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A Rare Case of Pituitary Gland Metastasis from Rectal Cancer: A Case Report and Mini Review

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Abstract

Colon cancer is one of the most frequent cancers worldwide and often the diagnosis is made in a local advanced or metastatic stage. Brain metastasis represents a sign of poor prognosis and due to the variability of symptoms and clinical manifestation a challenge for each oncologist. In the following pages we will present a unusual case of pituitary metastasis from a rectal cancer.

Keywords: Brain metastasis; Colon cancer; Endocrine dysfunction

Introduction

Colon cancer is the third most frequent cancer in males and the second in women, with almost 1.1 million new cases and more than 550.000 deaths in 2018 according to GLOBOCAN database [1]. Metastases from colon cancer occur most frequently in the liver, lungs and peritoneal cavity [2]. Brain metastases from colon cancer are very rare. Pituitary gland metastases represent 0.4% of all intracranial metastatic cancers and the most common primary site is breast (37.2%) and lung cancers (24.2%) [3-5]. The incidence of pituitary metastasis arising from colorectal cancer is 2.4% [6-8]. Pituitary metastases are often asymptomatic, but when symptoms are present patients might present visual disturbances to severe endocrine dysfunction such as diabetes insipidus. Here we report a rare case of a patient, who developed pituitary metastases from a colorectal cancer 4 years after starting treatment.

Case Report

A 44-year old Caucasian male was admitted with rectal bleeding. A colonoscopy was performed and showed a hemorrhagic vegetative tumor located 9 centimeters from the ano-cutaneous line. Ultrasound revealed some liver hemangioma and circumferential thickening of the rectum wall extended on a length of almost 6 centimeters and 2 small lymphadenopathies. Based on the clinical and imaging criteria, we established the diagnosis of inferior rectal G2 adenocarcinoma (clinical stage T3, N1b and Mx). We started the treatment with a short course of radiotherapy, 25 Gy in 5 fractions, followed shortly after by an anterior recto-sigmoid resection with colo-anal anastomosis and a protective transversostomy. The final diagnosis after this intervention was pT3N2aMxL0V0R0 recto-sigmoid intermediate differentiated cancer. After surgery, the patient received 8 cycles of adjuvant chemotherapy, Capecitabine and Oxaliplatin, but with very important neurotoxicity due to the use of Oxaliplatin.

After 1 year of disease free, a CT (computer tomography) scan showed multiple pulmonary metastases (the biggest 36 mm), mediastinal adenopathies (21 mm). Taking in the considerations the previous chemotherapy toxicities and the presence of mutation c.35G>C (p.G12A) in exon 2 of the K-RAS oncogene, the patient started again this time with Capecitabine, Irinotecan and Bevacizumab for 25 cycles. The chemotherapy was associated with dermatological toxicity grade 3 from Capecitabine and diarrhea from Irinotecan, both of them resolved after dose reduction. After two years of chemotherapy, the patientt presented polydipsia and polyuria. Further investigations revealed the decrease of the antidiuretic hormone <1 ng/ml, but the CT scan excluded any brain metastasis and showed regression of the pulmonary metastasis. 4 months after continuing the same chemotherapy, the patient presented headache, vomiting, visual disturbances, legs pain, and diarrhea. The blood tests showed pituitary hypofunction through the decrease level of cortisol, follicle-stimulating hormone, luteinizing hormone, thyroid-stimulating hormone and elevated level of prolactin **(Table 1).** The brain magnetic resonance imaging shows a pituitary mass and a left cerebellar metastasis. Later the patient underwent brain surgery with the resection of the pituitary mass and the histopathological result revealed a metastasis from the colorectal cancer. After surgery, the patient received decompressive radiotherapy together with the administration of metronomic Capecitabine. After 4 months from the diagnosis of pituitary metastasis the patient presented with altered general condition, comatose and after a few days he died.

Discussion

Metastasis in the pituitary gland is very unusual with an incidence of 0.14-28.1% of all brain metastasis [8]. Pituitary metastases were first described by Benjamin in 1857 an autopsy of a patient with malignant

Hormone	Result	Normal value
Antidiuretic	<1 ng/L	2-8
Cortisol	8.2 nmol/L	172-497 (7-10 AM) 71.1-286 (4-8 PM)
Follicle-stimulating hormone	0.4 mUI/mL	1.5-12.4 in men
Luteinizing hormone	<0.1 mUI/mL	1.7-8.6 in men
Thyroid-stimulating hormone	<0.005 microUI/mL	0.27-4.2
Prolactine	734 micro/mL	98-456

Table 1: The blood levels modifications of the pituitary hormones in our patient.

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Reference	Clinical manifestation	Time after the initial diagnosis	Treatment	Survival after pituitary metastasis diagnosis
Javanbakht et al.	Visual impairment, headache	1 year	TSS	3 years
Ratti et al.	Diabetes insipidus, right temporal hemianopsia	5 years	TSS	8 days
Castle-Kirszbaum	Panhypopituitarism		TSS	NR
Issa et al.	Left temporal hemianopsia	4,5 years	Gamma knife radiation therapy + palliative chemotherapy	17,5 mo
Tomita et al.	Subarachnoid hemorrhage	NR	TSS	NR
Neromi et al.	Bitemporal hemianopsia	NR	NR	NR
Nimura et al.	Diabetes insipidus	NR	NR	NR
Salldecker	Panhypopituitarsm	2 years	TSS	NR
Noga et al.	Progressive blurred vision, incomplete hemianopsia	5 MO	Right frontotemporal craniotomy	
Ozturk et al.	Bitemporal hemianopsia, Diabetes insipidus, central hypothyroidism	5 years	Gamma knife raiosurgery	4 MO
Thewjitcharoen et al.	Apoplexy	NR	TSS	9 MO
TSS: Transsphenoidal Surgery; NR: Not Reported				

Table 2: List of pituitary metastasis from colorectal cancer reported worldwide.

melanoma [9]. Patients with pituitary metastasis seem to have also a very advanced disease, more than five metastatic sites [10]. Komninos et al. reported in the largest review of literature that included 380 patients with pituitary metastases, only 9 cases were metastases from colorectal cancer. Studies also revealed that the majority of pituitary metastases can be found in the posterior lobe, 57%, 13% in the anterior lobe, 12% in both lobes and the remaining to the capsule or stalk [10,11]. Symptoms of pituitary metastases are reported in approximately 18% of cases. The most common manifestations are diabetes insipidus (30-60%), panhypopituitarism (7-47%), retro-orbital pain and headache (0-40%), ophthalmoplegia (15-43%) and other visual disturbances the most common being the bitemporal hemianopsia. Each category of manifestations results from a different way of dissemination. The central diabetes insipidus usually has its origin in the posterior lobe and patients can present polyuria, nicturia and polydipsia [12,13]. Panhypopituitarism diagnosis is established by the development of new-onset hypocortisolism, hypothyroidism and hyperprolactinemia. These syndromes are manifestations of pituitary failure and in the majority of the cases means that the disease in very advanced [12-14]. The visual disturbances and the ophthalmoplegia are caused by the involvement of the anterior lobe, invasion of cranial nerves III and invasion of the optic chiasm [2-17]. Pituitary apoplexy is a clinical syndrome secondary to haemorrhage in the pituitary gland and is characterized by the sudden onset of headache, visual impairment, vomiting and decreased consciousness. Usually pituitary apoplexy appears in pre-existing macroadenoma, but has been described also in patients with normal pituitary gland, lymphocytic hypophysitis and in rare cases of metastases [17,18]. Metastatic deposits can reach the pituitary gland by several routes like direct haematogenous spreading, spread from hypothalamo-hypophyseal through the portal vessels, extension from juxtasellar and skull base metastases and by meningeal spreading through suprasellar cistern [16,17] (Table 2).

Our patient symptomatology suggests us the severity of the disease and the metastatic invasion of both anterior and posterior pituitary lobes. The first symptoms developed by our patient guided us to the suspicion of diabetes insipidus. In the same time the laboratory tests showed the decrease of the antidiuretic hormone, but the CT scan of the brain was normal. Later, the patient presented signs of anterior lobe invasion such as visual disturbances, orbital pain and headache. The laboratory test revealed raised the suspicion of global pituitary insufficiency and the brain magnetic resonance imaging showed a pituitary mass. The diagnosis of pituitary metastases is based on histology due to the lack of specific clinical and radiological data. The best option is represented by complete excision because very often a simple biopsy can be irrelevant due to the fact that metastatic tumors can mimic a pituitary adenoma. In our case the diagnosis of pituitary metastases was confirmed through histopathological examination of the resection piece. The management of these type of cases must be oriented at treatment of the primary cancer, local treatment through surgery, radiation or both of them and symptomatic treatment. The supplemental endocrine treatment such as corticosteroids for hypocorticolism, thyroid hormones for hypothyroidism, desmopressin or carbamazepine for diabetes insipidus, seems to have also a significant role. Our treatment consisted of a multidisciplinary approach including surgical treatment, radiotherapy, chemotherapy and supportive treatment. The prognostic depends on many factors such as advanced disease with multiple sites of metastasis, patient's clinical status and other complications. In one study which included 52 patients, the mean survival after the diagnosis of pituitary metastases was 17 months and the overall 1-year mortality rate of 67%. The same study has showed the longest mean survival for melanoma and renal cell carcinoma, while patients with colorectal, lung, liver, prostate, breast, gastric cancer had a mean survival less than 1 year.

Conclusion

Pituitary metastases from colorectal cancer are very uncommon and usually are a sign of an advanced disseminated disease. The management of endocrine abnormalities is important to obtain a good quality of these terminally ill patients. For treating this rare complication of colorectal cancer we need a multidisciplinary team consisting of oncologist, neurosurgeon, endocrinologist and radiotherapist.

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