Amelanotic melanoma of the anterior mediastinum
— a case report —

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Background: Malignant melanoma of the mediastinum is rare. To our knowledge, 17 cases of malignant melanomas of the mediastinum have been reported to date, only one of which was an amelanotic melanoma.

Case: A 55-year-old male patient was found to have two well-demarcated, round tumor masses, measuring 2 cm and 0.3 cm in diameter, in his parietal and frontal lobes. A well-demarcated tumor mass, measuring 5×3.5 cm in size, was also detected in the anterior mediastinum. The tumors were yellowish-white in color, soft and hemorrhagic. Cytologically, numerous spindle-shaped and epithelioid tumor cells were observed. The nuclei were eccentrically located and possessed distinct, large nucleoli and inclusion bodies, so-called 'Apitz's bodies'. The cytoplasm was abundant, and slightly brown granules were observed in parts of a few tumor cells. Histologically, the findings were basically the same as the cytological findings. A Fontana-Masson stain was positive. Immunohistochemically, the tumor cells also tested positive for vimentin, S-100 protein and HMB-45. Melanosomes were observed using electron microscopy. In spite of radiation and chemotherapy, the patient died 10 months after the onset of symptoms from metastases to other organs.

Conclusion: To our knowledge, the present report is the first to describe an amelanotic melanoma of the anterior mediastinum from a cytological point-of-view. The present case emphasizes the usefulness of cytology for the rapid diagnosis of amelanotic melanomas during surgery.

Key words: Amelanotic melanoma — Mediastinum — Cytology — Immunohistochemistry — Electron microscopy — Case report

I. Introduction

Malignant melanoma of the mediastinum is very rare, and amelanotic melanoma of the mediastinum is extremely rare; to our knowledge, only one other case of an amelanotic melanoma of the mediastinum
has been reported to date\(^1\). Amelanotic melanoma is morphologically very difficult to differentiate from anaplastic carcinoma and anaplastic large cell lymphoma. The present report is the first to describe the cytological findings for an amelanotic melanoma of the anterior mediastinum.

II. Case Report

A 55-year-old man was admitted in October to the Tama-Nagayama Hospital, Nippon Medical School, complaining of a loss of strength in the left upper extremity. A computed tomography (CT) and magnetic resonance imaging (MRI) revealed a well-demarcated tumor mass, measuring 2 cm in diameter, in the parietal lobe (Photo. 1), and another small tumor mass, measuring 0.3 cm in diameter, in the right frontal lobe. Clinically, metastatic brain tumors were suspected because of the presence of multiple tumor masses, but glioblastoma and malignant lymphoma could not be ruled out. During a complete medical check up, a CT scan revealed a well-demarcated tumor mass, measuring 5 x 3.5 cm in size, in the anterior mediastinum (Photo. 2), and a mediastinal thymoma was clinically suspected. Tumor markers in the serum (CEA, CA19-9, CA125, SCC, AFP) were negative at this stage. During a consultation for the brain tumors, which was held on the day before the operation, the possibility of metastatic brain tumors from the mediastinum was discussed.

A tumorectomy for the tumor in the parietal lobe was performed 16 days after admission. The tumor mass in the parietal lobe was completely removed, and an intraoperative cytopathologic diagnosis was performed. Macroscopically, the tumor was yellowish-white in color, soft and hemorrhagic. Crushed and touched smears were prepared for cytological diagnosis using Papanicolaou and Giemsa stains. Cytologically, a large number of spindle-shaped and epithelioid tumor cells were observed in both smears. The tumor cells were large and discohesively arranged. The nuclei of the tumor cells were eccentrically located and possessed large distinct, nucleoli and a few inclusion bodies, so-called "Apitz’s bodies" (Photo. 3). The cytoplasm of the tumor cells was abundant, and brownish-black pigments were observed in a few tumor cells (Photo. 4). Histiocytes with brownish-black pigments were scattered around the tumor cells (Photo. 5). Cytologically, a diagnosis of amelanotic melanoma appeared to be the most probable, although the possibility of an anaplastic carcinoma or an anaplastic large cell lymphoma could not be ruled out. Histologically, the findings were basically the same as the cytological findings. The tumor consisted of nests of spindle-shaped and epithelioid cells. Brownish-black pigments were also observed in a few tumor cells (Photo. 6). Tumor necrosis was observed, and nuclear mitoses were fre-
quently noted. A Fontana-Masson stain was positive for the tumor cells. Immunohistochemically, the tumor cells stained positive for vimentin, S100 protein and HMB45 (Photo. 7) and negative for keratin, CEA, CAM5.2, LCA, Ki-1, AFP, HCG, NSE, chromogranin A, synaptophysin and GFAP. Melanosomes, mainly stage I and stage II, were observed in the cytoplasm of the tumor cells using electron microscopy (Photo. 8).

Based on the above findings, the diagnosis of amelanotic melanoma was confirmed. A whole-body gallium scintigraphy examination revealed hot spots in the head and anterior mediastinum. At this stage, the possibility of brain metastases from the amelanotic melanoma of the mediastinum was also considered. An extensive clinical examination was performed, including the skin, oral mucosa, alimentary tract and abdominal cavity, but no other tumors were detected, other than those in the brain and thymus. At this time, the serum 8-S-cystinal/dopa level was examined and found to be 8.8 nMol/L (standard value: 1.5-8.0 nMol/L). Therefore, a diagnosis of primary amelanotic melanoma of the mediastinum was considered to be the most likely, in spite of its extreme rarity. A tumorectomy for the tumor in the anterior mediastinum was performed 1 month and 20 days after admission. Macroscopically, the tumor was well demarcated, yellowish-white in color, hemorrhagic and necrotic (Photo. 9). Congestion was also observed at the periphery of the tumor. The cytological, histological, immunohistochemical and electron microscopic findings for the mediastinum tumor were the same as those for the metastatic brain tumors. Consequently, a morphological diagnosis of amelanotic melanoma of the mediastinum with brain metast-
tases was made. After the operation, radiation therapy and chemotherapy were administered, but the patient died 10 months after the onset of symptoms from metastases to other organs.

III. Discussion

An extremely rare case of amelanotic melanoma of the mediastinum with brain metastases is reported, including a description of the cytological, histological, immunohistochemical and electron microscopical findings. Malignant melanomas account for only 1.9% of metastatic brain tumors, compared to 5.4% for anaplastic large cell carcinomas and 5.9% for malignant lymphomas.

A melanoma in which pigment deposition cannot be observed macroscopically is termed an amelanotic melanoma, even if melanin formation is detected in a few tumor cells under careful histological observation.

In this case, a slight melanin pigment was observed in only a few tumor cells, making a definitive diagnosis of amelanotic melanoma difficult to support based only on the findings of an intraoperative HE stain preparation.

Histologically, the tumor cells tested positive when exposed to the Fontana-Masson stain. The tumor cells also tested positive immunohistochemically for S100 protein and HMB-45, and melanosomes, mainly stage I and stage II with a few stage III and stage IV bodies were observed in the cytoplasm of the tumor cells using electron microscopy. These observations are compatible with a diagnosis of amelanotic melanoma. Furthermore, the possibility of a melanotic neuroectodermal neoplasm and a pigmented carcinoid tumor were excluded by the negative immunohistochemical stains for NSE and chromogranin. Furthermore, in spite of a detailed whole-body examination, no other primary site for a malignant melanoma was detected, other than in the anterior mediastinum. Therefore, a diagnosis of amelanotic melanoma of the mediastinum with brain metastases was confirmed.

The histogenesis of malignant melanomas of the mediastinum is unclear. Regarding the histogenesis of malignant melanomas of the posterior mediastinum, the possibilities of tumorigenesis from the sympathetic chain or neuroendocrine cells have been proposed. On the other hand, the histogenesis of malignant melanomas of the anterior mediastinum is difficult to speculate upon. Benign nevus cells of the thymus have been proposed as the original cells in malignant melanomas of the thymus. In our case, however, thymic tissue, nerve cells, and nevus cells were not detected histologically. Therefore, the origin of the amelanotic melanoma in this particular case cannot be determined. However, nevus cells in the neural crest are generally considered to be the origin of malignant melanomas of the mediastinum. Thus, the tumor cells in this particular case may have originated from nerve cells in the neural crest.

In conclusion, the possibility of an amelanotic melanoma should be considered when cases are encountered where a definitive diagnosis of carcinoma or sarcoma is difficult to obtain, even if the primary tumor is located in the mediastinum. Furthermore, we would like to emphasize that brain tumor consultations prior to surgery are extremely important.
要約

背景: 細胞内の黑色素がまれで、これまでに17例の報告をみるが、その中でも無色素性黑色腫はきわめてまれてで、これまでに1例の報告をみるに過ぎない。転移をきたし、その術中迅速診断に細胞診が有用であった前縦隔無色素性黑色腫を経験したの報告する。

症例: 55歳、男性、頭頂葉を前頭葉に直径2cmと0.3cmの境界明瞭な円形腫瘤を認めた。前縦隔にも境界明瞭な5×3.5cmの腫瘤がみられた。腫瘤の術中迅速組織診断では、紡錘型～類円形の異型細胞が多数みられた。未分化癌、未分化大細胞性リンパ腫も考えられた。細胞診では、核は偏位性で大型の核小体を有し、核内細胞体である。いわゆるアピッツ小体もみられ、また一部の細胞にわずかに褐色顆粒を認め、無色素性黑色腫を疑った。術後の病理で、フォンクンタ・マッソ染色。ビメンチン、SiO2蛋白、HMB45が陽性で、電顕でメラノソームも確認され、無色素性黑色腫と診断した。前縦隔腫瘍摘出術が施されたが、灰白色腫瘍で、細胞組織学的、免疫組織学的、電顕的所見は腫瘍と同じ所見であり、前縦隔無色素性黑色腫の転移と診断した。

結論: たとえまれた無色素性黑色腫でも、細胞所見が広範かつ詳細に観察できる細胞診が術中迅速診断に有用であることを強調したい。

References


写真説明

Photo. 3 The tumor cells are large and discohesively arranged. The nuclei of the tumor cells are eccentrically located and contain distinct, large nucleoli and a few inclusion bodies, so-called "Apitz's bodies" (The arrows in photos a and b show the "Apitz's bodies") (a: Pap. stain, x 40. b: Giemsa stain, x 40).

Photo. 4 The cytoplasm of the tumor cells is abundant, and brownish-black pigments are observed in only a few tumor cells (The arrow shows the brownish-black pigments.) (Pap. stain, x 40).

Photo. 5 Histiocytes with brownish-black pigments are scattered around the tumor cells (The arrow shows the brownish-black pigments.) (Pap. stain, x 40).

Photo. 6 Brownish-black pigments are observed in only a few cells (The arrow shows the brownish-black pigments.) (HE stain, x 40).

Photo. 7 A few tumor cells were immunohistochemically positive for HMB45 (Immunohistochemical stain for HMB45, x 200).

Photo. 8 The tumor is well demarcated, yellowish-white in color, soft and hemorrhagic. Congestion is visible at the periphery of the tumor.