Colon and Lung Choriocarcinoma

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KEY WORDS: choriocarcinoma of colon, lung choriocarcinoma, non-gestational choriocarcinoma

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/m², ifosfamide 1.2 g/m², cisplatin 20 mg/m²) and mesna 1.2 g/m². 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 (< 51 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

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**Reported cases of colon choriocarcinoma**

<table>
<thead>
<tr>
<th>Author, journal (yr)</th>
<th>Patient’s age (yrs) and gender</th>
<th>Tumor site</th>
<th>Management</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Park et al. Cancer (1980)</td>
<td>49 female</td>
<td>Sigmoid chorio- and adenocarcinoma with metastasis</td>
<td>Hartman’s operation + 5 FU</td>
<td>Patient died 1 month post-surgery from liver and cardiopulmonary insufficiency</td>
</tr>
<tr>
<td>Gia-Khanh Nguyen Dis Col Rectum (1982)</td>
<td>74 male</td>
<td>Sigmoid chorio- and adenocarcinoma</td>
<td>Hartman’s operation</td>
<td>Patient died 10 weeks after bowel resection with liver metastasis. Elevated levels of βhCG were documented</td>
</tr>
<tr>
<td>Hitoshi Kubosawa et al. Cancer (1984)</td>
<td>50 female</td>
<td>Sigmoid chorio- and adenocarcinoma</td>
<td>Hartman’s operation</td>
<td>Patient died 5.5 weeks after bowel resection with liver, parapankreatic lymph node metastasis</td>
</tr>
<tr>
<td>Ordonez &amp; Luna Am J Gastroenterol (1984)</td>
<td>35 female</td>
<td>Right colon chorio- and adenocarcinoma</td>
<td>Right colectomy</td>
<td>Patient died 10 weeks after bowel resection with metastasis to liver, lungs, pleura, pericardium, iliac bone, mediastinal, mesenteric and periaortic lymph nodes</td>
</tr>
<tr>
<td>Lind et al. Am J Clin Pathol (1986)</td>
<td>42 male</td>
<td>Metastatic right colon choriocarcinoma</td>
<td>Laparotomy, whole brain irradiation and chemotherapy with bleomycin and cisplatin</td>
<td>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</td>
</tr>
<tr>
<td>Mitsuru Tokisue et al. J Gastroenterol (1996)</td>
<td>29 female</td>
<td>Rectal chorio- and adenocarcinoma</td>
<td>Chemotherapy: 4 courses of methotrexate, etoposide, actinomycin-D. Tumor resection, another two courses of methotrexate, etoposide, actinomycin-D, cisplatin, doxorubicin</td>
<td>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</td>
</tr>
<tr>
<td>Kiran et al. Eur J Surg Oncol (2001)</td>
<td>68 male</td>
<td>Distal colon chorio- and adenocarcinoma, 31 month after Hartman’s operation for rectal carcinoma</td>
<td>Tumor resection</td>
<td>Patient died of liver failure before chemotherapy was begun</td>
</tr>
<tr>
<td>Duy T. Le et al. Dis Colon Rectum (2003)</td>
<td>73 male</td>
<td>Metastatic Rt colon choriocarcinoma</td>
<td>Rectal biopsy</td>
<td>Patient died 10 days after admission. Postmortem report revealed a choriocarcinoma in the colon, brain, lungs, pancreas, kidney and in mesenteric lymph nodes</td>
</tr>
</tbody>
</table>
Case communications

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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**Capsule**

**Complement-mediated regulation of the IL-17A axis is a central genetic determinant of the severity of experimental allergic asthma**

Severe asthma is associated with the production of interleukin 17A (IL-17A). The exact role of IL-17A in severe asthma and the factors that drive its production are unknown. Lajoie et al. demonstrate that IL-17A mediated severe airway hyperresponsiveness (AHR) in susceptible strains of mice by enhancing IL-13-driven responses. Mechanistically, the authors demonstrate that IL-17A and AHR were regulated by allergen-driven production of anaphylatoxins, as mouse strains deficient in complement factor 5 (C5) or the complement receptor C5aR mounted robust IL-17A responses, whereas mice deficient in C3aR had fewer IL-17-producing helper T cells (T_{H17} cells) and less AHR after allergen challenge. The opposing effects of C3a and C5a were mediated through their reciprocal regulation of IL-23 production. These data demonstrate a critical role for complement-mediated regulation of the IL-23–T_{H17} axis in severe asthma.

*Nat Immunol* 2010; 11: 928
Eitan Israeli

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**Capsule**

**Peripheral innervation is necessary for organogenesis and may be involved in organ repair or regeneration**

Organ development requires the differentiation and coordination of nerves and blood vessels with multiple cell types. The peripheral parasympathetic nervous system innervates many organs during embryogenesis; however, the function of this interaction during organogenesis is unclear. By exploiting the close association during development of the parasympathetic ganglion with the mouse embryonic salivary gland epithelium, Knox et al. found that neuronal innervation preserves an epithelial progenitor cell population via muscarinic receptor and epidermal growth factor receptor signaling. These progenitor cells are then maintained in the adult salivary gland. A similar system was observed in the developing prostate gland. Peripheral innervation is thus necessary for organogenesis and may also be involved in organ repair or regeneration.

*Science* 2010; 329: 1645
Eitan Israeli

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“*I detest racialism, because I regard it as a barbaric thing, whether it comes from a black man or a white man*”

Nelson Mandela (b. 1918), first South African president to be elected in a fully representative democratic election. Before his presidency, Mandela was an anti-apartheid activist, and leader of the African National Congress (ANC). Mandela served 27 years in prison, mostly on Robben Island. Following his release in 1990, he represented his party in the negotiations that led to multiracial democracy in 1994. As president from 1994 to 1999, he frequently gave priority to reconciliation. In South Africa, Mandela is often known as Madiba, an honorary title adopted by elders of Mandela’s clan. Mandela has received more than 250 awards over four decades, including the 1993 Nobel Peace Prize.

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**References**