A case report: gastric adenocarcinoma in childhood

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Primary gastric adenocarcinoma is extremely rare in children, and accounts for 0.05% of all gastrointestinal malignancies during childhood. The initial symptoms of epigastric pain, feeling of fullness, belching, and loss of appetite are non-specific and misleading. Nausea, vomiting and weight loss may accompany, which also complicate reaching a prompt diagnosis. In the presented case, a 15-year-old girl admitted with ascites, pleural effusion, right supra-clavicular lymphadenopathy, and back pain. No primary focus of a malignancy was accomplished in radiological evaluation, and the diagnosis of gastric carcinoma was achieved with upper gastrointestinal system endoscopy. We point out the importance of upper gastrointestinal system endoscopy in patients with ascites and uncertain diagnosis of the primary focus of malignancy.

Key words: gastric adenocarcinoma, ascites, childhood.

Gastric tumors in children, the great majority of which are lymphomas and sarcomas, are uncommon, and account for 0.05% of all gastrointestinal malignancies¹,². The initial symptoms, such as epigastric pain, feeling of fullness, belching, nausea, vomiting, weight loss, and loss of appetite, are non-specific³. Although peritoneal metastasis and ascites are well-known symptoms in adult patients, they are not frequently encountered in children. In the presented case, the importance of upper gastrointestinal system endoscopy for prompt diagnosis in pediatric patients with ascites is emphasized⁴-⁶.

Case Report

A 15-year-old girl was presented on 4 January 2008 with complaints of progressively increasing abdominal distension, generalized abdomen and back pain, nausea, and vomiting lasting for one month. She had lost 4 kg in 20 days. Family history was unremarkable.

Her weight and stature were 46 kg (10th percentile) and 158 cm (25th-50th percentile), respectively. The patient was afebrile, pale and in marked discomfort. She refused to move due to her back pain. No respiratory distress was encountered. An enlarged (4x4 cm), firm, and painful right supraclavicular lymph node was detected. Abdominal distension was present, which was attributable to massive ascites rather than hepatosplenomegaly.

The complete blood count revealed: hemoglobin 10 g/dl, white blood cell count 10,700/µl, and platelet count 152,000/µl. Aspartate aminotransferase and lactate dehydrogenase levels were 71 U/L and 2,198 U/L, respectively. The blood chemistries and the erythrocyte sedimentation rate were in normal ranges. The chest X-ray demonstrated bilateral pleural effusion, and abdominal ultrasound examination revealed widespread ascites without an accompanying abnormality. Thorax computed tomography showed sub-segmental atelectasia in lower lobes with bilateral and massive pleural effusion. Biochemistry analysis study of the ascites and pleural effusion fluid showed elevation in lactate dehydrogenase (1280 U/L). Cytopathologic examination of these fluids revealed cells with intracytoplasmic vacuoles, loose nuclear chromatin, and profuse nuclei, which were suggestive of epithelial malignancies. Alpha-fetoprotein, B-human chorionic gonadotropin, CA 15-3, and CA
19-9 were within normal ranges. On the other hand, carcinoembryonic antigen (CEA) and CA-125 were found to be elevated \[86.30 \text{ ng/ml (0-2.5 ng/ml)} \text{ and 215.5 U/L (N: 0-35 U/L)}, \text{ respectively}\]. Histopathologic examination of the supraclavicular lymph node biopsy specimen revealed a diffuse, infiltrating tumor consisting of malignant cells with wide cytoplasms and atypical nuclei. The tumor was immunoreactive with pancytokeratin and epithelial membrane antigen, and did not stain with vimentin, desmin, leukocyte common antigen, CD3, placental alkaline phosphatase, CD99, calretinin, estrogen, or progesterone receptor. Results of the histopathologic examination of the supraclavicular lymph node biopsy together with CEA elevation were suggestive of gastrointestinal system epithelial neoplasm. Therefore, upper gastrointestinal system endoscopy was performed, which demonstrated highly fragile gastric mucosa with generalized edema, hyperemia, and thickened gastric folds (Fig. 1). Multi-nodular, hyperemic lesions were encountered in the greater curvature. Histopathologic examination of biopsies from the gastric mucosa revealed gastric signet-ring cell carcinoma (Fig. 2). Helicobacter pylori was not detected in the tissue specimens. Staging of gastric signet-ring cell carcinoma consisted of peritoneal cytopathologic examination as well as Tc-99m bone scintigraphy, as a result of which widespread metastases were detected in the vertebrae. The final TNM staging was: pT3 Nx M1. Due to extensive metastatic disease, no local radiotherapy or surgery was planned. Combination chemotherapy for metastatic gastric cancers of adults consisting of epirubicin (50 mg/m², on day 1), docetaxel (60 mg/m², on day 1) and cisplatin (60 mg/m², on day 2) was started and planned to be repeated for eight cycles with three-week intervals. Hematopoietic growth factor was administered following the first interval. The ascites decreased following the first course of the chemotherapy. Supraclavicular lymph node and back pain, which was due to vertebral metastases, improved after the second course. The patient continues to receive chemotherapy. Despite the absence of history of cancer in her parents and siblings, upper gastrointestinal system endoscopies were performed and biopsies were taken, all of which revealed no malignancy.

**Discussion**

Gastric cancer before the age of 40 years is an uncommon occurrence. Only 2-9% of all patients with gastric cancer are younger than 40 years of age; most are older than 35 years. Lymphomas and sarcomas constitute the great majority of gastric malignancies in children. Primary gastric adenocarcinoma is extremely rare and accounts for 0.05% of all gastrointestinal malignancies in children. If gastric adenocarcinoma appears at an unusually young age, as in our patient, genetic factors should be considered. The most common genetic abnormalities tend to be loss of heterozygosity of tumor suppressor genes, particularly p53 or adenomatous polyposis coli gene. In the case of gastric cancer, chromosomal changes (5q, 6q, 13q, 17p), microsatellite instability, E-cadherin mutations, and other factors have
been studied\(^3\). Therefore, it is important to take a detailed family history and screening. Our patient’s family history was not notable. Although no cancer was detected in endoscopic biopsy specimens, detailed genetic work-up was planned but could not be carried out because of financial issues.

The cause of gastric cancer is thought to be multifactorial, thus emphasizing environmental factors as much as genetic risk. Although chronic infection with \textit{H. pylori} has been suggested as playing a role in the pathogenesis of gastric cancer, especially MALT lymphomas, an association between \textit{H. pylori} infection and adenocarcinoma is under debate\(^1\). We were unable to find \textit{H. pylori} infection in the endoscopic biopsy specimens.

The majority of gastric carcinomas in children occur in the pyloric antrum, the esophagogastric junction, and the greater and lesser curvatures. Tumors in young patients are more likely to be diffuse and undifferentiated with signet-ring cells\(^1,8,10,12\), as in our patient.

Young patients with gastric adenocarcinoma are often misdiagnosed due to an unusual presentation and thus are only diagnosed properly in late stages\(^3,8\). In addition, the natural behavior of the tumor is more aggressive and the duration of symptoms is shorter in youngsters, providing another handicap for the physician for timely diagnosis in early stages\(^3,8\). Common presenting symptoms of gastric cancer are abdominal pain, dysphagia and weight loss. More unusual presentations such as left supraclavicular lymphadenopathy, a periumbilical nodule, a left axillary nodule, ascites, or a palpable liver mass should alert the clinician. Since gastric cancer can spread via lymphatics and transmural extension into the peritoneal cavity invading the lymphatics, a palpable left supraclavicular lymph node (Virchow’s node) or enlarged left axillary nodes are the most frequent sites of lymphatic metastases\(^1,13,14\). Although 25-50\% of adult patients with gastric cancer have distant or peritoneal metastases at presentation\(^2,4\), ascites has not been reported as a presenting sign of childhood gastric carcinoma. Radiologic evaluation failed to detect peritoneal carcinomatosis, but malignant cells were assumed to be dispersed transmurally to the peritoneal cavity. Right supraclavicular lymph node metastasis and malignant pleural effusion were supposed to be due to lymphatic metastasis. Distant metastases also occur to the skin, bone, ovaries and brain\(^1\). Bony metastasis with vertebral involvement is more common in younger patients\(^14\). Marked discomfort and back pain in the present case was because of widespread vertebral metastasis.

The prognosis of gastric adenocarcinoma in young patients is grave due to the high incidence of undifferentiated tumors and advanced stage at the time of diagnosis\(^3\). Because of its rarity, no established oncologic strategy exists for pediatric patients, for whom adult protocols are applied. The only potentially curative treatment for localized gastric cancer is complete surgical resection\(^10\). Adjuvant chemotherapy was proven to have no use in local or local advanced-stage gastric carcinoma in terms of survival\(^10,15,16\). Advanced gastric cancer, as in our patient, is considered to be a non-resectable disease, because it is locally advanced or presents as metastatic disease\(^2\). The prognosis for patients with advanced gastric cancer is poor, with a median survival of three to five months with the best supportive care alone. Although gastric cancer is a relatively chemosensitive disease, results of most combination regimens have been unsatisfactory in terms of survival\(^7\). Although 5-fluorouracil, leucovorin, adriamycin, cisplatin, etoposide, and epirubicin-containing protocols seem to have a limited effect in survival rates, they were reported to be effective in control of symptoms\(^2,17,18\). Newer chemotherapeutics with less toxicity are being developed for current use. Especially, docetaxel (a taxan group drug)-containing chemotherapy regimens are proposed as first-line therapies\(^2,7,17\). Recently, Di Lauro et al.\(^7\) reported that epirubicin, docetaxel and cisplatinum combination was useful in metastatic gastric carcinoma patients with a comparable efficacy and acceptable safety profile. This combination regimen provided early symptom control in our patient.

In conclusion, upper gastrointestinal system endoscopy and endoscopic biopsies are crucial in pediatric patients with vague gastrointestinal symptoms and malignant ascites in whom radiological intervention fails to demonstrate the primary site of the malignancy. Tissue diagnosis and anatomic localization of the primary tumor are best obtained by means of upper gastrointestinal system endoscopy.
Rare gastric adenocarcinoma should be kept in mind in childhood malignancies with their unusual presentation.

REFERENCES


