Extragonadal germ cell tumor (yolk sac tumor) arising in a case of familial adenomatous polyposis

Familial adenomatous polyposis (FAP) is an autosomal dominant condition that results in development of the large number of colorectal, and eventually, small intestinal or even gastric adenomas at an early age (late childhood to early adulthood). Extragonadal yolk sac tumors (YSTs) of the gastrointestinal tract are extremely rare neoplasms. Their greater rarity compared with other extragonadal YSTs suggests that different pathogenetic mechanisms could be involved according to the site of origin. Recent epigenetic studies suggest the involvement of some tumor suppressor genes, including the adenomatous polyposis coli gene in testicular YST. No case has so far been described in setting of FAP. Hereby, we describe a case of extragonadal germ cell tumor arising in colectomy stump of a patient with FAP.

Key words: Extragonadal germ cell tumor, familial adenomatous polyposis, fine needle aspiration cytology, metastasis, yolk sac tumor

INTRODUCTION

Familial polyposis of the large bowel is an autosomal dominant condition with a high degree of penetrance. The responsible gene adenomatous polyposis coli (APC) has been localized to chromosome 5q21. An alternative genetic mechanism is a germ-line mutation of base-excision repair gene MYH. Radiologically and grossly, the bowel is studded with polyps ranging from very slight elevations of the normal mucosa to relatively large masses. A minimum of 100 polyps need to be present before such a diagnosis can be justified on morphological grounds. Microscopic appearance of the individual lesions is indistinguishable by either light or electron microscopic criteria.[1]

Yolk sac tumors (YSTs) are uncommon malignant germ cell neoplasms that were described originally in gonads.Rarely, they also may arise in extragonadal sites, mainly in the same locations where other germ cell tumors (GCTs) are reported occasionally, such as the sacrococcygeal region, the upper aerodigestive tract, the lung, the anterior mediastinum, the female reproductive tract, the retroperitoneum, and the brain. The gastrointestinal tract is a very uncommon site for these tumors. The esophagus has been reported only once as a primary site for a YST, whereas few cases have been documented as arising in the stomach. Neoplasms that reproduce extraembryonal tissues also have been described in the colon and rectum.[2]

Chao et al. studied cytologic examination of fine needle aspirates (FNAs) of primary or metastatic lesions of primary extragonadal germ cell tumors (EGGCTs) (PEGCTs), stained either with romanovsky or papanicolaou stain. Tumor cell morphology was found to be same in primary and metastatic sites and was found to be of diagnostic value for such diseases. They concluded that fine needle aspiration cytology (FNAC), together with the characteristic clinical presentation and specific tumor markers, is crucial to the initial diagnosis and subsequent assessment of patients with PEGCTs.[3]

CASE REPORT

A 22-year-old male, a follow-up case of post colectomy for familial adenomatous polyposis (FAP) presented with bilateral inguinal lymphadenopathy for past 2 months. The patient's past history included complaint of bleeding per rectum for 8 months at an age of 10 years. Colonoscopy revealed rectum and ascending colon full of sessile and pedunculated polyp along with few polyps in descending and transverse colon. A diagnosis of FAP was made. The patient underwent proctocolectomy with ileal
pouch anal anastomosis (IPAA) and covering loop ileostomy. The polyps were >100 in number and confirmed to the morphology of adenomatous polyps. Hence, the histopathological examination was consistent with radiological diagnosis of FAP.

On examination, bilateral inguinal lymphadenopathy was present. Rest of systemic examination including testicular examination was within the normal limits. Complete hemogram revealed Hb of 8.8 gm%, total leukocyte count of 10,000/cm³, differential leukocyte counts P55 L40 M3 E2 B0 and platelet count of 4.5 lakhs/cm³. Chest X-ray revealed a lytic lesion in medial end of the clavicle and right pleural effusion [Figure 1]. Ultrasonography (USG) thorax revealed bilateral pleural effusion. USG abdomen revealed splenomegaly (17 cm) and few enlarged lymph nodes in peripancreatic and paraaortic region. Bilateral testes were normal. Enlarged lymph nodes were seen in bilateral inguinal region. Computed tomography (CT) scan thorax and abdomen revealed bilateral pleural effusion, consolidation in the right lower lobe of lung and bilateral inguinal lymphadenopathy.

18 fluorodeoxyglucose positron emission tomography (PET)-CT whole body scan revealed hypermetabolic metastatic disease involving mediastinal and abdominal lymph nodes and multiple skeletal sites (focal area in right frontal bone, head of left humerus, right clavicle, sternum, left ala of sacrum, body of D2, D5, L1, L4, L5 vertebrae, left transverse process of D3 vertebrae). The primary site was hypermetabolism in ileo-anal anastomotic region [Figure 2].

Fine-needle aspiration cytology was done from inguinal lymph node and clavicle. Smears from both the sites revealed similar morphology showing atypical cells arranged in groups, overlapping clusters, papillae, acini and dispersed singly [Figure 3a and b]. The cells revealed moderate nuclear pleomorphism, variable nuclear chromatin and prominent nucleoli in some. Cytoplasm was scant to abundant and vacuolated and granular in many [Figure 3c] with periodic acid Schiff positive pink intracytoplasmic inclusion in some [Figure 3d]. A few multinucleated giant cells were also seen and background focally gave a tigroid appearance [Figure 3c]. Cytologically possibility of YST and metastasis from colonic adenocarcinoma were rendered. Immunocytochemistry was also performed on FNA slides, which revealed positivity for cytokeratins-low molecular weight and α-fetoprotein (AFP). Serum AFP and β-human chorionic gonadotropin (HCG) were advised, which showed increased levels of AFP (3250 ng/ml). Considering raised levels of AFP and immunocytochemical findings, the possibility of colonic adenocarcinoma was excluded and a diagnosis of EGGCT with closest resemblance to YST was rendered.

The patient was advised biopsy of the involved lymph node as well as endoscopic biopsy from the primary site for histopathological confirmation, but the patient did not agree. Considering the raised AFP levels, the patient was advised chemotherapy (cisplatin and etoposide) for YST, but he did not comply and expired after 1 month. Postmortem autopsy for confirmation of diagnosis could not be performed as the relatives of the patient did not give consent for the same.

DISCUSSION

Familial polyposis coli (FAP) is an inherited disease involving truncating mutations of the tumor suppressor APC gene. The gene is located on chromosome 5 and suppresses canonical Wnt signaling. Clinically, the result in the colon is hundreds to thousands of adenomatous polyps that begin to appear as early as puberty. Early symptoms of patients with FAP include rectal bleeding and diarrhea. Diagnosis of FAP is based upon the finding of >100 adenomas

![Figure 1: Chest X-ray revealing a lytic lesion in medial end of clavicle and right pleural effusion](image1.png)

![Figure 2: 18 fluorodeoxyglucose positron emission tomography-computed tomography whole body scan revealing hypermetabolic metastatic disease involving mediastinal and abdominal lymph nodes and multiple skeletal sites and the primary site of hypermetabolism in ileo-anal anastomotic region](image2.png)
in the colon. Optimal operative therapy is a proctocolectomy with restorative ileo-anal reconstruction–IPAA. Most advocate surgical intervention when the patient is 15 years old and is able to understand and participate in treatment decisions.[6]

Extragonadal germ cell tumors are rare, accounting for only 1-4% of all GCTs. 95% of all testicular tumors are GCTs. These tumors originate in the sperm forming cells in the testicles (the male gonads) or egg producing cells in the ovary (female gonads). On rare occasions, however, GCTs develop elsewhere in the body without any evidence of cancer in the testes. When this happens, they are referred to as EGGCTs.[3]

Seminomas account for 30-40% of these tumors, and nonseminomatous tumors account for 60-70%. The most common site of EGGCTs is the mediastinum (50-70%) followed by the retroperitoneum (30-40%), the pineal gland (5%), and the sacrococcygeal area (<5%). In children, benign and malignant EGGCTs occur equally in males and females. In adults, only benign EGGCTs (teratomas) occur at equal frequency in both sexes; >90% of malignant EGGCTs occur in males. EGGCTs are aggressive and are usually seen in young adults. The treatment and prognosis of the disease depends on a variety of factors including the type of cancer, the tumor location, and the size of the tumor.[5]

Extragonadal pure YSTs are thought to arise from germ cells that are sequestered in midline during embryogenesis. The extreme rarity of YSTs of the gastrointestinal tract suggests a peculiar morphogenesis for these tumors with respect to those arising in other extragonadal sites. Some authors have proposed that these tumors could result from an aberrant differentiation or “retrodifferentiation” occurring in cells during carcinogenesis.[2]

Fine-needle aspirate smears from YSTs have a variety of patterns, including papillary and/or papillaroid fragments, cohesive clusters, acinar structures, and single tumor cells that contain moderate amounts of vacuolated cytoplasm and vesicular nuclei with prominent nucleoli. Basement membrane-like material (observed in 60% of cases) is the feature that assists most consistently in the cytodiagnosis of YST in combination with hyaline globules (observed in only 20% of cases). The presence of tumor with a glandular appearance in an appropriate clinical setting should arouse the suspicion of YST in cytology. FNAC, compared with a biopsy, is a rapid, reliable, and less invasive technique to make a diagnosis of GCTs at extragonadal sites, including metastatic lesions, which may be seen as the first clinical presentation.[9]

Workup of EGGCTs begins with lab studies with the tumor markers AFP and β-HCG. These tumor markers provide diagnostic, staging, and prognostic information. Pure seminomas and pure choriocarcinomas do not produce AFP. A CT scan of the chest, abdomen, and pelvis should be obtained. Treatment consists of surgery and chemotherapy.[5]

Recent epigenetic studies have suggested the involvement of some tumor suppressor genes, including the APC gene in infantile YST. Loss of heterozygosity at 9p21, where the APC gene is localized, was detected in at least 3 (30%) of the nine YSTs examined. These data indicate that inactivation of the APC gene, by allelic loss and/or promoter methylation, is related to the occurrence of infantile YSTs.[7] However, no case has so far been described in setting of FAP.

Oechsle studied prevalence of bone metastasis in GCT patients. 40 patients (9%) presented with primary bone metastases. Bone metastases were significantly more frequently observed in patients with primary mediastinal tumors, YST histology, and synchronous liver metastases.[8]

Our case describes an YST arising in prophylactic colectomy stump, which metastasized to abdominal and inguinal lymph nodes and multiple skeletal sites. To the best of our knowledge, this is the first case with this morphologic appearance in the remnant stump in setting of FAP, although few cases of YST with gastric adenocarcinoma have been described.[2,9]

The present case of YST arising in prophylactic colectomy stump (strongly suspected and endorsed by PET scan study) and metastasizing widely in body strongly points to a common molecular pathogenetic pathway.

Fine-needle aspiration cytology proves to be a reliable, rapid and less invasive diagnostic tool in conjunction with other ancillary investigations in such moribund patients.

REFERENCES


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