

Intestinal Metastases from Unknown Primary Masquerading as Primary Colonic Neoplasms- Diagnostic Dilemma Elucidated by Detailed Clinical Evaluation

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ABSTRACT

Intestinal metastasis from unknown primary may simulate a primary colonic neoplasm in its clinical presentation. The gross histopathological examination may also mimic primary intestinal pathology. The diagnostic dilemma is furthered by paucity of available knowledge due to the limited literature. This article discusses three such cases (50-year-old male, 60-year-old female and 65-year-old female), all of which clinically presented with bowel symptoms, either in the form of acute abdomen or intestinal obstruction. The imaging studies pointed towards an intestinal pathology. Although the initial presentation was dubious, on delving into the medical and surgical history, all of them had a previous known malignant neoplasm on different sites like skin, ovary and cervix. The diagnosis of intestinal metastasis of melanoma, High Grade Serous Carcinoma (HGSC) of ovary and Squamous Cell Carcinoma (SCC) of cervix, respectively, were supported by suggestive histomorphology and ancillary studies like immunohistochemistry in one of the cases. The most alluring of the above three cases was that of intestinal metastasis from melanoma, where lack of melanin pigment made the histological diagnosis difficult. After retrieving medical history along with diffuse S100 and HMB45 positivity, definitive conclusion could be opined. Thus, clinical history of the patient was the cornerstone for definitive diagnosis in all of the three cases. Primary colonic neoplasms and intestinal metastasis from previous known malignant neoplasms have totally different clinical and prognostic outcomes. So, identification of these cases is extremely important from treatment point of view. It is possible only based on detailed clinical evaluation, clear suspicion, suggestive histomorphology and suitable ancillary investigations.

Keywords: Acute abdomen, Colonic metastases, Intestinal obstruction, Melanoma, Serous carcinoma, Squamous cell carcinoma

INTRODUCTION

Colonic metastasis has occasionally been reported from primary sites of breast, cervix, ovaries, kidneys and malignant melanomas [1]. However, because of their rare incidence and an overlapping histomorphology with primary colonic pathology, they often pose a diagnostic challenge to the reporting oncopathologists. The problem is compounded by lack of proper history and awareness of patient party, where the exact clinical picture remains hidden to the clinician. It is only when there is suggestive histomorphology and on revisiting the history, the actual scenario is unveiled. Three of such alluring cases have been discussed here [Table/Fig-1].

CASE SERIES

Case 1

A 50-year-old male patient came to the Emergency Department with clinical presentation of diffuse abdominal pain, vomiting, constipation and abdominal rigidity for the last 24 hours. The clinical presentation was that of acute abdomen, where bowel sounds were absent on auscultation.

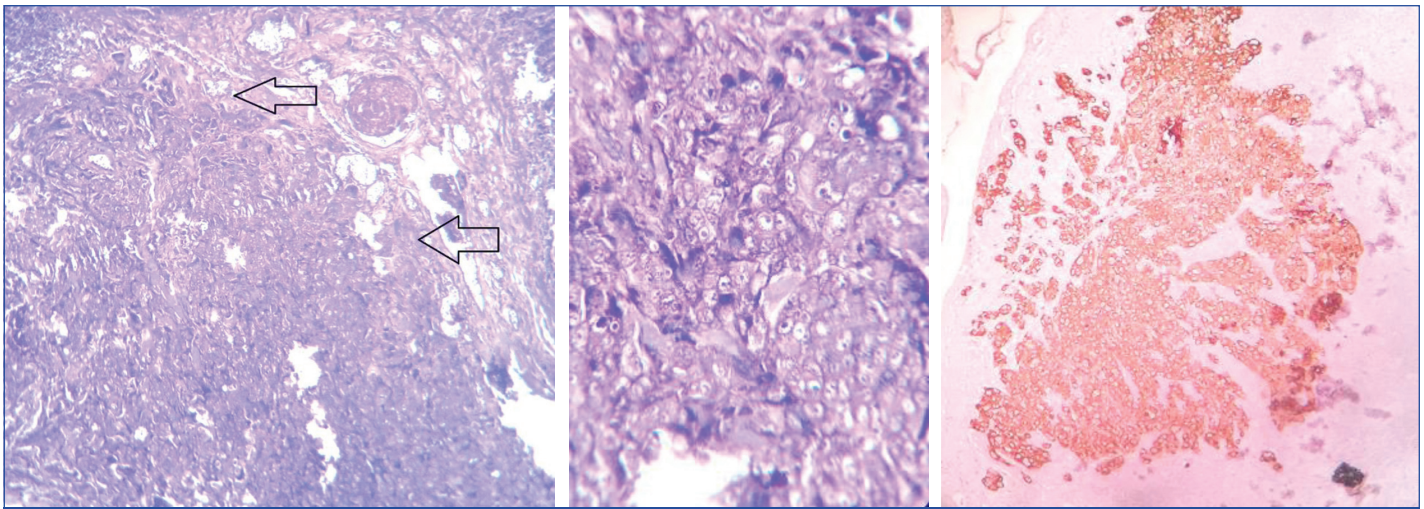
Straight X-ray abdomen was advised that showed free gas under the diaphragm and working diagnosis was that of hollow viscus perforation. On exploratory laparotomy, ileal perforation was noted and segmental resection was done. Serosal congestion and exudation surrounding a small ileal perforation were noted. No macroscopic growth or ulceration was seen.

On histological examination, serial sections surrounding the area of perforations showed deposits of markedly pleomorphic tumour cells with prominent nucleoli and bizarre mitosis in submucosae, muscularis propria and serosa, with unremarkable mucosae [Table/Fig-2,3]. A provisional diagnosis of undifferentiated carcinoma was made. Detailed past history revealed melanoma ten years back in lower extremity. Immunohistochemical (IHC) assessment with S100 followed by HMB45 was strongly positive [Table/Fig-4,5], and the final diagnosis was intestinal metastasis in a known case of melanoma.

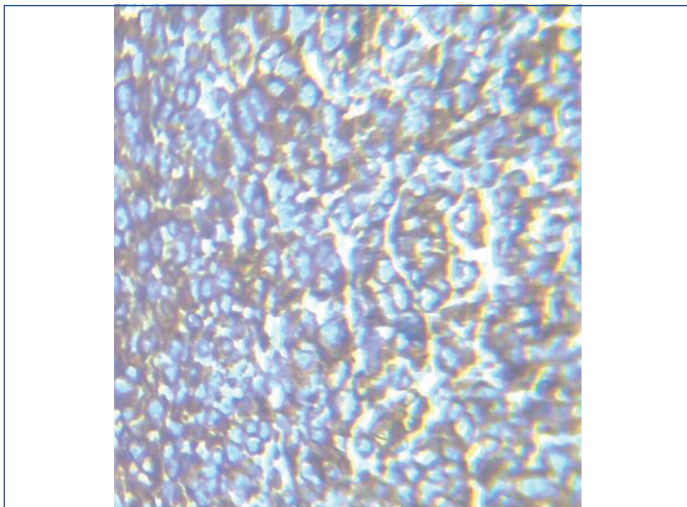
On follow-up the patient developed other extraintestinal sites of metastasis like liver, lungs and bones, and finally succumbed to death within five months of gastrointestinal resection.

Case	Age/Gender	Primary site of malignancy	Site of metastasis	Mode of presentation	Time from initial diagnosis to metastasis	Postsurgery follow-up
1	50 years/Male	Melanoma in lower extremity	Ileum	Acute abdomen due to ileal perforation	10 years	Further extra-intestinal metastasis followed by death within five months
2	60 years/Female	Squamous cell carcinoma of cervix	Sigmoid colon	Anaemia, positive occult blood in stool due to colonic constriction	5 years	Put on cisplatin and paclitaxel with no metastasis till three months
3	65 years/Female	Bilateral High Grade Serous Carcinoma (HGSC) of ovaries	Ileum	Intestinal obstruction due to constrictive intestinal growth	6 years	Platinum-based chemotherapy with good response till eight months

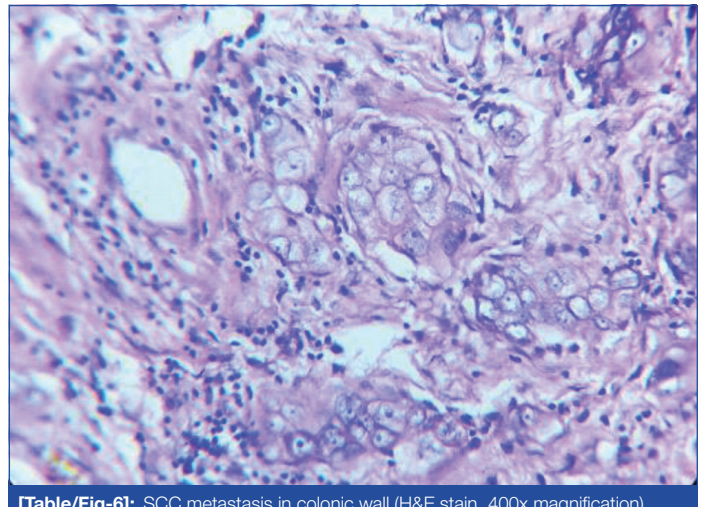
[Table/Fig-1]: Depicting case wise distribution with respect to demography, primary site of malignancy, metastatic site, mode of presentation, time from initial diagnosis to metastasis and follow-up postsurgery.



[Table/Fig-2]: Submucosal deposits (shown by open arrows) of melanoma in gut (H&E stain, 100x magnification); **[Table/Fig-3]:** Prominent nucleoli in melanoma metastasis (H&E stain, 400x magnification); **[Table/Fig-4]:** Immunohistochemistry showed S100 positivity in tumour cells (100x magnification). (Images from left to right)



[Table/Fig-5]: HMB45 positivity in tumour cells (400x magnification).



[Table/Fig-6]: SCC metastasis in colonic wall (H&E stain, 400x magnification).

Case 2

A 60-year-old female patient attended Outpatient Department with anaemia, lethargy, palpitation, bloating with vague abdominal pain for the last four months. Stool examination was positive for Occult Blood Test (OBT). Ultrasonography and colonoscopy showed a constriction in sigmoid colon. Biopsy was also taken from the area of constriction, in the same setting, and was found to be a poorly differentiated malignant neoplasm. Segmental resection of sigmoid colon was done. The provisional diagnosis was that of any primary colonic neoplasm.

Serial sections from constricted and thickened sigmoid colon showed sheets of atypical squamoid cells infiltrating the muscularis propria and serosa with occasional deposits in periserosal fat [Table/Fig-6,7]. Detailed history revealed SCC of cervix five years back. Thus, a diagnosis of colonic metastasis of cervical SCC was agreed upon.

The patient was put on Cisplatin and Paclitaxel based chemotherapeutic regimen, and had shown no further metastasis until three months till the date of reporting of this case.

Case 3

A 65-year-old female patient attended Surgical Emergency Department with symptoms of crampy abdominal pain and swelling, vomiting, loss of appetite and constipation for the last 48 hours. The patient had been experiencing mild abdominal discomfort with flatulence for the last three months. Straight X-ray abdomen showed dilated bowel loops with multiple air fluid levels and ultrasonography of whole abdomen showed constriction in small bowel with minimal ascites. The clinical and radiological presentation was in favour of intestinal obstruction. This was followed by segmental ileal resection.

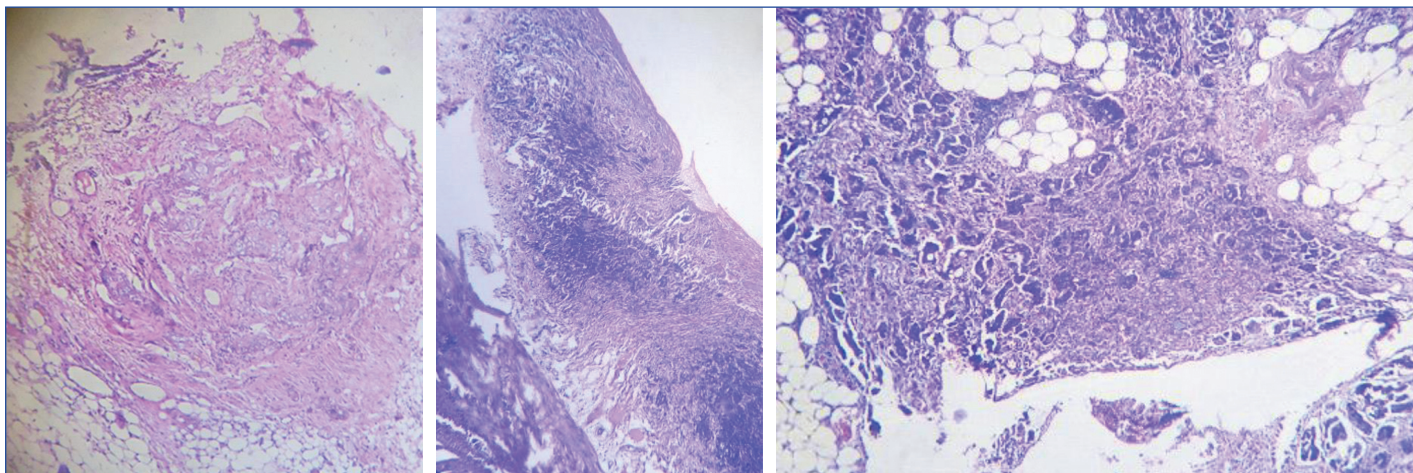
Constrictive growth with multiple serosal nodules and mesenteric deposits showed tumour cells with papillary architecture [Table/Fig-8,9]. Individual cells were pleomorphic, with vesicular chromatin, prominent nucleoli and increased mitosis. History of bilateral HGSC of ovaries six years back was elicited. Hence, it was a case of HGSC of ovary metastasising to small intestine.

Following the debulking surgery, the patient was put on platinum-based chemotherapeutic agents, which has shown good response till eight months of therapy, until the reporting of this case.

DISCUSSION

Gastrointestinal (GI) metastasis to colon with bowel symptoms as the presenting complaint, in a case with unknown primary, is exceedingly rare. It is further challenged by the fact that primary and secondary gastrointestinal tract malignancies are clinically indistinguishable [2]. Due to the rare occurrence, these are not recognised promptly. This may delay effective treatment and overall survival of the patients as treatment approaches for primary GI malignancies and metastases are drastically different [3,4]. Thus, awareness about these entities through available literature and case studies may guide the oncopathologists to arrive at a definitive diagnosis.

Melanoma usually metastasises within five years of initial diagnosis with GI symptoms, that require medical attention, and has an exceedingly low prevalence [5,6]. The latency between primary and metastatic disease in the present case series was also higher than a case series conducted by Tessier DJ et al., where it was documented as 7.47 years [7]. Moreover, lack of pigment made the diagnosis more difficult in the present cases. Proper history with supportive evidence of S100 and HMB45 positivity made the diagnosis clear. These cases have poor survival, which is further compounded by obstruction



[Table/Fig-7]: Periserosal fatty deposits of SCC (H&E stain, 100x magnification) (Case 2); **[Table/Fig-8]:** Serosal deposits of high grade serous carcinoma of ovaries (H&E stain, 100x magnification); **[Table/Fig-9]:** Papillary fragments invading mesenteric fat (H&E stain, 100x magnification). (Images from left to right)

and perforation, of which the latter was the acute presentation in this case [8]. Cervical metastasis to gastrointestinal tract has only been demonstrated in a handful of cases with presentation similar to primary colonic neoplasm, making it prone to get misdiagnosed [9,10]. A proper evaluation of past medical history was instrumental in this case following histopathological analysis. As for the third case, intestinal metastasis from ovarian serous carcinoma may be explained by intraperitoneal seeding or hematogenous spread [11]. Since ovarian carcinoma is notorious for having a high case fatality rate and a very low cure rate, it should always be considered as a differential for metastatic disease in any known case with atypical presentation following a period of latency [12]. Thus, the common histomorphology for all the above three cases was an unremarkable mucosa with predominant involvement of serosa and subserosa along with periserosal and mesenteric fatty deposits. This ruled out the possibility of any adenocarcinomas arising from bowel mucosa. Clinical history was inevitable in arriving at specific diagnosis in each of the above cases for adoption of proper treatment protocols.

CONCLUSION(S)

Intestinal metastases and primary colonic pathologies may have overlapping clinical and radiological presentation. But early detection and differentiation between the two is extremely important for appropriate therapeutic approach. All the cases with bowel metastases are stage IV disease with poor survival opportunities, with palliative care as the mainstay of treatment. Here comes the important role of pathologists for arriving at a definitive opinion in all such doubtful cases. Proper clinical evaluation, judicious histomorphological approach and appropriate immunohistochemistry are the warp and woof of accurate diagnosis. The importance of all these aspects has been highlighted in this series, where clinical history has served as a main footing for precise pathological diagnosis.

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