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Thyroid metastases from colorectal cancer: The Institut Gustave Roussy experience

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ABSTRACT

The prevalence of thyroid metastases in colorectal cancer (CRC) patients is unknown. We retrieved the records of all patients with CRC and pathologically proved thyroid metastasis for the period 1993–2004. Among 5862 consecutive patients with CRC, 6 (0.1%) were diagnosed with thyroid metastases, a median of 61 months after the diagnosis of primary tumour, and a median of 19 months after the last surgical resection or radiofrequency ablation of other metastases (which were present in all cases). Signs and symptoms, when present (n = 3), consisted of cervical pain, cervical adenopathy, goitre, dysphagia, and/or dysphonia. In other cases, the diagnosis was made by positron emission tomography scanning. Thyroidectomy was performed in the 5 patients with isolated thyroid metastases, with cervical lymph node dissection being required in all cases. The only patient treated conservatively because of concomitant liver and lung metastases developed life-threatening dyspnoea, which required emergent tracheal stenting. Median overall survival was 77 months, 58 months, and 12 months after the diagnosis of primary CRC, initial metastases, and thyroid metastasis, respectively. It is concluded that thyroid metastases are rare and occur late in the course of CRC. Thyroidectomy (with cervical lymph node dissection) may result in prevention or improvement of life-threatening symptoms and prolonged survival.

1. Introduction

Thyroid metastases are uncommon, accounting for 1.5–7.5% of all thyroid malignancies.[1–3] They most commonly arise from renal, lung and breast carcinomas.[2–6] Thyroid metastases of colorectal origin seem to be very rare, as several large series of patients with thyroid metastases did not report it.[2,4,6] This retrospective study reports on all patients with thyroid metastases from colorectal cancer (CRC) seen at the Institut Gustave Roussy (Villejuif, France) during a 12-year period.

2. Patients and methods

The records of all patients with cytologically or histologically proved thyroid metastases arising from colorectal

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adenocarcinoma, seen at our institution from January 1993 to June 2004, were retrieved from our medical, surgical, and pathological computerised databases. The following data were collected and analysed: age at diagnosis, gender, primary tumour site (colon or rectum), clinical presentation and complications of thyroid metastases, interval from diagnosis of primary colorectal tumour to thyroid metastasis, presence of other metastatic sites, therapeutic management, outcome, and duration of survival.

3. Results

3.1. *Patient characteristics and clinical presentation*

Among 5862 CRC patients seen at our institution between January 1993 and June 2004, 6 (0.1%) (4 women, median age, 56 years) were diagnosed with thyroid metastases, a median of 61 months (range 14–94 months) after the diagnosis of primary tumour, and 19 months (range 3–36 months) after the last surgical resection or radiofrequency ablation (RFA) of other metastases (Table 1). In asymptomatic patients (n = 3), thyroid metastases were diagnosed by positron emission tomography (PET) scanning, ordered for pre-operative staging before lung metastasectomy, follow-up after RFA of an adrenal gland metastasis, and isolated carcinoembryogenic antigen (CEA) increase 3 years after surgical resection of primary colon cancer and liver metastasis. The remaining 3 patients presented with symptoms related to thyroid metastases (Table 1). In all 6 patients, thyroid hormone levels were normal. Thyroid metastases occurred after curative resection ±RFA of liver, lung, or adrenal gland metastases in all patients, which were considered disease-free after these procedures in all cases but one. In the remaining patient, the thyroid metastasis was diagnosed while she was receiving chemotherapy for liver and lung metastases.

3.2. *Diagnosis*

Ultrasound-guided fine-needle aspiration (FNA) cytology allowed the diagnosis of malignancy in all patients. The diagnosis of thyroid metastasis from colorectal adenocarcinoma was confirmed histologically in the 5 patients who underwent thyroidectomy. For the remaining patient with colon cancer metastatic to the liver and lungs, the diagnosis of thyroid metastasis was made on FNA findings, normal thyroglobulin serum levels, and no clinical, computed tomography (CT), or PET scan evidence of other primary cancer. Tumoural thyroglobulin immunostaining was negative in the 2 patients in which it was performed.

3.3. *Treatment*

Thyroidectomy with central and lateral neck lymph node dissection was performed in 5 patients (Table 1). In all cases, jugulocarotid or recurrent nerve chain lymph node metastases were found. One patient did not undergo thyroidectomy, because of concomitant liver and lung metastases. Despite chemotherapy, metastatic goitre progressed and caused dyspnoea and dysphagia, which promptly resolved after radiotherapy and tracheal stent insertion.

3.4. *Survival*

Median overall survival after the diagnosis of thyroid metastasis was 12 months (range 8–18 months). For the 5 patients who underwent thyroidectomy, postoperative survival was 10 months (range 2–18 months). Median overall survival was 77 months (range 24–102 months) after the diagnosis of primary CRC, and 58 months after the first diagnosis of metastases (range 25–75 months).

4. Discussion

The actual frequency of thyroid metastases in patients with CRC is not known. To our knowledge, this study is the first specifically to address this issue in a large cohort of CRC patients. We found only 6 cases (0.1%) of thyroid metastases among 5862 consecutive CRC patients prospectively registered over more than a decade in our institution. This prevalence is much lower than that previously reported in autopsy studies, ranging from 1.25% in unselected patients up to 24% in cancer patients.[1,7–11] The reasons for the apparent rarity of thyroid metastases in patients with CRC are obscure, with respect to the rich vascularisation of the thyroid gland and the frequency of CRC, in which haematogenous metastatic spreading is common. Indeed, renal, breast and lung carcinomas have been the most frequently identified sources of thyroid metastases, followed by melanomas and lymphomas,[1–6,10] and colorectal origin has been very rarely reported.[2,4,6] Thyroid metastases have been found in 1.7% of 118 patients with CRC in an autopsy series of 1000 cancer patients.[12] The prevalence of thyroid metastases in our series is probably underestimated, as half of the patients were asymptomatic, and metastases occurring in sites other than the lungs, liver and peritoneum were not systematically searched for. The wider diffusion of PET scan and of thoracic CT scan is likely to lead to an increased frequency of thyroid metastases in CRC patients, as it was observed in our series (in which 2 cases were observed in the first 10-year period while the other 4 were diagnosed in the last 2 years), as well as in others.[4,11,13–17] Moreover, overall survival in patients with metastatic CRC has nearly doubled in the last 10 years with the advent of more effective anticancer drugs that may favour the occurrence of metastases in unusual sites, such as the thyroid gland. Accordingly, survival was remarkably long in our patients (median, 77 months) and exceeded 24 months in all patients since the first diagnosis of metastases.

The diagnosis of thyroid metastases in patients with CRC may be challenging. First, the median interval from the diagnosis of colorectal primary to that of thyroid metastasis may be long (61 months in our series, and up to 9 years in others).[18] Secondly, symptoms are often lacking and thyroid function mostly remains normal, although hypothyroidism[19] and hyperthyroidism[13] have been reported. Increased CEA level may be the only manifestation in asymptomatic, isolated cases.[14,15] Finally, thyroid metastases may not be distinguishable from primary thyroid malignancies on imaging.

Patients with thyroid metastases arising from any cancer are often deemed to harbour a dismal prognosis, owing to an usually long-standing history of associated, non-thyroid metastatic disease.[4,5] However, all patients but 1 in our series were

Table 1 – Patient characteristics and outcome

Sex, age (years)	Primary	Non-thyroid metastases	Time to diagnosis of thyroid metastases (months)		Revealing symptoms	Thyroidectomy (resection margin status)	Other treatments	Survival (months)		Current status	Overall survival (months)
			From diagnosis of primary	From last surgery or RFA for other metastases				After diagnosis of thyroid metastases	After thyroidectomy		
M, 65	Colon	Liver (1*) Adrenal gland (1**)	14	3	–	Right (R0) then total (R0) (left thyroid recurrence)	–	11	10	Alive, recurrence-free	24
F, 48	Rectum	Lung (3*/1**)	79	21	–	Total (R0)	–	10	7	Alive, recurrence-free	88
F, 55	Colon	Liver (1*) Lung Brain	38	34	–	Total (R0)	CT	18	17	Dead (lung and brain metastases)	56
M, 45	Colon	Lung (2*)	53	16	Pain Dysphonia	Total (R1)	CT	18	18	Dead (lung metastases)	71
F, 47	Colon	Liver (2*) Lung (3*)	94	5	Goitre Pain Dysphonia	Total (R1)	CT+RT	8	2	Dead (digestive haemorrhage)	102
F, 51	Colon	Liver (2*) Ovary (1*) Lung	69	36	Dysphonia Adenopathy	–	CT RT Tracheal stent	14	–	Dead (lung metastases)	82

RFA, radiofrequency ablation; CT, chemotherapy; RT, radiotherapy.
*/**n, number of *surgical or **RFA procedures.

disease-free after curative resection or RFA of non-thyroid metastases, and cases of isolated thyroid metastases have been reported.[14] Moreover, median overall survival after the diagnosis of thyroid metastasis was 12 months in our series, and other studies have reported survivals up to 26 months[17] after surgical[15,17] or medical[16] management of thyroid metastases from CRC. These data argue in favour of an active diagnostic and therapeutic management of such patients.

The role of thyroidectomy in the management of colorectal thyroid metastases is unknown. In case of isolated thyroid metastases from other cancers than CRC, thyroidectomy has been advocated since it has been shown to improve patient survival compared with historical, non-surgical controls,[4] and may even be curative.[2,4,6,11] In our series, postoperative survival was 10 months, which is lower than that currently observed after resection of lung or liver metastases. As 2 of our patients died from metastatic recurrence in sites other than thyroid metastases, one may suggest that thyroidectomy should be indicated only for patients with symptomatic thyroid involvement. However, although conservative management may result in long survival, and seems the most logical approach in patients with multi-metastatic disease,[16,20] the only patient who did not undergo thyroidectomy in our series developed life-threatening respiratory symptoms, suggesting that thyroidectomy should be discussed systematically even in asymptomatic patients. Radiotherapy may be advocated in case of life-threatening or disabling symptoms (e.g. dyspnoea, dysphagia), but its efficacy is inconstant.[3,17,20] In such cases, oesophageal or tracheal stenting may result in rapid symptomatic improvement. If thyroidectomy is performed, in our opinion it should be a total thyroidectomy with extensive lymph node dissection, since all cases in our series presented lymph node metastases. In fact, such lymph node involvement is less common in non-colorectal thyroid metastases (data not shown).

In conclusion, thyroid metastases are rare and occur late in the course of CRC, but may be seen increasingly as more effective treatments will result in longer survival. Symptomatic improvement and prolonged survival may be obtained with thyroidectomy and lymph node dissection.

Conflict of interest statement

None declared.

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