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Colon and Lung Choriocarcinoma

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Choriocarcinoma is a rare tumor that usually arises in the uterus and gonads. However, it can also occur in extragenital locations such as the lung [1], mediastinum [2], retroperitoneum [3] and gastrointestinal tract [4]. Choriocarcinoma of the gastrointestinal tract is extremely rare. It is usually located in the stomach, esophagus, small bowel and colon. Only nine cases of colon and rectal choriocarcinoma have been reported in the English-language medical literature. In addition, choriocarcinoma of the colon and the lung in association with adenocarcinoma of the contralateral lung has never been reported. We present the first case of a coexisting colon and lung choriocarcinoma with lung adenocarcinoma, describe the management, and review the literature on this unique clinical presentation.

PATIENT DESCRIPTION

A 57 year old woman with a history of heavy smoking presented with hemoptysis. Chest X-ray showed bilateral shadowing in the upper lobes. Chest computed tomography scan demonstrated bilateral infiltrative lesions. Fine needle aspiration revealed non-small cell carcinoma in both lungs. Positron emission tomography-CT demonstrated uptake in the lung lesions and in retrocaval and paratracheal lymph nodes (stage IV disease). Before undergoing a combined chemotherapy and immunotherapy protocol the patient was required to undergo a full-body CT, which demonstrated a tumor in the left colon. Colonoscopy revealed a left colon lesion and biopsy showed poorly differentiated adenocarcinoma. At this time it was assumed that the patient had two primary lesions: adenocarcinoma of the lung and adenocarcinoma of the colon. Although the patient was asymptomatic we decided to perform a left colectomy to prevent colonic obstruction or bleeding during chemotherapy. At surgery, a polypoid tumor in the splenic flexure was detected. Left colectomy was performed, the postoperative course was uneventful and the patient was discharged after 8 days.

The pathologic finding was a solid malignant tumor invading the muscularis propria and composed of two populations of cells: large polygonal clear cells and atypical multinucleated giant cells. Giant cells were strongly positive for human chorionic gonadotropin and negative for carcinoembryonic antigen. Eight negative lymph nodes were resected. Histology and the immunohistochemical pattern of the tumor were consistent with choriocarcinoma.

An immunohistochemical dye showed that the colon biopsy that had been taken during colonoscopy demonstrated choriocarcinoma rather than adenocarcinoma as previously assumed.

Further history taking revealed that the patient had had an abortion. This raised the possibility of a microgerminal cell tumor from a hydatiform mole, but transvaginal ultrasound was interpreted as normal. Serum levels of βhCG were 13,000 IU/L before chemotherapy. The patient received four courses of VIP combination chemotherapy (VP-16 100 mg/m^2, ifosfamide 1.2 g/m^2, cisplatin 20 mg/m^2) and mesna 1.2 g/m^2. The chemotherapy cycles were one every 3 weeks, with each cycle given for 4 days. βhCG levels decreased by a log per course to less than 5 IU/L after three courses. A PET-CT scan later detected only the two lesions in the lungs. Eight weeks later a right upper lung lobectomy revealed adenocarcinoma. After recovery a left upper lobectomy was performed, and the histologic appearance showed interstitial fibrosis surrounded by foam macrophages and necrotic tissue, which is expected following chemotherapy. However, immunohistochemical staining showed one area that was strongly positive for βhCG. The patient did not receive further chemotherapy and died 16 months after the diagnosis of choriocarcinoma was made, with metastasis to the bone and brain.

COMMENT

Choriocarcinoma is a germ cell tumor that can be gestational or non-gestational. Non-gestational choriocarcinoma is a rare malignancy that can occur in the lung [1], mediastinum, kidney, stomach, small bowel and large bowel [2]. Gestational choriocarcinoma usually occurs in young females and has no connection with gonadal choriocarcinoma, which is more common in males. Both gestational and non-gestational choriocarcinoma are associated with a high serum level of βhCG.

There have been nine cases of colonic

βhCG = beta-human chorionic gonadotropin

PET-CT = positron-emission tomography-CT

choriocarcinoma reported in the English literature [Table]. Of these, all but two were associated with adenocarcinoma. In this report, the two remote lesions, both in the colon and the lungs, showed a combination of two different histologic characteristics as described above.

This patient was totally asymptomatic with regard to the colon choriocarcinoma, in contrast to previous reports of gastrointestinal choriocarcinoma. The PET-CT detected only the lung lesion, emphasizing the problematic issue of PET-CT as a low sensitivity diagnostic modality in choriocarcinoma. Knowing the patient had had an abortion raises the possibility of microgerminal cell tumor from a hydatiform mole. However, the normal report of transvaginal ultrasound made this option unlikely.

It was speculated by McKechnie and Fechner [4] that choriocarcinoma may originate from adenocarcinoma. Even if no histologic evidence of adenocarcinoma is documented, this theory could still be valid if adenocarcinoma was ruled out by choriocarcinoma [5]. The histopathologic report in our case found no indication for adenocarcinoma in the colon. In this complex case, the source of the tumor is conjectural since choriocarcinoma rarely arises also in the lung. The diagnosis of choriocarcinoma in the colon was suspected by the histologic hematoxylin and eosin examinations and was confirmed by high βhCG serum levels and immunohistochemistry. The patient received four courses of VIP, and serum βhCG levels returned to normal towards the end of the chemotherapy regimen. When first measured, 3 weeks after the colectomy, βhCG levels were 13,000 IU/L. βhCG decreased to 27 IU/L after the first and second courses of chemotherapy and only after the third course reached normal levels (< 5I U/L). The half-life of βhCG is 24 hours and this raised concern that the choriocarcinoma was active.

Since time is critical following the diagnosis of choriocarcinoma, prompt treatment with chemotherapy is crucial for prolonging survival if there is metastatic spread. In the present case the reduction of βhCG in the serum indicates response to treatment. The choriocarcinoma responded to chemotherapy only after three courses of VIP. βhCG did not

VIP = VIP-16 100 mg/m², ifosfamide 1.2 g/m², cisplatin 20 mg/m²

Reported cases of colon choriocarcinoma

Author, journal (yr)	Patient's age (yrs) and gender	Tumor site	Management	Outcome
Park et al. *Cancer* (1980)	49 female	Sigmoid chorio- and adenocarcinoma with metastasis	Hartman's operation + 5 FU	Patient died 1 month post-surgery from liver and cardiopulmonary insufficiency
Gia-Khanh Nguyen *Dis Col Rectum* (1982)	74 male	Sigmoid chorio- and adenocarcinoma	Hartman's operation	Patient died 10 weeks after bowel resection with liver metastasis. Elevated levels of βhCG were documented
Hitoshi Kubosawa et al. *Cancer* (1984)	50 female	Sigmoid chorio- and adenocarcinoma	Hartman's operation	Patient died 5.5 weeks after bowel resection with liver, lung, parapancreatic lymph node metastasis
Ordonez & Luna *Am J Gastroenterol* (1984)	35 female	Right colon chorio- and adenocarcinoma	Right colectomy	Patient died 10 weeks after bowel resection with metastasis to liver, lungs, pleura, pericardium, iliac bone, mediastinal, mesenteric and periaortic lymph nodes
Lind et al. *Am J Clin Pathol* (1986)	42 male	Metastatic right colon choriocarcinoma	Laparotomy, whole brain irradiation and chemotherapy with bleomycin and cisplatin	Patient died 1 month following admission. Metastases were found in both lungs, paratracheal lymph nodes, liver, spleen, kidneys and paraaortic lymph nodes. High probability for bone and brain metastases as well
Mitsuru Tokisue et al. *J Gastroenterol* (1996)	29 female	Rectal chorio- and adenocarcinoma	Chemotherapy: 4 courses of methotrexate, etoposide, actinomycin-D. Tumor resection, another two courses of methotrexate, etoposide, actinomycin-D, cisplatin, doxorubicin	Patient died 10 months after treatment initiation. Although both primary (rectal) foci and pulmonary metastasis showed regression after chemotherapy, pulmonary metastasis enlarged and brain metastasis were detected
Kiran et al. *Eur J Surg Oncol* (2001)	68 male	Distal colon chorio- and adenocarcinoma. 31 month after Hartman's operation for rectal carcinoma	Tumor resection	Patient died of liver failure before chemotherapy was begun
Duy T. Le et al. *Dis Colon Rectum* (2003)	73 male	Metastatic Rt colon choriocarcinoma	Rectal biopsy	Patient died 10 days after admission. Postmortem report revealed a choriocarcinoma in the colon, brain, lungs, pancreas, kidney and in mesenteric lymph nodes
Verbeek et al. *Hum Pathol* (2004)	54 female	Low rectal choriocarcinoma	Abdominoperineal resection, hysterectomy, adnexectomy, paraaortic and locoregional lymph node resection. Chemotherapy 4 cycles of cisplatin, etoposide, ifosfamide. thoracotomy for resection of lung metastasis.	Patient died 8 month after diagnosis

decrease to normal levels after surgery, implying that micrometastatic disease not recognized by PET-CT was still present after surgery.

Choriocarcinoma is a systemic disease and it is sometimes difficult to determine the site of the primary lesion. As choriocarcinoma of the colon and digestive system is rare and usually not identified until the tumor has spread, our assumption is that this patient had a primary colon choriocarcinoma that had spread to her lungs and later to the bones and brain. New tests in the future might be more sensitive for the detection of choriocarcinoma cells [5]. However, the prognosis is worsened by the presence of metastatic disease involving the central nervous system, liver, or gastrointestinal tract.

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