

# Neuroendocrine carcinoma arising in a wound of the postoperative maxillary sinus

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## Abstract

We report a case of a neuroendocrine carcinoma arising in a wound of the postoperative maxillary sinus that was difficult to distinguish from a postoperative maxillary cyst. The patient was a 65-year-old Japanese woman who complained of left exophthalmos with cheek swelling and eye movement disorders. In past history, she had, 40 years previously undergone operation on the bilateral maxillary sinus by Caldwell-Luc's method. In a preoperative computed tomography, a mass occupied the left maxillary sinus showing irregular densities with destruction of the posterior bone walls and invasion into the left orbital. Both T1 and T2 weighted magnetic resonance imaging showed low intensities and unevenness in the mass. We performed a biopsy of the maxillary tumor according to Caldwell-Luc's method. Histological examination diagnosed neuroendocrine carcinoma. Radiation therapy (total 66Gy) resulted in partial response for this tumor. However, sinonasal neuroendocrine carcinoma has been identified as highly aggressive, with a high probability of recurrence and metastasis.

## Introduction

Maxillary carcinoma has seldom been known to arise in the postoperative maxillary sinus. Primary neuroendocrine carcinomas of the paranasal sinuses are newly recognized, extremely uncommon, and aggressive tumors with the capacity to metastasize locally and distantly.<sup>1-3</sup> We encountered neuroendocrine carcinoma arising in the wound of a postoperative maxillary sinus. In preoperative diagnosis, it was difficult to discriminate between maxillary carcinoma and postoperative maxillary cyst. Biopsy of the maxillary mass revealed neuroendocrine carcinomas. After biopsy, tumors became partial remission in response to radiation therapy. This case suggests that the possibility of a carcinoma should be kept in mind in cases of postoperative maxillary sinus. Below we describe our case, as well as some of

the considerations suggested by the literature on this topic.

## Case Report

A 65-year-old Japanese woman consulted our hospital with a 1-week history of left exophthalmos with cheek swelling and eye movement disorders. Forty years prior, she had undergone an operation on the bilateral maxillary sinus by Caldwell-Luc's method. In a preoperative computed tomography (CT) scan, a mass occupied the left maxillary sinus showing irregular densities with destruction of the posterior bone wall and invasion into the left orbital (Figures 1 and 2). Both T1 and T2 weighted magnetic resonance imaging (MRI) showed low intensities and unevenness in the mass (Figure 3). Thus, CT and MRI suggested a solid mass in the maxillary. At the first medical examination, we suspected carcinoma arising in the postoperative maxillary sinus in addition to postoperative maxillary cyst. We performed biopsy of the maxillary tumor according to Caldwell-Luc's method. On the histological examination, the carcinoma tissues showed nesting patterns with necrosis, proliferation of cells with round nuclei and numerous abnormal mitotic features (Figure 4). Immunohistochemical studies showed positive staining for keratin, CAM5.2, and CD56, but not LCA (leukocyte common antigen). From the above results, we diagnosed neuroendocrine carcinoma. After biopsy, radiation therapy (total 66Gy) resulted in partial remission (PR) for this tumor. We consulted her concerning radio-chemotherapy or chemotherapy after radiation therapy for the remains of the tumors, but she refused the above combined chemotherapy. Regression of the tumor after therapy has been continued 24 months.

## Discussion

Forty years previously, the patient had undergone an operation on the bilateral maxillary sinus by Caldwell-Luc's method. The majority of histopathological classifications of maxillary carcinomas are squamous cell carcinoma. Squamous cell carcinoma can be seldom observed in wounds of the postoperative maxillary sinus because removal of the maxillary mucosa membranes by Caldwell-Luc's method eliminates the place where squamous cell carcinoma arises. Silva<sup>2</sup> and Mendeloff<sup>3</sup> suggested olfactory epithelium as the original cell of neuroendocrine carcinoma. Schall<sup>5</sup> reported sphenopalatine nerve. A main aggressive finding in this case showed destructions of the posterior bone wall in the maxillary sinus.

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Therefore, the origin of this neuroendocrine carcinoma may be sphenopalatine nerve. Neuroendocrine carcinoma consists of carcinoid and small cell carcinoma. It is difficult to be discriminate between carcinoid and small cell carcinoma. Moreover, the neuroendocrine carcinoma of nasal-paranasal has not been classified. Therefore, Tojima<sup>6</sup> described it as small cell neuroendocrine carcinoma. In general, the cyst showed high intensities by T2weighted MRI.<sup>7</sup> In this case, T2 weighted MRI showed low intensities with unevenness in the maxillary mass. Therefore, it was difficult to preoperatively distinguish carcinoma from a postoperative maxillary cyst. Finally, we diagnosed neuroendocrine carcinoma by biopsy. Silva *et al.*<sup>2</sup> the first proposed sinonasal neuroendocrine carcinoma as an entity. In this case, destruction of the posterior bone wall and aggressive invasion into the orbital were found on CT. Smith *et al.*<sup>3</sup> reported that sinonasal neuroendocrine carcinoma was a rare, and aggressive neoplasma.<sup>6,8,9</sup> Our hematoxylin and eosin staining showed nesting patterns with the cells having round nuclei. These findings have been reported as one of features of the neuroendocrine carcinoma. It has been known that it is difficult to discriminate between the neuroendocrine carcinoma and olfactory neuroblastoma because the olfactory neuroblastomas as well as neuroendocrine carcinomas have filaments, microtubules, and secretory granules on electron microscopy.<sup>10</sup> Immunohistological examinations are helpful for the diagnosis. Our case showed positive staining for keratin, CAM5.2, and CD56. Their

antibodies can be used to detect neuroepithelia. CAM 5.2, epithelia membrane antigen, neuron specific enolase, synaptophysin, and chromogranin were reported to be reactive for neuroendocrine epithelia.<sup>1,3,9</sup> Keratin is negative for olfactory neuroblastoma.<sup>11</sup> Our patient was treated by radiation therapy alone. She has been alive 24 months after therapy with regression of the tumor. Presently, radiation therapy has been considered to be the first choice for the therapy of neuroendocrine carcinoma.<sup>12,13</sup> Some cases have undergone chemo-radiotherapy.<sup>6,13,14,15</sup> Morikawa<sup>13</sup> reported that a patient treated with chemo-radiotherapy was alive 21 months after diagnosis without local recurrence and distant metastasis. Reversely, Tojima<sup>6</sup> documented that a patient received chemo-radiotherapy died from bone metastasis 7 month after diagnosis. Takahashi<sup>14</sup> performed chemo-radiotherapy in 2 cases. But they died 6 months (bone metastasis) and 15

months (liver and brain metastasis) after diagnosis. Georgiou<sup>15</sup> described that despite radiotherapy and chemotherapy; the patient died 4 months after diagnosis due to widespread dissemination and bone marrow failure. From the above reports, there has been no evidence of any difference in effectiveness between radiation therapy alone and chemo-radiotherapy. Bailey<sup>16</sup> and Cartrell<sup>17</sup> reported that only radiation therapy contributed to remission. Sinonasal neuroendocrine carcinoma is identified as highly aggressive, with a high probability of recurrence and metastasis. Takahashi *et al.*<sup>14</sup> reported that the 5-year mortality of nasal-paranasal neuroendocrine carcinoma (30 cases) was 69%. Perez-Ordenez *et al.*<sup>1</sup> reported that, out of 6 patients, 4 were alive with disease recurrence and 2 had died of the disease. Slivia *et al.*<sup>2</sup> reported that recurrences and metastasis in 70% of the case occurred later than the third year. Multiple recurrences

were present in 54% of the cases. The metastases affected lymph nodes, brain and spine. Therefore, careful follow-up after treatment of this disease is indicated.

## Conclusions

We encountered a very rare case that a neuroendocrine carcinoma arising in a wound of the postoperative maxillary sinus was difficult to distinguish from a postoperative maxillary cyst. MRI and immunohistological examinations (e.g., Keratin, CAM5.2 and CD56) were helpful for diagnosis of this case. Radiation therapy has been considered the first choice for the therapy of neuroendocrine carcinoma. In our case, radiation therapy (total 66Gy) resulted in PR for this tumor. Regression of the tumor after therapy has been continued 24 months.

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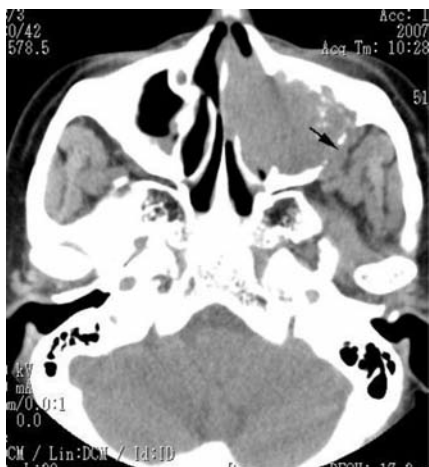


Figure 1. In the preoperative computed tomography, a mass occupied the left maxillary sinus, showing irregular densities with destructions of the posterior bone wall (arrow).



Figure 2. In the preoperative computed tomography, a mass occupied the left maxillary sinus, invading the orbita (arrow).



Figure 3. T2 weighted magnetic resonance imaging showed low intensities with unevenness in the mass and destructions of the posterior bone wall (arrow).

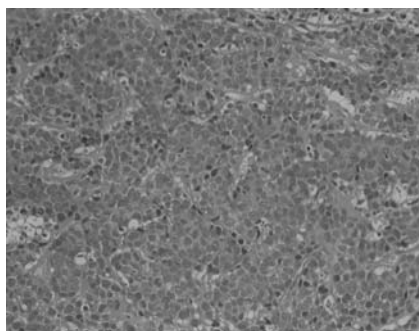


Figure 4. Histopathological examination (H&E staining, X200) revealed nesting patterns with necrosis and the proliferation of cell round nuclei.

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