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Colonic mucinous adenocarcinoma with secondary in the breast: A case report and literature review

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ABSTRACT

INTRODUCTION: Secondary breast metastasis from the colonic origin is a rare phenomenon in the literature, and an estimation of an increase in the incidence has been reported in the literature to reach approximately 7%.
PRESENTATION OF CASE: We report a case of a 56-year-old male with constipation who underwent extended right hemicolectomy after confirmation of adenocarcinoma of the right colon. The patient was diagnosed with multiple metastases over 5 years and endured numerous resections of the costal margins, ribs, diaphragm, liver wedges, abdominal wall, and the small bowel. Eventually, the patient's right breast mass measured about 2.1 cm on ultrasonography and revealed metastatic adenocarcinoma of the same colonic origin. The patient started on palliative chemotherapy and was deceased after 11 months.
DISCUSSION: Comparing this case to the 56 similar cases, we found our case with an almost average time to metastasize but unfortunately with aggressive metastatic behavior to various organs. Nevertheless, the triple assessment of the breast by physical examination, radiological, and pathological studies assisted in diagnosis and early establishment of the treatment. Currently, there is no definitive guideline for the management of secondary breast metastasis from the colonic origin. We estimated the average survival rate as 6.1 months, and it was reported to reach an average of 8–10 months in the literature.
CONCLUSION: During the surveillance program of colorectal cancer, a full-body examination is warranted. Secondary breast cancer metastasis from colorectal origin behaves aggressively and a multidisciplinary approach is essential for the establishment of personalized treatment.

1. Introduction

Secondary breast cancer is an uncommon occurrence, and even more uncommon is the case of colorectal cancer (CRC) metastasizing to the breast [1]. The incidence of extramammary metastasis to the breast accounts for 0.5–3%, and it is predicted to increase to approximately 7% [2]. Despite their rare occurrence, the differentiation between primary and secondary breast cancers must be established by triple assessment: the physical examination, the radiological studies, and most importantly, the pathological assessment as it is the definitive diagnostic method [3]. Here, we report a case of a 56-year-old male with multiple colonic metastatic tumors to the abdominal wall, the liver, the chest wall, and eventually the breast. Our case clearly demonstrates how careful follow-up and vigilant observation assisted in the discovery and diagnosis of secondary breast cancer. This work was reported in line with the SCARE criteria [4].

2. Presentation of case

An otherwise healthy 56-year-old male was referred to King Fahad Specialist Hospital - Dammam with a 4-day history of constipation associated with abdominal pain and vomiting with no significant past medical or surgical history. On examination, the patient had a blood pressure of 136/89 mmHg, heart rate 83 beats/min, respiratory rate 22 breath/min, and the temperature was 37.2 °C; the abdominal was soft and lax, symmetrical with mild distention. The rectal examination showed a small amount of liquid stool with no blood present. The complete blood count, liver, and renal panels were within the normal range.

The erect abdominal x-ray showed multiple air-fluid levels and the abdominal computed tomography (CT) scan was significant for focal circumferential wall thinning of the splenic flexure causing stricture with proximal colonic and small bowel distension (Fig. 1A, B). Thereafter, colonoscopy was done and showed an obstructive

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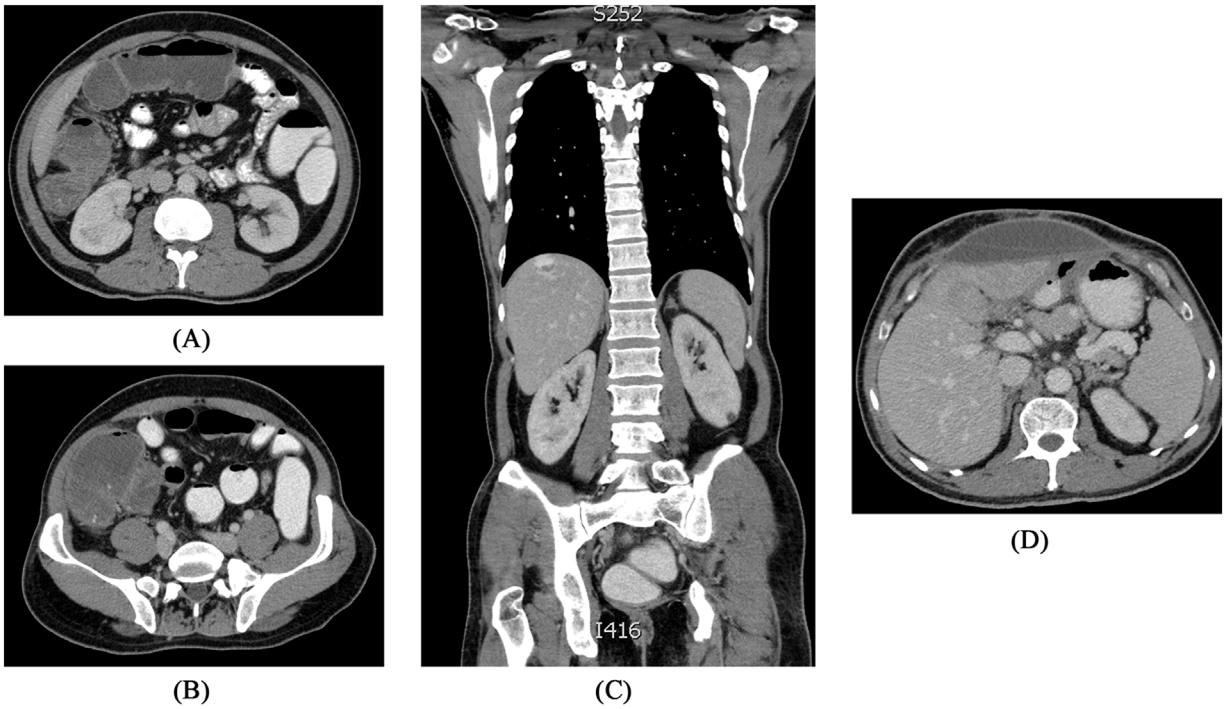

Fig. 1. (A–B) A contrast-enhanced CT scan showing a mass involving the splenic flexure extending for approximately 5.2 cm in length. (C–D) Anterior abdominal wall collection with a thick wall measuring 13 × 3.5 × 9 cm on its maximum transverse likely to be seroma. The liver is enhancing homogeneity and appears to be pulled to the anterior abdominal wall likely due to fibrosis, stable hemangioma at segment VII measuring 2.6 cm in diameter. The small bowel is the anterior abdominal wall without obstruction.

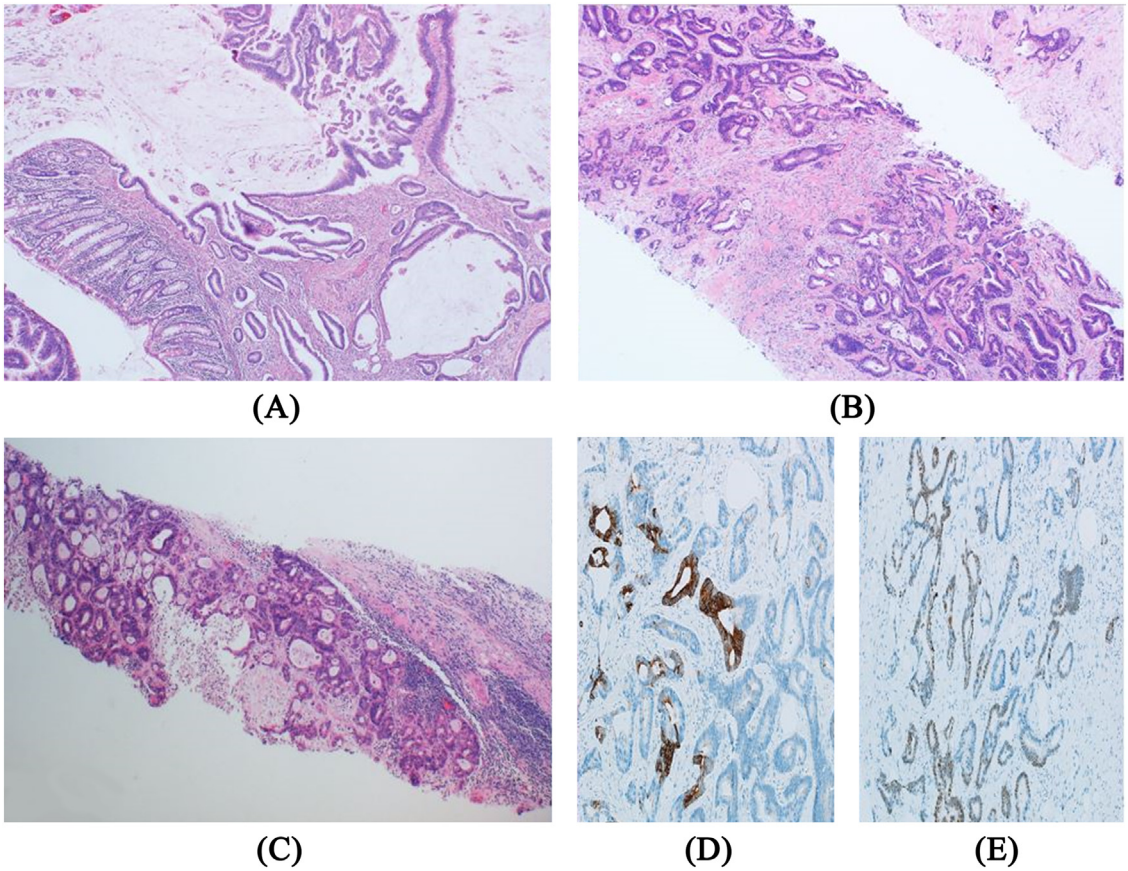

Fig. 2. (A) Histological examination of the colonic mass shows infiltration by variably sized malignant glands with pools of intra and extra glandular mucin. (B–C) Infiltration of the breast and the axillary lymph node by adenocarcinoma showing similar histological features of the primary colonic adenocarcinoma. (D–E) Well-controlled immunohistochemical stains show that the neoplastic cells in the metastasis are positive for CK20 and CDX2 supporting a primary colonic origin.

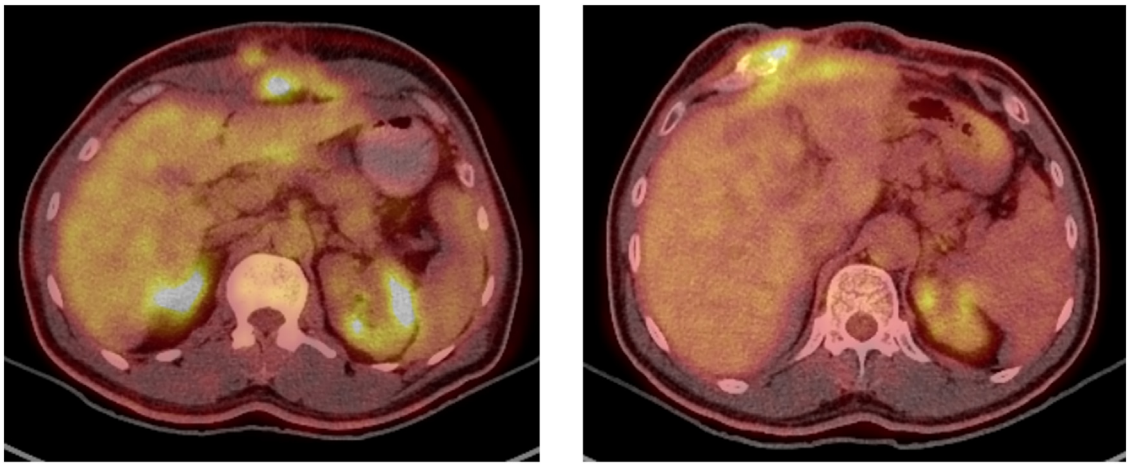

Fig. 3. (A) Fluorodeoxyglucose ($_{18}$F) PET/CT scan of the abdomen showing intense heterogeneous uptake in upper anterior abdominal wall measuring roughly 8.5 × 2.5 cm. (B) Fluorodeoxyglucose ($_{18}$F) PET/CT scan of the abdomen showing interval progression in size of FDG activity of a soft tissue nodule at in the right upper anterior abdominal wall, with SUVmax of 7.7. New FDG avid peritoneal nodulehepatic focal lesion at the tip of the right hepatic lobe adjacent to the capsule of segment IV with SUVmax of 4.8. Small seroma fluid collection in the midline upper abdominal wall measuring 4.5 × 0.9 cm surrounded by FDG avid wall and fat stranding suggestive of an inflammatory process.

mass beyond the anal verge by 65 cm and the scope was unable to go beyond this point; biopsies were taken and the histopathology report confirmed adenocarcinoma. Preoperative lab work was white blood counts (WBCs): 11300 × 10^9/L, Hg 15.3 g/dL, platelet: 328 × 10^9/L, fasting blood glucose (FBG): 68 mg/dL, creatinine: 78 U/L, urea: 4.9 mg/dL, lactate dehydrogenase (LDH): 254 U/L, total bilirubin: 32 μmol/L, amylase: 19 μmol/L, carcinoembryonic antigen (CEA): 39.32. Chest x-ray and electrocardiogram results were normal. Thereafter, the patient underwent emergency laparotomy by a colorectal surgeon due to colonic distension; extended right hemicolectomy and ileocolonic side to side anastomosis were performed. Gross examination of the specimen revealed a fungating mass at the distal of the transverse colon measuring 4 × 3.5 × 3 cm. Histological examination of the sections taken from the mass revealed low-grade mucinous adenocarcinoma with no lymph node metastasis and negative surgical resection margins pT3N0Mx (Fig. 2A). The postoperative recovery course went smoothly, and the patient was discharged after 7 days. The patient received 8-cycles of oxaliplatin and capecitabine (XELOX) adjuvant chemotherapy and this was tolerated very well without adverse events. The patient was followed up by the oncology and colorectal team every 3 months for the first 2 years, and every 6 months after the second year.

At the 7th follow-up of the patient (2½ years), the CEA level had increased rapidly from 2.88 to 19.79. Positron emission tomography with 18-F fluorodeoxyglucose integrated with CT ($_{18}$F-FDG-PET/CT) showed a metastatic solitary upper abdominal mass (Fig. 3A). Ultrasound-guided fine-needle aspiration (FNA) was done and malignant cells were confirmed. The case was discussed in the multidisciplinary meeting and a decision was made to excise the mass. So, excision was done, and the histopathology confirmed metastatic adenocarcinoma of colonic origin. Furthermore, genetic testing was performed and K-RAS mutation was detected. Palliative chemotherapy of folinic acid, fluorouracil, and irinotecan (FOLFIRI) + bevacizumab was started, but the patient could not tolerate the course and the regimen was stopped.

Seven months later CEA increased from <0.5 to 10.3 and evaluation by CT-scan showed soft tissue nodules at the surgical site indicating recurrence, a mass invading the lower 4 costal cartilage, and a query liver lesion at segments 3 and 4 (Fig. 1C, D). The patient underwent en bloc resection of segments 3 and 4A of the liver, the lower 4 costal cartilage on the left side, and an abdominal lesion. Later, the patient received a consolidated dose of radiotherapy 20 Gy/5 with 7 cycles of pseudo-adjuvant XELOX chemotherapy.

After 6 months of follow-up, the patient's CEA level elevated from 6.92 to 19.46, and the $_{18}$F-FDG-PET/CT showed a new FDG avid peritoneal nodule and hepatic focal lesion (Fig. 3B). The patient underwent resection of the 7th, 8th, and 9th right ribs, a part of the diaphragm, segments 4B and 5 of the liver, and a cancerous nodule on the omentum and the peritoneum. All the resected specimens were positive for adenocarcinoma metastasis and all margins were negative for malignancy.

After 10 months, the patient was admitted because of a 5-day history of right lower quadrant abdominal pain associated with vomiting food in content and obstipation. On examination, the abdomen was soft and lax, but distended. An x-ray ordered and showed multiple air-fluid levels and the CT scan of the abdomen showed small obstruction with a transition point at mid distal ileum proximal to ileocolic anastomosis, but distal to small bowel anastomosis, most likely due to adhesion. The patient was kept on conservative treatment but unfortunately did not improve and was taken to the operating room. Intraoperative findings included multiple metastatic masses on many levels causing an obstruction and dilated small bowel. The abdominal wall nodules were excised. An extensive adhesiolysis of the adhesion between small bowel, the abdominal wall, and a loop ileostomy was fashioned. Post-operatively, the patient developed a high output enterocutaneous fistula that was treated conservatively. The histopathology report of the excised small bowel was positive for adenocarcinoma metastasis.

During the same admission, the patient revealed having a mass on the right breast for the preceding 2 months. According to the patient, the mass was slowly increasing in size with no nipple discharge. Examination of the right breast and axilla showed a 2 × 2 cm hard mobile mass in the lower outer quadrant of the right breast with hard mobile right axillary lymph node. The patient had an ultrasound of the right breast and axilla which showed a mass and followed by an ultrasound-guided biopsy (Fig. 4). With the patient's history of metastatic colon cancer in mind, the differential diagnosis of clinically suspicious breast lump with ipsilateral hard axillary lymph node is commonly diagnosed as either primary or secondary

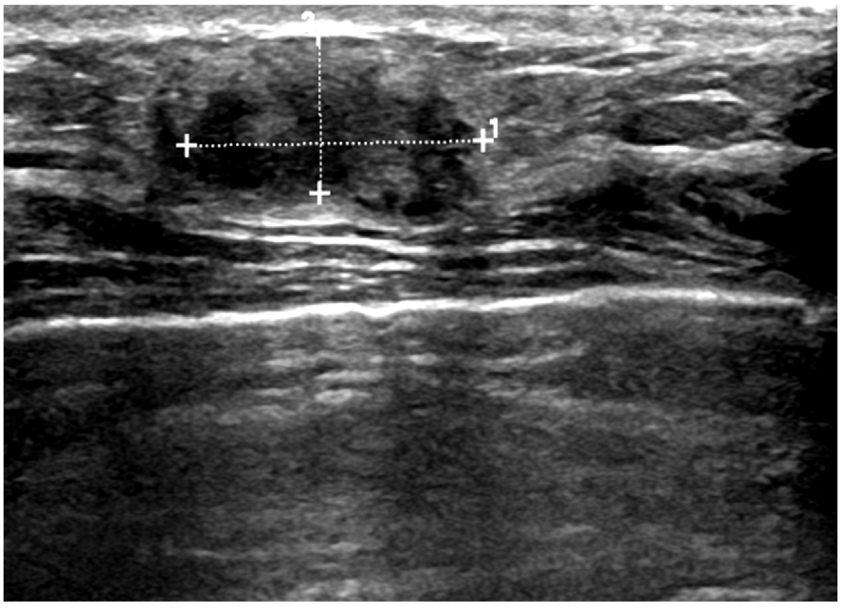

Fig. 4. Ultrasound imaging of the right breast showing 9 o'clock hypoechoic anti-parallel mass measuring 1.6 × 0.8 × 2.1 cm, suggestive of highly aggressive malignancy with BIRADS V.

breast malignancy. The differentiation between the two diagnoses can only be reached through systematic evaluation of the lump through the medical history, the clinical examination, as well as the radiological and histopathological assessments. The specimen was confirmed as metastatic adenocarcinoma with positive CK20, CDX2 while negative for CK7, GCDFP15, GATA-4, estrogen (ER) and progesterone (PR) (Fig. 2B–E).

The patient's condition was re-discussed with the multidisciplinary team and the decision to start palliative chemotherapy was made. Unfortunately, the patient was deceased after 11 months of follow-up.

3. Discussion

By using PubMed, Google Scholar, and Microsoft Academic to search academic articles in the English language published between January 1976 and August 2019, our team identified 141 similar studies but included only 56 which were relevant to our case (Fig. 5). Search terms used were colon, colonic cancer, rectum, rectal cancer, colorectal, colorectal cancer, breast, breast cancer, adenocarcinoma, colonic adenocarcinoma, colorectal adenocarcinoma, and metastasis.

Of the 56 cases relevant to our case (Table 1), most cases were of female patients with a ratio of 52:4 compared to males. The minimum age of presentation was 21 years old, the maximum age was 86 years old, and the average age was 49 years old. Most of the cases 23 (41%) were metastasized from rectal origin, 22 (39%) cases from colonic origins, 2 (4%) cases from cecal origin, and 9 (16%) cases with no specific colorectal origin. The left breast was the most common site for metastasis from colorectal origins with 25 (44.64%) cases and the right breast with 21 (37.5%) cases. Moreover, bilateral metastasis to the breast is also not that rare as there were 8 (14.29%) cases, and 2 (3.57%) cases with no specific location. Additionally, 32 (57.14%) of the identified cases had multiple colorectal metastases to other organs besides the breast. The average time of survival rate for 13 of the deceased cases was 6.1 months. The summary of the result is demonstrated in Table 2.

CRC is the most common cancer and the leading cause of death after prostate and lung cancer for males; and the third leading cause of death in females following breast and lung cancer [5]. Local metastasis of CRC to the regional lymph nodes accounts for 40–70% during the diagnostic period [6]. Hence, early localization and staging of the tumor may account for 90% survival after 5 years of resection [6]. Primary metastasis of CRC to the breast is rare, as it usually metastasizes from contralateral breast cancer, leukemia, lymphoma, melanoma, gynecological gastric and pulmonary tumors [6].

The differentiation between primary and secondary breast tumors is made based on medical history, clinical examination, radiological imaging, and immunohistopathological studies [7]. Most of the secondary breast tumors are readily palpable, freely movable, and characterize by rapid growth. They usually arise from the left breast and at the upper outer quadrant [3,6]. In addition, the adherence of breast tumors to the skin is not rare, but it does not cause retraction to the skin or the nipple, and it is not associated with nipple discharge [6]. Moreover, metastasis of secondary breast tumors to the regional axillary lymph nodes has been reported in some cases [6]. Moreover, the mammographic assessment may support in creating a differential diagnosis, as the classical mammographic features are round, well-circumscribed masses without skin speculation, microcalcification, or thickening [6]. Further, fluorodeoxyglucose positron emission tomography (FDG-PET) in combination with CEA can help determine the tendency of the tumor to be malignant [8]. Consequently, the standard of care is to assess the lesion by a core needle biopsy guided with ultrasound as it is a more sensitive and specific diagnostic tool in comparison to an FNA biopsy [5]. The histological assessment of a core biopsy may show a lack of tissue elasticity as a result of the rapid growth, a transition sharp border, and the periodical and perilobular location of the tumor favoring secondary malignant metastasis with the absence of in situ ductal carcinoma [5]. Furthermore, specific immunohistochemical markers used to identify breast and colorectal adenocarcinoma are CK7, CK20, CDX2, and villin. The vast majority of breast tumors are CK7 (+) and CK20 (−), whereas CK7 (−) and CK20 (+) which are suggesting colorectal adenocarcinomas [8]. Also, the positivity of the CDX2 and CK20, and the negativity for CK7, ER, PR, HER2, GDCP15, and BCA favor secondary breast tumors of colonic origin [5].

Table 1
Detailed clinical characteristics of 56 patients with primary colorectal cancer with metastasis to the breast.

No.	Year	Author	Age	Gender	Primary CRC			Metastasis organ	Breast metastasis			Survival (months)
					Time (months)	Stage	Location		Laterality	Size (cm)	Treatment	
1	1976	[11]	44	F	1	NS	NS		NS	NS	WLE (Ex)	4 AWD
2	1980	[12]	30	F	10	Dukes B	NS		Left	3	NS	72 AWD
3	1980	[12]	67	M	12	Dukes B	NS		NS	NS	NS	NS
4	1981	[13]	59	F	6	NS	NS	Liver, peritoneum	Left	2 & 4	NS	4
5	1981	[13]	68	F	24	NS	NS	Peritoneum	Right	3	NS	6
6	1989	[14]	28	F	11	T4N2	Rectum		Right	NS	WLE (Ex)	48 DOD
7	1997	[15]	86	F	Synchronous	Dukes B	Ascending colon		Right	2	WLE (Lx)	18 AWD
8	1998	[16]	36	F	12	NS	NS		Bilateral	Multiple	NS	NS
9	1999	[17]	69	F	12	T3N0	Rectum		Left	NS	WLE	4 DOD
10	2001	[18]	42	F	6	NS	Sigmoid colon	Retroperitoneal space, peritoneum	Right	3	WLE (Ex)	6 AWD
11	2001	[19]	66	F	120	T2	NS	Thoracic, skin, lung	Right	NS	OBx	NS
12	2001	[20]	77	F	3	T4N2	Cecum		Left	2	WLE (Ex)	6 AWD
13	2003	[21]	52	F	20	T4N2	Rectum		Left	1.4	NS	2
14	2004	[22]	40	F	≈ 48	Dukes C	Ascending colon	Retroperitoneal space	Left	4	Mx	6 AWD
15	2004	[23]	53	F	60	Dukes B	Rectum	Skin	Left	1	WLE	4 AWD
16	2006	[24]	32	F	10	T4N2	Rectum	Vertebra, brain	Left	4	OBx	0.5 DOD
17	2008	[25]	45	F	24	Dukes C	Rectum	Liver, lung	Bilateral	2.2 (Right), 2 (Left)	OBx	NS
18	2008	[25]	74	F	2	Dukes C	Cecum		Bilateral	4 (Right), 6 (Left)	OBx	NS
19	2008	[26]	36	F	4	T4	Rectum		Left	6	OBx	NS
20	2009	[27]	50	M	6	T3N1M1	Ascending colon		Right	1.5	OBx	12 AWD
21	2009	[28]	43	F	<1	Dukes D	Transverse colon	Liver bone	Right	4.5	OBx	NS
22	2009	[29]	54	F	>2	T4NxM0	Rectum	Skull, adjacent to kidney	Right	3.7	CTx	12 DOD
23	2009	[30]	42	F	11	T4N1M0	Rectum	Liver, brain	Right	5	NS	2 DOD
24	2010	[31]	78	F	16	T4N0	Transverse colon	Abdominal wall	Left	1	OBx	4 DOD
25	2011	[10]	63	F	48	T3N1	Sigmoid colon	Lung	Right	2.8	WLE	NS
26	2011	[32]	46	F	36	T3N1	Sigmoid colon	Lung	Left	1	WLE (Lx)	16 DOD
27	2011	[33]	37	F	18	T3N0	Sigmoid colon		Left	1	OBx	NS
28	2011	[34]	44	F	84	Dukes A	NS	Brain, lung, mediastinum	Left	11	NS	NS
29	2011	[35]	76	F	84	T3N1M0	Colon	Lung	Left	1.6 & 3	WLE (Ox)	1.5 AWD
30	2011	[36]	38	M	84	NS	Rectum	Liver	Right	6.2	CTx then Mx	2 DOD
31	2011	[37]	47	F	36	T4N1M0	Rectum		Left	3	WLE then CTx	NS
32	2011	[33]	37	F	18	T3N3M0	Sigmoid colon		Left	1	CTx	NS
33	2012	[38]	76	F	96	T4N0	Sigmoid colon	Lung	Left	1.2	WLE	132 AWD
34	2012	[7]	31	F	9	T4N2M1	Rectum	Bone	Bilateral	1.4 (Right), 1.3 (Left)	NS	NS
35	2012	[39]	63	F	30	T3N1M0	Rectum	Liver, peritoneum	Right	3	CTx	4 DOD
36	2013	[40]	28	F	9	NS	Rectum		Bilateral	Multiple	NS	2 AWD
37	2013	[41]	32	F	24	NS	Sigmoid colon	Ovaries	Left	3	NS	NS
38	2014	[2]	28	F	Synchronous	T4N2M1	Rectum	Liver	Right	2	CTx	NS
39	2014	[42]	38	F	15	T3N1	Ascending colon	Ovarian	Left	9	Mx	8 AWD
40	2014	[43]	36	F	20	T3N1M0	Rectum	Uterus, peritoneum	Bilateral	9 (Right), 10 (Left)	NS	2 DOD
41	2014	[44]	38	F	NS	NS	Sigmoid colon		Right	3	Planned CTx	NS
42	2015	[45]	45	F	NS	Stage IV	Ascending colon		Right	0.68 & 0.9	OBx	NS
43	2015	[45]	56	F	NS	Stage IV	NS	Liver	Right	1.46	OBx	NS
44	2015	[6]	37	F	14	NS	Colon	Ovaries	Right	3	CTx	20 AWD
45	2015	[46]	22	F	Synchronous	NS	Rectum	Bone	Bilateral	NS	NS	NS
46	2015	[45]	45	F	NS	Stage IV	Colon		Right	0.68, 0.93	OBx	NS
47	2015	[45]	56	F	NS	Stage IV	Colon		Right	1.46	OBx	NS
48	2016	[5]	80	F	NS	T3N2Mx	Sigmoid colon		Right	1.8	WLE	NS
49	2016	[9]	21	F	10	Dukes C	Rectum	Uterus, cervix, left ovary, left fallopian tube	Bilateral	Multiple	CTx	12 DOD
50	2016	[47]	26	F	120	NS	Rectum		Left	>2.5	CTx then Mx	3 DOD
51	2016	[48]	47	F	36	NS	Rectum	Abdominal wall, urinary bladder, uterus	Left	1.7	WLE	16 DOD
52	2016	[49]	45	F	NS	NS	Rectum		Left	2	Mx	NS
53	2017	[1]	82	M	30	NS	Colon	Lung	Left	3.6	Mx	NS
54	2017	[3]	47	F	9	NS	Transverse colon	Ovaries, omentum	Left	2.5	WLE	NS
55	2019	[8]	68	F	78	Dukes A	Rectum	Skin, multiple viscera	Left	4	CTx	3 DOD
56	2019	[50]	43	F	NS	T3N1Mo	Rectum		Right	2.6	NS	NS

M, male; F, female; NS, not specified; Ex, excision; Qx, quadrantectomy; Lx, lumpectomy; Mx, mastectomy; CTx, chemotherapy; OBx, observation; DOD, died of disease; AWD, alive with disease.

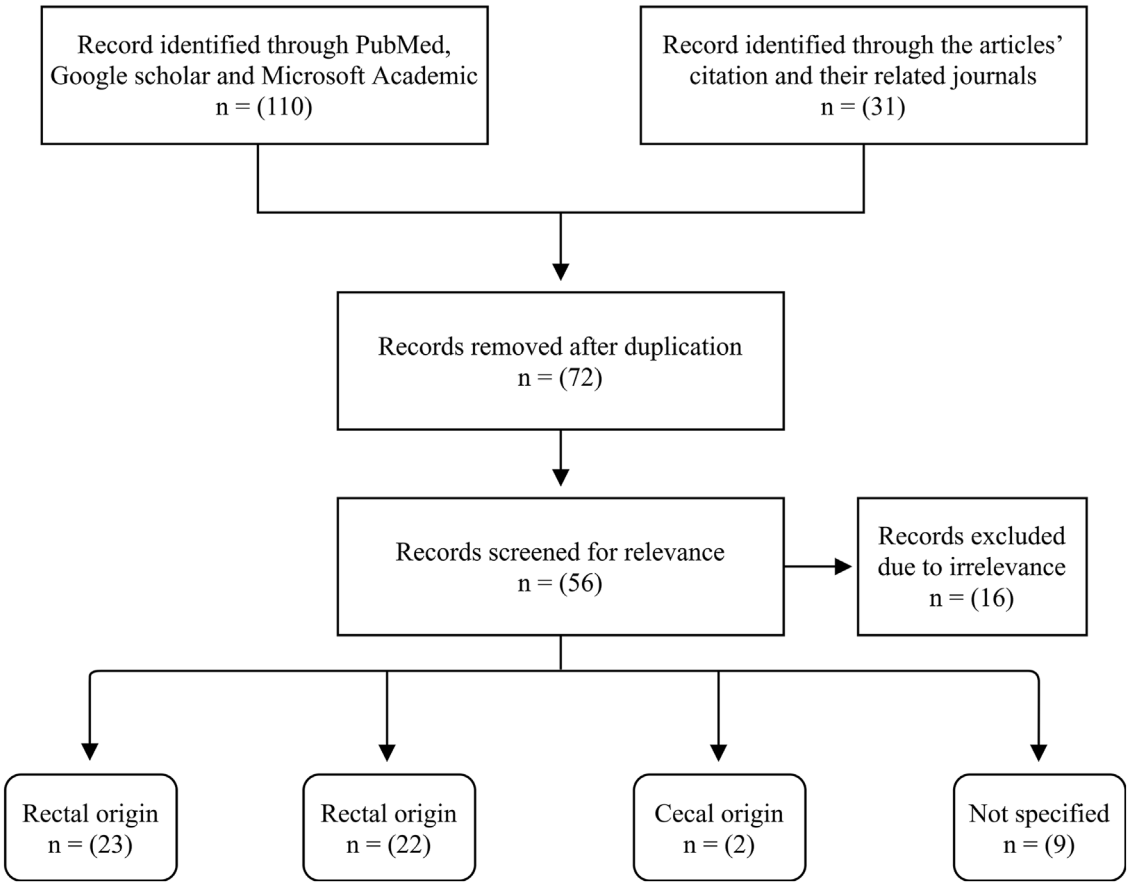

Fig. 5. Flowchart showing the number of cases that we identified through the medical databases and the journals' websites.

Table 2
Patient and tumor characteristics.

	No. of cases (%)
Age	
21–44	24 (42.86%)
44–59	16 (28.57%)
59–75	9 (16.07%)
75+	7 (12.5%)
Gender	
Female	52 (92.86%)
Male	4 (7.14%)
Origin of metastasis	
Colonic origin	22 (39%)
Rectal origin	23 (41%)
Cecal origin	2 (4%)
Not specified	9 (16%)
Metastasis site to the breast	
Right breast	21 (37.5%)
Left breast	25 (44.64%)
Bilateral	8 (14.29%)
Not specified	2 (3.57%)

Limited data have been proposed regarding the management of metastatic colorectal cancer to the breast [1]. Surgery is not recommended due to the fear of short life expectancy and the seeding of breast tumors to the adjacent skin [6]. Nevertheless, surgery is recommended in the case of sizable masses and painful tumors [6]. Therefore, the major palliative management is by chemotherapeutic agents [6]. First line palliate therapy is a combination of irinotecan/5-fluorouracil (FOLFIRI), FOLFOX or XELOX and the second line is a combination of oxaliplatin (FOLFOX and CAPOX) and an anti-VEGF (bevacizumab) or anti-EGFR (cetuximab) antibody with the exclusion of K-RAS mutation [8].

This condition has a poor prognostic factor, as it is the beginning of the rapid widespread dissemination of the disease, especially to cerebral and skeletal organs [9]. Despite the advancement of treatment over the years, the prolonged survival rate after diagnosis is unlikely as the estimated survival time is 8–10 months [10], while our estimation was 6.1 months.

4. Conclusion

To conclude, metastatic colorectal cancer to the breast is not widely common but should raise the vigilance of the physician toward any abnormal breast changes. Hence, during the surveillance program of colorectal cancer, a full examination of the body from head to toe is warranted, and radiological and pathological studies can help in the differentiation between primary and secondary breast tumors. Secondary breast metastasis from colorectal origin behaves aggressively and a multidisciplinary team should establish the optimal personalized treatment as there is no definitive management guideline.

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Ethical approval

The study is exempt from ethical approval in our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy

of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

- Study concept or design: Balhareth A, AlQatari AA.
- Participation in the pre/post-operative management of the patients: Balhareth A, Aldulaijan F, Joudeh A.
- Data collection: AlQatari AA.
- Data interpretation: AlQatari AA.
- Literature review: Balhareth A, AlQatari AA, Aldulaijan F, Joudeh A.
- Drafting of the paper: Balhareth A, AlQatari AA, Aldulaijan F, Joudeh A.
- Editing of the paper: Balhareth A, Aldulaijan F.

Registration of research studies

This case report in not first in men.

Guarantor

Ameera Balhareth.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of Competing Interest

The authors report no declarations of interest.

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