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CASE REPORT

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Metastasis of colon cancer to the thyroid: a case report and review of the literature

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ABSTRACT

In France, colorectal cancer is the third most common cancer in males and the second most common cancer in females. Thyroid metastasis from CRC is rare. The incidence of metastasis to the thyroid gland in autopsy series varies from 4% to 9%, while in clinical series the prevalence of intra-thyroid metastasis is not more than 1%. We present a case of a fifty years female patient who

presented a right neck pain. Clinical and imaging examinations found an isolated right thyroid metastasis five years after the initial diagnosis of colon cancer. The thyroid metastasis was surgically resected and had adjuvant chemoradiotherapy was delivered. All patients with history of malignancy with thyroid nodule should be investigated for secondary deposits even after many years of cancer treatment. Fine nodule aspiration is a sensitive method of diagnoses. Surgical resection followed by radiation and chemotherapy should be proposed in a curative intent. Radiotherapy alone should be considered for palliation goal.

1. INTRODUCTION

In France, colorectal cancer (CRC) is the third most common cancer in males and the second most common cancer in females [1]. Intra-thyroid metastasis (ITM) is rare. The incidence of ITM in autopsy series varies from 4% to 9 % [2, 3], while in clinical series its prevalence is ranged between 1% and 2.2 % [4, 5]. The most common primary cancers that metastasize to the thyroid in autopsy series are breast, lung, and kidney [6], while in clinical series, renal cell carcinomas is the most common primary site followed by breast and lung cancer [7]. ITM from CRCs considered being extremely rare. In some clinical series, only 3 cases out of 25 patients that metastasize from colon cancer [8], and in some other series , none of the patients had a CRC [7, 9]. We present a case of a 50 year-old female with an solitary ITM 5 years after the initial diagnosis of adenocarcinoma of the right colon. In addition, we performed a review of the literature.

2. CASE REPORT

A 50 years old woman with a history of adenocarcinoma of the right colon, which was treated in March 2009 with right colectomy. The tumor was classified as pT3 N1 M0. The patient received adjuvant chemotherapy till October 2009 by 10 cycles of FOLFOX (Fluorouracil, leucovorin, Oxaliplatin) and 2 cycles without oxaliplatinum because of neuropathy toxicity. In March 2010, ovarian metastases have been diagnosed and the patient underwent bilateral ovariectomy followed by chemotherapy by FOLFIRI (Fluorouracil, leucovorin, Irinotican) until August 2010. Finally, in December 2013, she presented with a painful right neck pain, which was palpable in physical examination. CT-scan showed a right thyroid lesion in a preexisting nodule (figure 1). Fine needle aspiration (FNA) was done with a suspicion of papillary carcinoma, and in January 2014, she had undergone a right thyroid lobectomy. Pathological examination revealed adenocarcinoma, consistent with metastatic colon adenocarcinoma. During the postoperative stay the surgeon observed an abnormal expectoration in the tracheotomy tube, which was analysed by the pathology lab. Results revealed adenocarcinoma cells. However, 18F-fludeoxyglucose positron emission tomography (18FDG-PET) which was done in post operative did not retrieve any pathological uptake.

The patient had radiotherapy with concomitant chemotherapy. The dose of cabicitabine was 800 mg/m² two times per day. The radiotherapy consisted on an IMRT (intensity modulated radiotherapy) delivered with Tomotherapy Hi-ART. Prescribed dose was 66 Gy in 33 fractions, one fraction daily and 5 fractions per week. The clinical target volume (CTV) included the tumor bed and the lymph node areas that drain the thyroid (III R, IV R, VI, III L). PTV (Planning target volume) was the CTV plus an automatic expansion of 3 mm (Figure 2). The radiotherapy treatment was moderately supported by the patient. The cabicitabine was stopped at 48 Gy. However, the patient received the total irradiation dose. The patient developped a grade 3 dermatitis and grade 2 dysphagia. One year after the radiotherapy, the patient developped a recurrence in the controlateral thyroid lobe diagnosed by a pathological uptake in PET scan follow-up. The patient undergone a left thyroid lobectomy and histopathology confirmed the diagnosis. Notably, the removal was considered as complete.

The thyroid function was normal before the second surgery. After it, the patient was treated with thyroid hormone replacement until she became euthyroid. At time of last news, the patient still alive without any local recurrence or distal metastasis, and without any late complications from radiotherapy.

3. DISCUSSION

Generally, the intra thyroid metastasis is rare in autopsy series with an incidence between 3% to 8.3%, and the incidence of ITM from CRC is range between 3% and 19% [2, 3, 10, 11]. In clinical series, either the surgical or the fine needle biopsy series, the intra thyroid metastasis range between 0.15% to 1%, and the incidence of ITM from CRC are between 3.5% to 12% [4, 8, 12, 13]. In some large

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Figure 1 CT scan showing right thyroid mass (*)

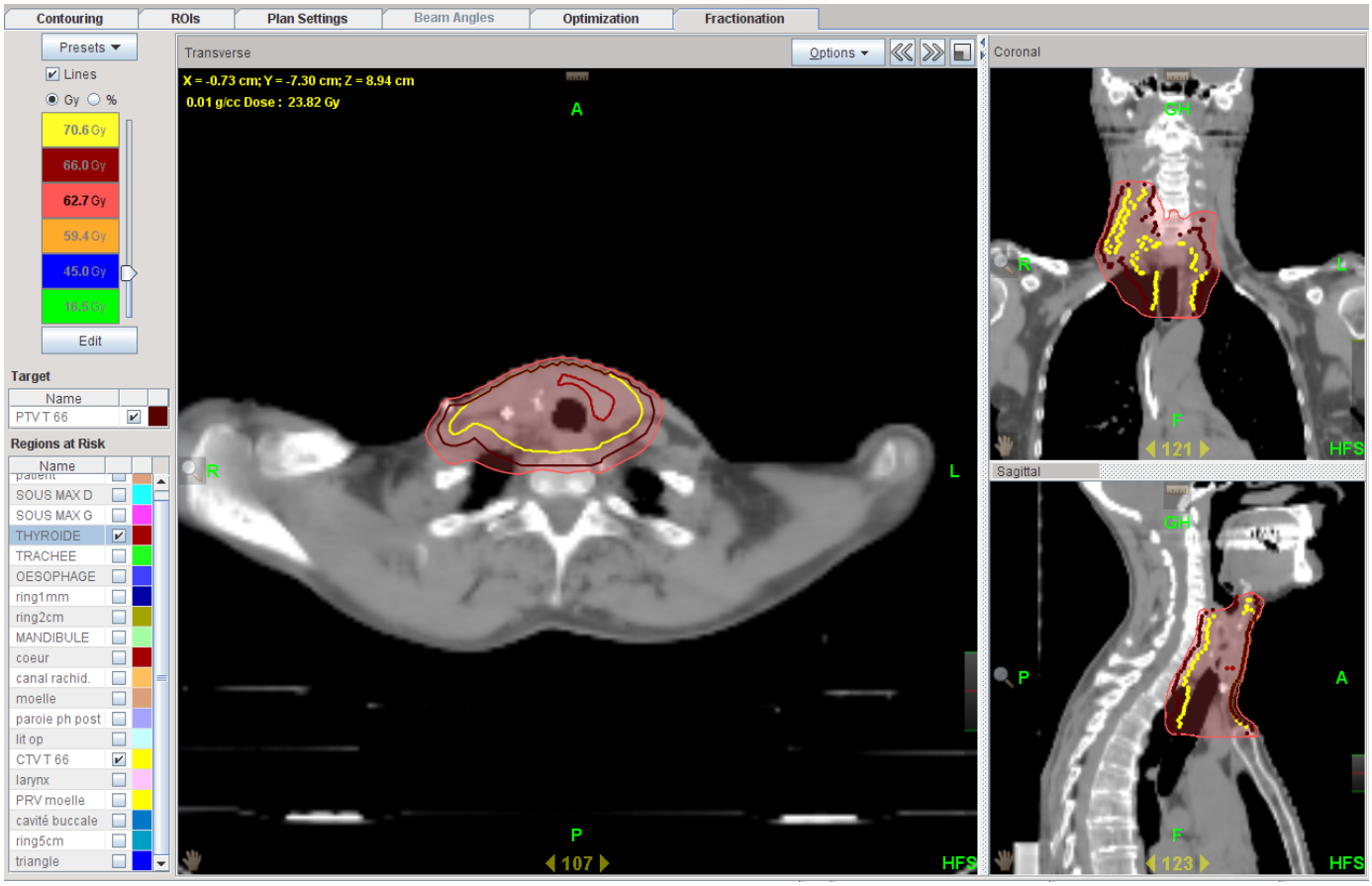

Figure 2 Dose distribution showing 95% isodose in light red, CTV (yellow), PTV (dark red), left lobe thyroid (light red).

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clinical series did not report any thyroid metastases from CRC [5, 7, 14]. Chung et al [15] reviewed all clinical reports available in the literature from 2000 to 2010. Authors found that 48% of cases were from renal cancer, 10% from CRC, 8.3% from lung cancer, 7.8% from breast cancer, and 4.1% from melanomas. The only specific CRC series was done by Lièvre et al.[16]. The reviewed all the cases of CRC in their institution and found only 6 patients with ITM from 5862 patients diagnosed with CRC (0.1%). Currently, the number of clinical cases with ITM from CRC is 65 case reports including our case (table 1). The patient age ranged from 28 to 85 years (average, 62 years). The female: male ratio was (2:1). This could suggest some influence of the hormonal environment on the development of metastasis but the origin of breast primary cancer is a reason *per se* to find this sex ratio. The delay between the initial primary diagnosis and the diagnostic of the thyroid metastasis was between 6 months and 8 years (average, 3.5 years). The reasons for the apparent rarity of ITM in patients with CRC are obscure, despite the fact that the thyroid gland has one of the richest blood supplies in the human body and the frequency of CRC. Willis [2] described factors that could explain the thyroid microenvironment unsuitable for metastasis. He hypothesized that the fast arterial flow and the high concentration of both oxygen and iodine may act as barriers to the spread of metastatic cells. Author assumed that when the thyroid gland presents adenomatous or fibrous features, the blood flow could dramatically slow down and the iodine is more diffuse leading the cancer cells to metastasize more easily., Smith et al seemed to confirm these suppositions [17] when the authors reported 11 out of 19 patients of their series that have had either adenomatous or multinodular thyroid.

In our case, the patient metastasized only to the thyroid. That suggests the presence of another way to metastasize than the classical haematogenous pathway (portal vein, vena cava), and Batson et al proposed that the vertebral venous system could be an alternative way to metastize, which could explain the dissemination into the thyroid [18].

Table 1 All cases in the literature

Number	Author	Reported year	Age	Sex	Location	Time after initial treatment (years)	Treatment	Other metastatic lesions	Prognosis (months)
1	Willis (2)	1931	54	M	Right colon	4	No	Liver, kidney, lungs	----
2	Sklaroof (24)	1954	73	F	Rectum	7	Prophylactic tracheostomy	None	2
3	Elliott and Frantz	1960	56	F	Rectum	Synchronous	Total thyroidectomy	----	3
4	Shimaoka et al. (3)	1962	50	F	Sigmoid colon	4	Total thyroidectomy	Lungs	----
5	Wychulis et al.	1964	37	F	Rectum	0.5	Rt thyroidectomy and isthmectomy	Lungs	3
6	B.Make et al.	1974	68	M	Sigmoid colon	4	Palliative RT	Liver	8
7	J.A. Thombson	1975	44	F	Right colon	4	Total thyroidectomy	Brain	9
8	Cotin et al. (27)	1979							
9	T.Ishida et al.	1982	34	M	Rectum	2	Total thyroidectomy	Generalized metastasis	7
10	Ito et al.	1983	34	M	Right Colon	2	Total thyroidectomy	Liver, Lungs	7
11	J.W Lester Jr. Et al.	1986	56	F	Colon	2.5	----	Liver, Lungs	----
12	C.Rigaud et al.	1987	68	F	Colon	2	Total	Liver, Lungs	3

							thyroidectomy and Chemotherapy		
13	C.Rigaud et al.	1987	77	M	Rectum	4	Total thyroidectomy and Chemotherapy	Liver, Lungs	1
14	E.G. Cristallini et al.	1990	64	F	Colon	4	Total thyroidectomy	Liver	>12
15	Jingu et al.	1990	48	F	Right Colon	2.5	Left lobectomy	Liver, Lungs	10
16	Matsusako et al.	1991	78	F	Right Colon	1	SubTotal thyroidectomy	----	----
17	D. Nachtigal et al.	1992	69	F	Left Colon	8	Total thyroidectomy	Lungs	8
18	Y. Shibutani et al.	1992	52	F	Sigmoid colon	3	SubTotal thyroidectomy	Lungs	8
19	Maeda et al.	1992	66	F	RightColon	1	Right lobectomy	Liver	2
20	Mase et al.	1993	----	----	Sigmoid colon	4	----	-----	----
21	Cohen Solal et al.	1993	----	----	----	----	----	----	----
22	S. Kim et al.	1994	37	F	colon	7	----	LN, Skin	>2
23	T. W. Mesko et al.	1996	59	F	Rectum	2	Right lobectomy	Vertebrae, Kidney	>36
24	P. Osin et al.	1996	70	F	Rectosegmoid Colon	Synchronous	Right lobectomy	Liver	----
25	Masuda et al	1996	73	M	Right Colon	1	Total thyroidectomy	Liver	>4
26	Masuda et al	1996	38	F	Right Colon	4	Total thyroidectomy	Liver, Lungs	5
27	Yoshimatsu et al.	1996	50	F	Right Colon	0.5	SubTotal thyroidectomy	Brain	5
28	Nakamura et al.	1997	71	F	Right Colon	5	Chemotherapy	Lung	6
29	Takashima et al.	1998	67	M	Rectum	2	----	----	----
30	Tazuke et al.	1998	61	F	Right Colon	2	Right lobectomy	----	Alive
31	C. H. Kim et al	1999	68	F	Sigmoid Colon	2	Left lobectomy and RT	Lung	----
32	K. Kameyama et al.	2000	82	M	Sigmoid Colon	2	No	Generalized metastasis	----
33	Shinohara et al.	2000	66	F	Transverse Colon	4	Subtotal thyroidectomy	Liver, Lung	>4
34	Shiga et al.	2001	36	F	Right Colon	3	Left lobectomy	Lung	>2
35	Kanaya et al.	2001	80	F	Right Colon	1.5	Total thyroidectomy	None	----
36	M. De Ridder et al. (22)	2001	75	F	Left colon	7	Total thyroidectomy and RT	None	9
37	M. S. Boleas Aguirre et al.	2001	80	F	Colon	7	----	Larynx	----
38	Ogisawa et al.	2002	58	M	Rectum	----	Tracheotomy	Lung	----

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39	Akimaru rt al.	2002	67	M	Right Colon	6	Chemotherapy	Brain, Lung	4
40	Giammaria et al.	2002	42	M	Sigloid Colon	4	Total thyroidectomy	Liver, Lung	6
41	Yamada et al.	2003	60	F	Rectum	3	Subtotal thyroidectomy	Brain, Lung	4
42	G. P. Perinu et al.	2003	43	M	Left Colon	4	----	Liver	----
43	Hacker et al. (25)	2003	----	----	Rectum	7	Total thyroidectomy	None	----
44	R. L. Witt	2003	71	M	Colon	7	Right lobectomy	Liver, Lung	----
45	Fujita et al.	2004	28	F	Rectum	Synchronous	Left lebectomy and neck dissection	Lung	6
46	Poon et al.	2004	64	M	Right Colon	1	Tracheotomy	Lung	18
47	Poon et al.	2004	53	F	Sigmoid Colon	Synchronous	Total Thyroidectomy	Liver, Lung	10
46	O. Fadare et al	2005	59	F	Sigmoid Colon	Synchronous	Total thyroidectomy and chemotherapy	Liver, Peritoneum	>12
47	Malani AK et al.	2005			Colon				
48	Phillips et al. (23)	2005	81	F	Colon	2	Total thyroidectomy	None	----
49	J. C. Youn et al.	2006	85	M	Right Colon	1.5	Chemotherapy	Adrenals, Lung	----
50	K. Kumamoto et al.	2006	66	F	Right Colon	3.5	Left lobectomy and neck dissection	Liver, Lung	----
51	W. C. Hanna et al.	2006	48	F	Left Colon	Synchronous	Right Lobectomy	Lung	----
51	Iguchi et al. (26)	2007	51	M	Sigmoid Colon	----	Total thyroidectomy	None	----
52	Cherk et al.	2008	52	M	Rectum	1.5	Right Lobectomy and Chemotherapy	Lung	----
53	Trivedi et al. (20)	2008	30	F	Rectum	8	Total Thyroidectomy and neck dissection	None	>4
54	Y. Cheung et al.	2008			Rectum				
55	Y. Cheung et al.	2008			Rectum				
56	Hyun Yoon et al.	2010							
57	I. Cozzolino et al. (29)	2010	60	M	Rectosigmoid Colon	6	Palliative RT	Liver, Lung, Bones	>72
58	K. Nakamura et al.	2011	58	F	Sigmoid Colon	5	Subtotal thyroidectomy and chemotherapy	Lung	----
59	Goatman et al.	2012	82	M	Rectum	5	Total Thyroidectomy	Lung	----

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							and neck dissection		
60	Froylich et al.	2013	62	F	Sigmoid Colon	5	Total Thyroidectomy	Lung	>24
61	Alherabi et al.	2014	40	M	Colon	----	Tracheostomy	Liver, Lung	10
62	Jin et al. (21)	2014	62	F	Rectum	2	Total Thyroidectomy and Chemotherapy	None	>24
63	Yeo et al	2014	53	M	Sigmoid Colon	1	Chemotherapy then total thyroidectomy and neck dissection	Lung	12
64	Sagarra Cebolla et al.	2015	70	F	Sigmoid Colon	Synchronous	Total Thyroidectomy and neck dissection	None	----
65	**Our Case**	**2017**	**50**	**F**	**Right Colon**	**5**	**Right Lobectomy then Concurrent Chemoradiation**	**None**	**>24**

Clinical presentation of thyroid metastasis as a palpable mass in 72% of the case, while the other 28% other cases were detected incidentally by imaging studies [19]. Isolated thyroid metastasis seems to be very rare. Only 8 cases were reported [20–26]. It's a real challenge to diagnose this relapse, especially if it occurred several years after the initial diagnosis [20, 22, 24, 25, 27]. Any patient with previous history of malignancy with thyroid mass should be evaluated for recurrent biopsy. FNA remains a sensitive and specific method to detect metastasis to the thyroid [12]. The diagnosis method of choice according to the American thyroid association guidelines is fine needle aspiration (FNA) [28]. Immunohistochemical staining should be performed to differentiate between primary thyroid carcinoma and metastatic lesions to the thyroid, these stains include ck7, ck20, thyroglobuline, and the thyroid transcription factor1 (TTF1) [29].

Also, the increase in using advanced imaging modalities like CT scans and PET scans leads to an increase in detecting thyroid metastasis from CRC [7, 16, 30]. F-18 FDG PET in particularly is useful to detect thyroid metastasis from colon cancer [26].

The modality of treatment depends on whether the goal is palliative or curative. Although the role of thyroid surgery in thyroid metastatic CRC Is unknown, the only series with several patients treated in a single institution reported that patients treated with thyroidectomy had better palliation of respiratory symptoms than those who were merely observed [16]. The treatment, surgery is considered the treatment of choice either with thyroid lobectomy or even total thyroidectomy. Patients who underwent thyroidectomy with or without adjuvant treatment had 34 months mean survival, while the patients that treated without surgery had 25 months [7]. Patients treated with total thyroidectomy have better survival results than patients treated with thyroid lobectomy [8]. In our reported case, we observed a relapse in the remained lobe, which could be a additional reason to perform total thyroidectomy.

Radiotherapy was currently proposed in a palliative intent [20, 22, 29]. All cases treated with palliative radiotherapy did mention neither the dose of radiotherapy nor the technique. We considered the patient to have an oligometastatic disease, which justified curative intent's treatment. Consequently, the cervical lymph nodes, draining the thyroid gland, were irradiated. Indeed, it was showed that the ITM from CRC are commonly associated with invaded lymph nodes [16, 20]. The delineation was performed according to the 2013 update of the guidelines of delineation of the neck nodes levels for head and neck tumors [31]. The IMRT

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chosen to treat the patient was used because this technique is the recommended for head and neck tumors as demonstrated in prospective randomized trials [32, 33].

4. CONCLUSION

ITMs are scarce. Suspicion of ITM should be diagnosis via a FNA. Treatment must be aggressive for a curative intent and triple combination, surgery followed by radiotherapy and chemotherapy, seems relevant. However, most the case can be treated only in a palliative intent and the treatment have to offer the best quality of life as possible.

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