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Anaplastic thyroid carcinoma transformation in a lateral neck node metastasis – A case report and a review of the literature

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ABSTRACT
Anaplastic thyroid carcinoma is thought to be derived from previous existing papillary or follicular thyroid carcinoma that dedifferentiates into its anaplastic counterpart. We present a case where this type of dedifferentiation occurs at a metastatic site in a regional lymph node, years after the primary papillary thyroid tumor had metastasized.

Introduction
Papillary thyroid carcinoma (PTC) is the most common malignancy of the thyroid and accounts for up to 80% of all thyroid carcinomas. It carries an excellent prognosis, with 10-year survival of over 90% [1]. Anaplastic thyroid carcinomas are much rarer, representing approximately 2% of all thyroid cancers. These, however, are aggressive in behavior and carry a very poor prognosis, with mean survival of six months after diagnosis. Anaplastic thyroid carcinomas are responsible for almost half of thyroid cancer-related deaths [2].

It has been widely accepted that anaplastic thyroid carcinomas arise from a previous existing papillary (PTC) or follicular carcinoma of the thyroid, with PTC being the most common pre-transformational subtype [3]. It is much rarer that anaplastic transformation occurs at a metastatic site, whether this being a metastatic lymph node or distant metastatic site. We present a case where an anaplastic carcinoma developed in a lateral neck node metastasis without transformation of the primary.

Clinical summary
A 79-year-old male presented to his primary physician because of intermittent fevers for a few months without any other symptoms. His prior medical history was remarkable for prostate cancer, depression and repeated lower respiratory tract infections and urinary tract infections.

During the workup he developed a rapidly growing tumor on the right side of his neck which had developed over just a few days. A CT scan of the neck and chest was obtained urgently. It showed a large tumor (6 × 7 × 4 cm) in the lateral neck compartment, fairly well circumscribed but with central necrosis (Figure 1). A calcified nodule in the right thyroid lobe was discovered as well. When reviewing CT scans of the patient from three years prior it appeared as if this tumor was also present then, but much smaller in size (Figure 2). At that time, it was described as an enlarged lymph node, but no further workup was performed. There were no signs of distant metastases.

The patient was referred urgently to our department for further workup. On ultrasound the tumor was hypoechogenic with microcalcifications (Figure 3). Core biopsies taken from the tumor showed findings most consistent with a metastasis from an anaplastic thyroid carcinoma. When discussing the diagnosis with the patient a week later the tumor had gotten visibly larger. He was scheduled for urgent surgery.

Two days later the patient was admitted for a right hemithyroidectomy and a radical right neck dissection.

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At surgery the tumor in the neck was fairly well circumscribed, but with visible invasion of the prevertebral musculature. The right lobe of the thyroid gland was removed as well.

The pathologic examination showed a large metastasis with mixed PTC and anaplastic thyroid carcinoma (Figure 4) as well as metastases of PTC in 2 of 25 lymph nodes. In the right lobe of the thyroid

Figure 1. CT scan of the neck showing a well circumscribed large tumor (6 × 7 × 4 cm) in the lateral neck compartment with central necrosis.

Figure 2. CT scan of the neck three years prior; a tumor present at the same site, then described as an enlarged lymph node.

Figure 3. Ultrasound image of the tumor showing the hypoecho genetic mass with multiple microcalcifications.
there was multifocal PTC but no focus of anaplastic carcinoma.

Postoperatively the patient did well. He was discharged on the fourth postoperative day and was referred to the radiation oncology department for postoperative radiation therapy. He started radiation therapy 3 weeks after surgery and received 66 Gy to the neck. Three months after he finished the radiation he developed aspiration pneumonia and died of sepsis. There was evidence of metastases in the lungs and carcinomatosis in the abdomen on CT scans. An autopsy was not performed.

Discussion

Prognosis of primary anaplastic carcinoma of the thyroid is poor. However, the prognosis of patients with a PTC primary but a dedifferentiated anaplastic carcinoma metastasis is less known. A few case reports have been published, but no statistic mortality rate can be deduced from these case reports.

Ito et al. presented five cases of PTC showing anaplastic transformation in regional lymph nodes that were curatively resected. Of these 5 patients two died from the malignancy, two patients survived up to the publication of the article (6 and 85 months after resection) and one patient died from other causes [4].

Presentation of these type of malignancies, i.e. dedifferentiation of metastatic PTC in lymph nodes, is often that the patient notices a rapidly enlarging cervical mass [5,6]. If distant metastasis is already present at the time of diagnosis the presentation can vary; the patient can present with systemic symptoms of lethargy, anemia, tiredness, etc. [7], or the patient can present with local pain in the area of metastasis [8]. In the case presented by Benedict and Costa the diagnosis of metastatic anaplastic transformation of a primary PTC was made incidentally [9].

There are reports of anaplastic transformations of PTC tumors at distant metastatic sites. Both Al-Qsous and Miller and Abe et al. reported, in two separate case reports, anaplastic transformation in multiple lung metastases from differentiated PTC [7,10]. In both cases the patient had been treated for PTC a decade earlier. This behavior, i.e. metastatic anaplastic transformations of PTC many years after discovery of the thyroid primary tumor, seems to be a common denominator in case reports similar to ours. Sotome et al. reported a case of anaplastic transformation of a metastatic PTC in the retroperitoneum that presented 17 years after the primary thyroid tumor was resected [8]. It is also of interest that anaplastic transformation of PTC metastasis has been reported to occur synchronously at several metastatic sites, as reported by Benedict and Costa [9]. In our case the anaplastic transformation of the PTC metastasis probably occurred more than three years after the primary PTC tumor had metastasized, considering the CT scan results from 2014 when a tumor at the exact same site was described as an enlarged lymph node.

Treatment for metastatic anaplastic transformation of PTC depends on the location but in our case consisted of ipsilateral hemithyroidectomy with ipsilateral modified radical neck dissection, followed by radiotherapy. Ito et al. reported five separate cases in their article, where all patients underwent curative resection, although postoperative radiotherapy was only reported in three of the patients [4]. When distant metastasis is present upon diagnosis the treatment is radiation therapy, with or without surgical treatment, but always with the addition of chemotherapy [11].

Figure 4. Metastatic PTC (on the right) with anaplastic transformation (on the left).
Our case highlights the aggressive nature of anaplastic tumors, considering that in a matter of less than two weeks an anaplastic dedifferentiated tumor had grown from being unpalpable to a mass over 8cm in diameter.

Conclusions
Anaplastic thyroid carcinoma is thought to arise by progressive accumulation of genetic mutations in previously existing papillary or follicular thyroid carcinoma. Very rarely this transformation occurs at a metastatic site, as in the case we are reporting. Not much is known about prognosis for these patients because of how rare these occurrences are.

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Written informed consent for publication was obtained from relatives.

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