrence, and the VMA/HVA levels have re
within normal ranges.

Peripheral neuroblastic tumors are the most common extracranial solid t
children, including ganglioneuroma, intermediate ganglioneuroblastoma,
differentiating ganglioneuroblastoma. The natural history of neuroblastoma
progress with an aggressive clinical course or differentiate spontaneously. The best example
of spontaneous differentiation is Stage IVS neuroblastoma
MS with widespread subcutaneous nodules, massive hepatic and lim
involvement, and a small primary tumor without oth
involvement. The prognosis of patients with bone metastas
[1] Few reports have described spontaneous differentiation of
neuroblastoma cases with bone metastasis.[2,3] Several pathological assessments of each
tumor in our case demonstrated a mixture of neuroblastic and
ganglionic components. Furthermore, we compared th
ganglioneuroma and ganglioneuroblastoma to reveal the same molecular sig
suggesting that the ganglioneuroma in this case originated from

differentiate toward ganglioneuroma.

In conclusion, we experienced an extremely rare case of neuroblastoma with multiple bone metastases that differentiated to ganglioneuroma spontaneously. We need to be aware of the potential for spontaneous differentiation from neuroblastoma with bone metastasis to ganglioneuroma in order to avoid unnecessarily administering chemotherapy during the natural course of spontaneous terminal differentiation toward ganglioneuroma.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest in association with the present study.

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FIGURE LEGENDS

Figure. (A) Cranial magnetic resonance imaging (MRI) sh
metastases in the upper orbital walls, zygomatic bones, and sphenoid bones. (B) Abdominal
MRI showing a large mass (54 × 52 × 56 m)mininthsizeft adrenal gland. (C) An
I^{123}- metaiodobenzylguanidine scintigram showing accumulations in the left adrenal g
and right humerus. (D) Positron emission-computed tomography showing increased uptakes
in the left adrenal mass and multiple bones (right scapula, right humerus, bilateral femurs and
bilateral tibias). (E) Histology of the subcutaneous mass resected from
revealing ganglioneuroma. Sacnwdamnaitaurestgraomglion cells were
(Hematoxylin-eosin staining, original magnxif4ic0a0t)i.o(nF)Histology of the resected
adrenal tumor revealing(Hgeamnagtloixoyn leiunr-oebolsaisnt osmaini
magnifxicla0t0i)o.n,Differentiating neurobla
original magnification, x 400).