

### Olfactory Neuroblastoma Visualized by Technetium-99m-ECD SPECT

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We describe a case of olfactory neuroblastoma diagnosed by <sup>99m</sup>Tc-ECD SPECT. Although MRI and CT are very important for delineating these tumors, they are, by no means, specific for neuroblastomas. <sup>131</sup>I-MIBG scintigraphy, the standard method for imaging tumors of neural crest origin, also failed to detect a histologically proven esthesioneuroblastoma.

*Key words:* Technetium-99m-ethyl cysteinate dimer, iodo-131-metaiodobenzylguanidine, olfactory neuroblastoma, esthesioneuroblastoma, SPECT

#### INTRODUCTION

A CASE OF OLFACTORY NEUROBLASTOMA demonstrating increased uptake of Technetium-99m-ethyl cysteinate dimer (<sup>99m</sup>Tc-ECD) is presented. Radioiodinated metaiodobenzylguanidine (<sup>131</sup>I-MIBG) was developed for imaging the adrenal medulla and its diseases, neuroblastomas, and a wide range of tumors originating from the neural crest.<sup>1-3</sup> However, a number of MIBG-negative studies,<sup>4,5</sup> especially in neural crest tumors other than pheochromocytomas, raises the question that grouping these tumors together is a mere simplification. <sup>99m</sup>Tc-ECD has been developed for cerebral blood flow (CBF) imaging.<sup>6-10</sup> Although further studies are necessary, this case demonstrates that <sup>99m</sup>Tc-ECD has many potential applications, including detection of tumors of neural crest origin.

#### CASE REPORT

A 43-year-old man complaining of impaired movement of his left eyelid – noticed 2 years prior to the first examination – and progressive weight loss, sought for medical assistance.

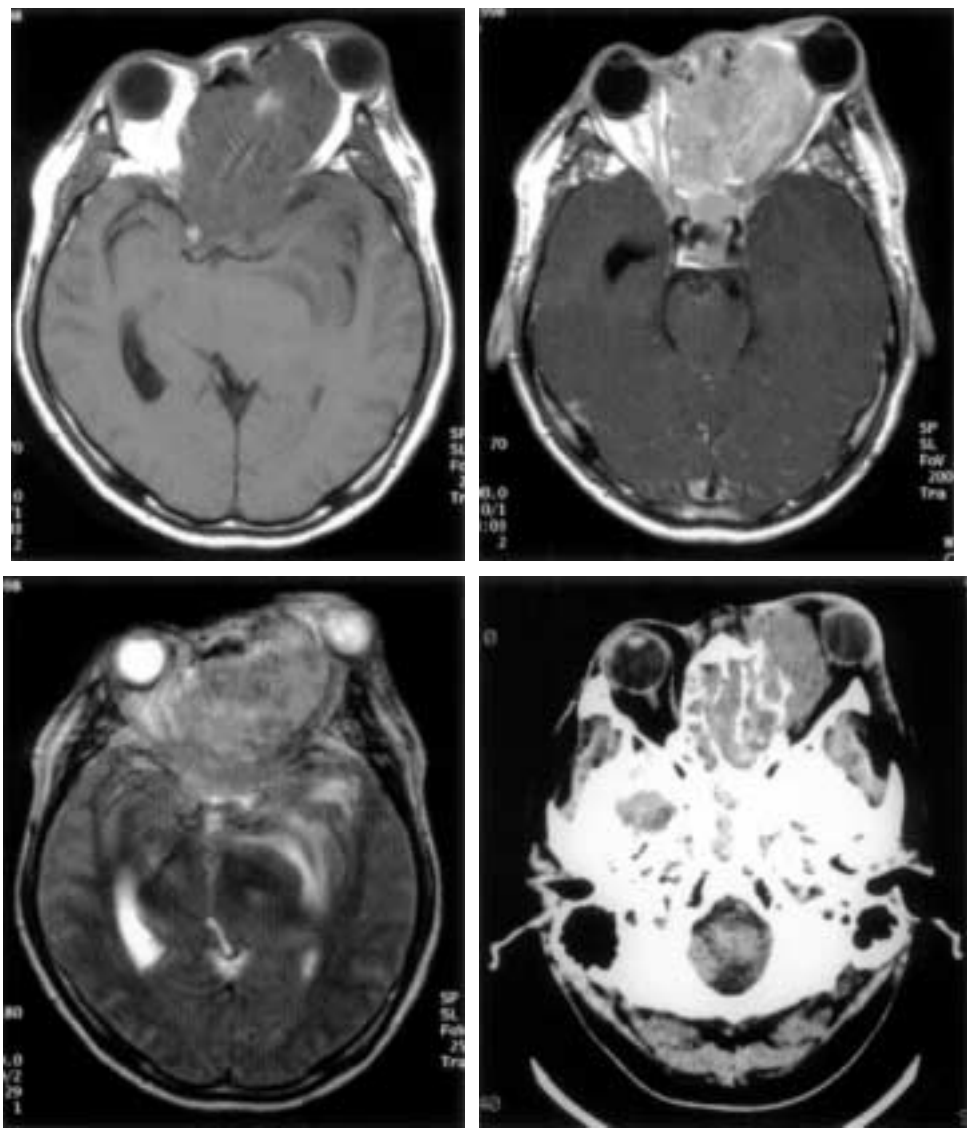
A magnetic resonance imaging (MRI) study revealed a mass destroying the skull base and infiltrating intracranially. The bulk of the mass was located in the paranasal sinus abutting the medial wall of the left orbit

(Fig. 1a-c). Computed tomography (CT) demonstrated extensive bone destruction with an enhanced tumor causing mass effect, including peritumoral edema and midline shift to the right (Fig. 1d). A paranasal tumor of olfactory mucosal origin, including neuroblastoma, was suspected. Scintigraphic study (Siemens, Multi Spect 2, High Energy Parallel Collimator, 30 minutes delay) using approximately 20 MBq of <sup>131</sup>I-MIBG (Daiichi Radioisotope Laboratories; Tokyo, Japan) was performed, but it failed to demonstrate accumulation of the tracer in the tumor or in any other site (Fig. 2a). At the time, a brain-flow study by means of single photon emission computed tomography (SPECT) (Siemens, Multi Spect 3, Fanbeam Collimator, 20 minutes delay) using approximately 740 MBq of <sup>99m</sup>Tc-ECD (Daiichi Radioisotope Laboratories, Tokyo, Japan) was done, and an incidental high uptake of the radiocompound in the area corresponding to the tumor was observed (Fig. 2b).

One week later, a biopsy was performed. Histologically, the tumor tissues revealed acinar proliferation of primitive tumor cells of small round cell type which were associated with fibrillary stroma without rosette formation. Immunohistochemically these tumor cells showed positive immunoreactivity for neurospecific enolase and neurofilaments, resulting in a diagnosis of round-type neuroblastoma of the nose. The patient was referred to neurosurgery, where unsuccessful transcatheter arterial embolization of the tumor was performed. The surgical approach was also difficult due to the size and position of the mass, so the patient was referred for radiotherapy.

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**Fig. 1. a: Plain and b: contrast enhanced axial T1-weighted MR images (SE TR/TE=600/12), c: axial T2-weighted MR image (SE TR/TE=4,000/98), and d: unenhanced CT at the same level depict a mass in the superior paranasal sinus. Although MR and CT are good for delineating size and extension of the tumor, the findings are non-specific.**

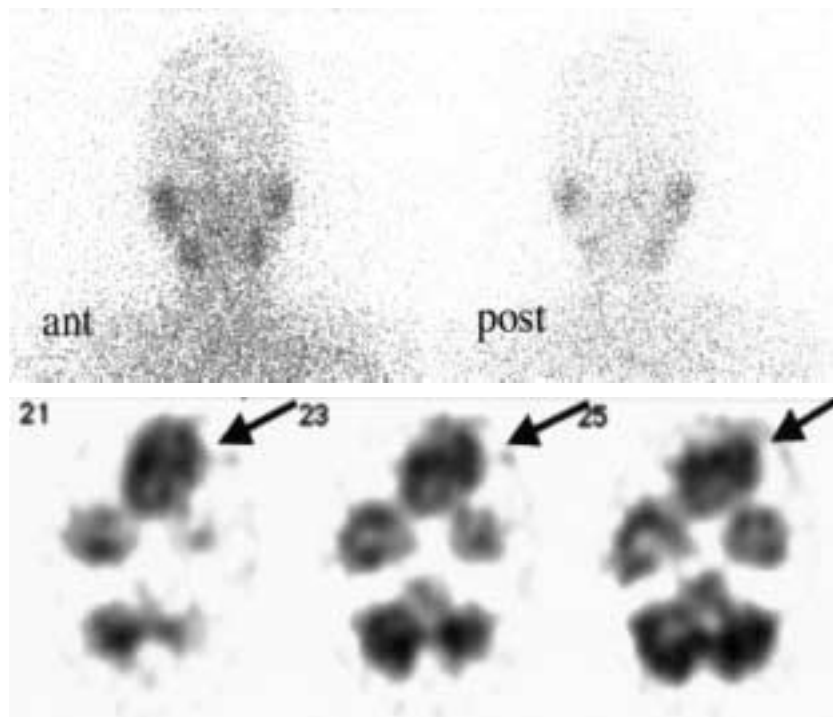
a	b
c	d

DISCUSSION

Olfactory neuroblastomas cover several types of esthesioneurogenic tumors, including esthesioneuroepithelioma, esthesioneuroblastoma, and others. They are thought to be of olfactory mucosal origin and present with typical light microscopical “neurogenic features,” e.g., rosettes and/or axon production. The literature review strongly supports the hypothesis that olfactory neuroblastomas are most likely of neural crest origin and thus belong to a group of neoplasms of the amine precursor uptake and decarboxylation series, collectively known as “APUDomas” or neurocristomas.

Olfactory neuroblastomas slowly invade and destroy bony structures and readily spread through the lymphatics to involve regional and distant lymph nodes. Hematogenous metastasis is less frequent. The 5-year survival rate is 50%, and death is usually due to invasion of the cranial cavity.<sup>11-13</sup>

Olfactory neuroblastomas should be suspected in all ages following identification of a mass in the superior nasal cavity that demonstrates both expansile and destructive growth patterns. In the evaluation of olfactory neuroblastomas, MRI is most useful in delineating the extent of the tumor and may be more accurate than CT. However, the signal intensity characteristics of olfactory



**Fig. 2. a:** <sup>131</sup>I-MIBG scintigraphic study failed to locate the primary site of the tumor, **b:** incidental finding on cerebral blood flow study. <sup>99m</sup>Tc-ECD SPECT demonstrates tracer accumulation in the tumor (arrows).

neuroblastomas may overlap those of other tumors.<sup>13-15</sup>

Radioiodinated-MIBG, first developed in 1980 for imaging the adrenal medulla and its diseases, was subsequently shown to depict neuroblastomas and a wide range of APUDomas.<sup>1-3</sup> Although the use of MIBG became very common, worldwide experience has shown a number of MIBG-negative studies, especially in neural crest tumors other than pheochromocytomas.<sup>4,5</sup> Histological differentiation might influence the uptake of MIBG, as negative results have been observed in patients with well-differentiated tumor.<sup>5</sup> However, in our reported case, <sup>131</sup>I-MIBG failed to demonstrate a histologically undifferentiated tumor. More studies will be required to clarify this point.

<sup>99m</sup>Tc-ECD has been developed for CBF studies, and is widely available nowadays. It is a lipophilic chelating agent that penetrates the normal blood brain barrier (BBB); it then accumulates in brain parenchymal tissue in proportion to the CBF and persists stably for a long time by rapid deesterification into a polar metabolite that cannot recross the BBB. Data have already provided *in-vitro* evidence supporting the hypothesis that esterase is the determinant factor in tissue retention of ECD.<sup>8,9</sup> The pathological specimen of this case did not support another reason for retention of ECD by tumor-invading monocytes and macrophages, which have strong esterase

activity. While this enzyme's activity is the cut-off point in this reported case, yet to be determined, the depiction of the tumor by <sup>99m</sup>Tc-ECD raises the suspicion that inner characteristics of neural crest tumors, including not only neurogenic features but also enzymatic presentation, may play an important role.

To our knowledge, there have been no reports of olfactory neuroblastomas being detected with <sup>99m</sup>Tc-ECD, and although <sup>131</sup>I-MIBG is the method of choice in situations like this, the case represents a call for more investigative studies between the diagnostic performances of <sup>131</sup>I-MIBG and <sup>99m</sup>Tc-ECD in the field of neurogenic tumors, especially considering that the clinical applications of <sup>99m</sup>Tc-ECD are still undergoing expansion.

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