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FAMILIAL ADENOMATOUS POLYPOSIS WITH BILATERAL OVARIAN AND LIVER METASTASIS : A CASE REPORT

Histopathology

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ABSTRACT

Familial adenomatous polyposis (FAP) is a rare genetic disease with autosomal inheritance caused predominantly by germline mutations in the adenomatous polyposis coli (APC) gene. The development of colorectal carcinoma in untreated patients is almost 100%, with the median diagnosis of CRC being approximately at 35-45 years. Metastases to the ovary occur in 0.8–9.7 % of colorectal cancer (CRC) cases. Here we present a case of 30 year old premenopausal female who presented with pain abdomen and was discovered to have multiple gastric and colonic polyps with carcinoma caecum and bilateral ovarian metastasis.

KEYWORDS

Familial adenomatous polyposis, APC gene, Colon carcinoma, Metastasis

INTRODUCTION

Familial adenomatous polyposis (FAP) is a rare genetic disease with autosomal inheritance caused predominantly by germline mutations in the adenomatous polyposis coli (APC) gene, with a family history in 70-80% of cases[1]. Most patients develop colorectal cancer (CRC) by the age of 35–40 years if left untreated. Some people have a variant of the disorder, called attenuated FAP, in which polyp growth is delayed, with an average CRC onset at 55 years of age[2]. Extraintestinal manifestations of the disease may occur in attenuated FAP; however, this occurs far less commonly than in the classical form of FAP[3]. Seven percent of ovarian masses are metastatic malignant tumors[4]. Approximately 3.6% to 7.4% of patients with colon cancer have ovarian metastasis at the time of initial presentation, of which 45% are mistaken for primary ovarian tumors[5]. Here we describe a 30 year old premenopausal female who presented with pain abdomen and was discovered to have multiple gastric and colonic polyps with carcinoma caecum and bilateral ovarian metastasis.

CASE HISTORY

A 30 year old premanopausal female who presented with pain abdomen in the gynaecological department. Contrast enhanced computed tomography (CECT) abdomen and pelvis revealed bilateral large abdominopelvic masses with omentum, peritoneal deposits along with multiple space occupying lesions in liver suggestive of bilateral ovarian serous cystadenocarcinoma. Serum CA 125, CEA and CA19-9 were raised. Trucut biopsy from ovarian mass was suggestve of adenocarcinoma. She then received 6 cycles of chemotherapy. After six months, her PETscan showed residual ovarian disease with hypermetabolic polypoid lesion in large bowel. Colonoscopy showed more than 100 sessile and pedunculated polyps throughout the colon with an ulceroproliferative growth in ascending colon. Given colon malignancy with possible FAP and synchronous bilateral ovarian masses with omental and liver metastasis, the patient was given the option of exploratory laparotomy with a total abdominal hysterectomy and bilateral salpingo-oophorectomy on table colonoscopy, and total colectomy with omentectomy and pelvic lymph node dissection. After obtaining informed consent, exploratory laparotomy was carried out.On table colonoscopy showed > 100 polyps in the ascending, transverse and descending colon and a growth in ascending colon. Total proctocolectomy with end ileostomy was done and was sent to us for histopathological examination. On gross examination, the colon showed multiple(>100) sessile and pedunculated polyps with an ulceroproliferative growth in caecum invading the colonic wall upto the level of serosa[Figure 1A]. Bilateral irregular ovarian masses were seen which on cut section were solid and cystic grey white with no areas of necrosis and haemorrhage[Figure 1B]. Uterus, cervix and bilateral fallopian tubes were grossly normal . Omentum showed multiple solid grey white firm to hard masses (tumor deposits). On microscopic examination, sections rom the polyps showed histologic features of tubular adenomas with low grade and high grade dysplasia[FIGURE2]. Sections from the growth caecum showed features of moderately differentiated adenocarcinoma invading the serosal fat with lymphovascular invasion and metastatic tumor deposits in omentum. Bilateral ovaries reveals tumor cells in back to back arranged glands with focal cribriform pattern infiltrating the ovarian stroma[FIGURE3]. Imuunohistochemistry revealed the ovarian tumor to be immunoreactive for CDX2, CK20 and nonimmunoreactive for CK7, WT1, PAX 8 confirming it to be secondaries from colonic adenocarcinoma. Molecular tests showed *APC* gene mutation with loss of Mismatch repair genes like MLH1, MSH2 and MSH6. Thus, the final diagnosis of Familial adenomatous polyposis with caecal adenocarcinoma with bilateral ovarian, omental and liver metastasis was given. Her family was then advised for complete genetic profile screening so as to prevent another mishap in the family.

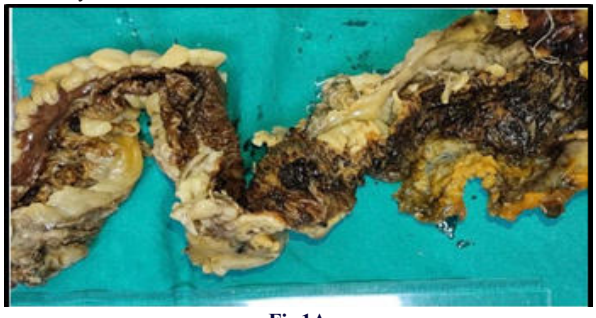

Fig 1A

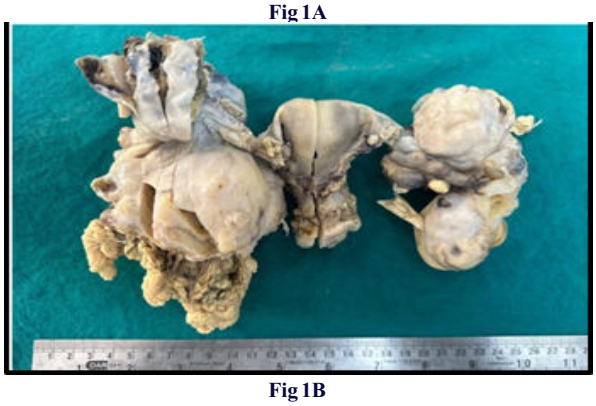

Fig 1B

Figure 1A: Gross Image Of Coloectomy Specimen Showing Multiple Sessile And Pedunculated Polyps.

Figure 1B: Gross Image Of Total Hystrectomy Specimen Showing Bilateral Ovarian Masses (METASTASIS)

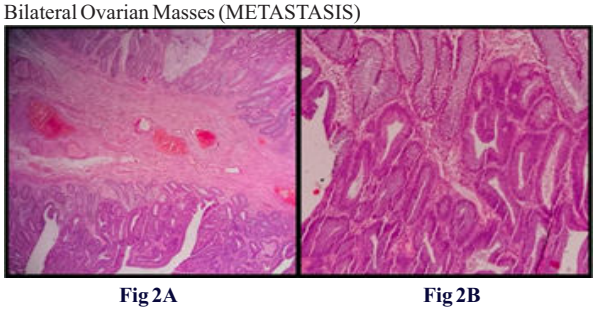

Fig 2A Fig 2B

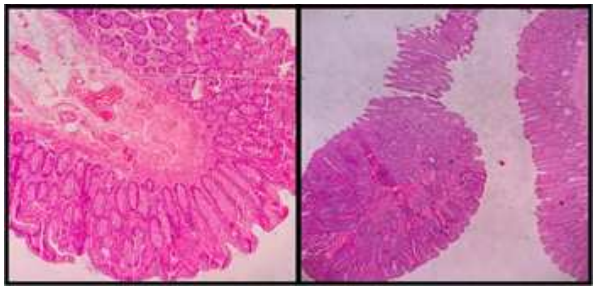

Fig 2C Fig 2D

Figure 2: H&E Stained Sections From Polyps Showing Histologic Features Of Tubular Adenoma ; Tubular Adenoma With Fibrovascular Stalk With Low Grade Dysplasia On Low Power View In 2A, 2C, 2D And On High Power View In 2B.

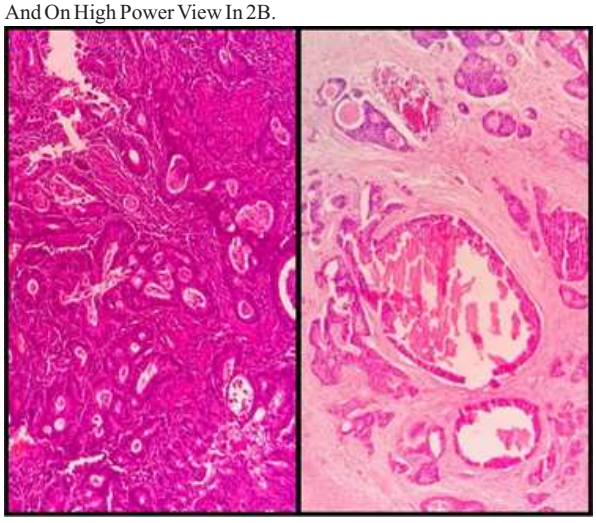

Fig 3A Fig 3B

Figure 3: H&E stained sections showing back to back arranged neoplastic glands in a desmoplastic stroma in caecum [3A] and metastatic tumor deposits in ovary showing multiple glands and cysts lined by tumor cells with intraluminal haemorrhage and necrosis[3B].

DISCUSSION

FAP is usually due to a germline mutation in the adenomatous polyposis coli (APC) gene. APC regulates the turnover of β-catenin, and inactivating APC mutations lead to aberrant accumulation of β-catenin in the nucleus, which in turn leads to dysregulated cellular proliferation. Clinical diagnosis of the "classical FAP" is made with 100 or more adenomatous polyps in the colon and rectum or fewer than 100 polyps with at least one family history of confirmed FAP.

Somatic mutations in APC are well-documented in colorectal cancers.The development of colorectal carcinoma in untreated patients is almost 100%, with the median diagnosis of CRC being approximately at 35-45 years [6]. In addition to colorectal cancer, FAP predisposes to patients to upper gastric and duodenal adenomas and fundic gland polyps, and FAP patients have an increased risk for malignancies of the pancreas, biliary tract, adrenals, and thyroid[7]. Metastases to the ovary occur in 0.8–9.7 % of colorectal cancer (CRC) cases[8]. The fundamental pillar of FAP management continues to be early screening and timely follow-up. According to international guidelines, patients with "classical FAP" should start a CRC screening program at 10-15 years with follow-up every one-to-two years, with colonoscopy being the procedure of choice[6].At the time of FAP diagnosis, surgery is the most offered method to mitigate the risk of CRC . In our case, the patient gave similar family history but due to poor follow up and lack of knowledge she developed colon cancer with metastasis to ovary, liver and omentum.

CONCLUSION

FAP is a genetic disease with an autosomal dominant inheritance that carries a high risk of developing CRC and other types of cancer, including duodenal/ampullary, thyroid, and gastric cancer. The management of this disease is based on early screening and timely follow up, with subsequent planning of risk-reducing or surgeries, including less invasive and safe surgical or endoscopic approaches. Consideration should also be given to the efficacy of prophylactic oophorectomy or intensive chemotherapy accompanying colon resections for carcinoma in such patients.

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