Carcinosarcoma with choriocarcinomatous and osteosarcomatous differentiation in a patient with juvenile polyposis syndrome

Rafael Parra-Medina,1,2 Patricia López Correa,1,2 Julian Jiménez Moreno,2 Paula Moreno Lucero,2 Edgardo Yaspe,1,2 Fernando Polo1,2

Department of Pathology, Hospital Infantil de San José, Bogotá; Fundación Universitaria de Ciencias de la Salud, Bogotá, Colombia

Introduction

Juvenile polyposis syndrome (JPS) is an infrequent autosomal dominant hereditary predisposition to the occurrence of hamartomatous polyps in the colon and rectum. We describe the case of a 12-year-old boy with JPS associated with an abdominal tumor. Histological sections of the abdominal tumor showed components of adenocarcinoma, carcinomatous and osteosarcomatous elements. This association has not been reported before.

Case Report

A 12-year-old boy who presented with an abdominal mass associated with B symptoms as well as anemia, requiring several blood transfusions, and no family history of gastrointestinal problems. On initial examination a large palpable ill-defined mass, fixed to deep underlying structures was found in the right flank. The mass was characterized by an abdominal computed tomography (CT) scan (Figure 1) that revealed a heterogeneous stenotic mass affecting the cecal lumen and compromising the colon. Severe hepateomaga was observed including several small nodular lesions corresponding to metastasis.

At the time the pathology report was received, the boy remained in critical condition and was discharged at the request of the family and due to his overall poor prognosis. Thus, a follow-up of this case was not possible and the surgical treatment outcome was not known.

Discussion

Juvenile polyposis syndrome (JPS) is a rare dominant autosomal hereditary disorder characterized by the presence of five or more juvenile polyps along the colorectum; or juvenile polyps throughout the gastrointestinal tract or any number of polyps in patients with family history of juvenile polyposis. Carcinosarcoma is a mixed biphasic tumor, characterized by a carcinomatous component and a sarcomatous component, an extremely rare and aggressive entity with poor prognosis. Carcinosarcoma has been described in the gastrointestinal tract predominantly in the esophagus, in the stomach and in the biliary tract, whereas the presence of this type of tumor in the colon has been reported only rarely. We report the case of a 12-year-old boy with JPS associated to a colon tumor characterized as a conventional adenocarcinoma exhibiting areas of choriocarcinomatous and osteosarcomatous elements.

Correspondence: Rafael Parra-Medina, Department of Pathology, Hospital Infantil de San José, Carrera 52 #67A-71, Bogotá, Colombia. Tel: +57.143.77540. E-mail: rsparra@fucsalud.edu.co; rasapa90@hotmail.com

Key words: Juvenile polyposis syndrome; adenocarcinoma; osteosarcoma; choriocarcinoma.

Acknowledgments: the authors express their gratitude to Elizabeth A. Montgomery. They also would like to thank the Radiology Department at Hospital Infantil de San José, Bogotá, Colombia.

Contributions: the authors contributed equally.

Conflict of interest: the authors declare no potential conflict of interest.

Received for publication: 23 December 2014. Revision received: 16 May 2015. Accepted for publication: 26 May 2015

This work is licensed under a Creative Commons Attribution NonCommercial 3.0 License (CC BY-NC 3.0).

©Copyright R. Parra-Medina et al., 2015

Licensee PAGEPress, Italy

Rare Tumors 2015; 7:5778
doi:10.4081/rare-tumors.2015.5778

[ Rare Tumors 2015; 7:5778]
This entity is rare in children; in fact, the first documented report was published in 2008. It localizes most commonly in the head, neck, and female urogenital system. In fact, only 23 cases of colon malignancies of this type have been reported in the literature.

In 2012, Ryu et al. reviewed the clinicopathological features of 17 reported cases of colonic sarcomatoid carcinomas. Mean age was 67.6 years. Ten patients were women. Some of these tumors, deeply invaded the bowel wall, metastasized to distant organs, resisted multi-agent chemotherapy and caused early patient death. Metastases were more frequent to the liver, lymph nodes, omentum, peritoneum and spleen.

The association of carcinosarcoma and choriocarcinoma has only been reported on the female urogenital system and bladder, making our case a clinicopathological challenge.

Hematoxylin & Eosin-based diagnosis may be difficult in these cases, which comprise various tumor components, thus, immunohistochemical diagnostic analyses can be a useful tool in an attempt to define the histogenesis of the tumor. In this case, we observed AE1/AE3 and CK7 positivity for epithelial components and SALL4 positivity for germinal components. Immunohistochemistry is extremely important for diagnosing these tumors. A choriocarcinoma was diagnosed based on the morphologic features and the presence of HCG and negativity of other germinal markers such as AFP, OCT3/4, PLAP, and CD117.

Conclusions

In summary, a case like the one presented here, of JPS associated with a conventional adenocarcinoma with choriocarcinomatous and osteosarcomatous differentiation has not been reported before. These changes may be explained by alterations in the TGF-β pathway.

Figure 1. Marked thickening of the ascending colon wall affecting 90% of the lumen with the resulting luminal stenosis.

Figure 2. Hematoxylin and Eosin 400× shows: A) Juvenile polyps with high and low-grade dysplastic changes. B) Components of conventional adenocarcinoma. C) Section of osteosarcoma component. D) Section of germinal tumor.

Figure 3. Immunohistochemistry: A) reactivity to cytokeratin (AE1/AE3) in the adenocarcinoma component; 4×. B) Reactivity to CK7 in the adenocarcinoma component; 50×. Reactivity to HCG is positive in the germinal tumor component; 400×.
Genes involved in JPS such as **SMAD4** and **BMPR1A** are also involved in the TGF-β pathway. TGF-β plays a crucial role in many cellular processes, including proliferation, differentiation, adhesion and migration. Disruptions in the TGF-β pathway have been reported in a uterine carcinosarcoma and choriocarcinoma. The role of TGF-β1 is associated with the initiation of the trophoblastic invasion process in choriocarcinoma by down regulation of the **SMAD4** gene. In addition, mutations in the **SMAD4** gene have been associated with predisposition to germinal tumors and other tumors.

**References**

1. Brosens LA, Langeveld D, van Hattem WA, et al. Juvenile polyposis syndrome. World J Gastroenterol 2011;17:4839-44.
2. Choi YY, Jeen YM, Kim YJ. Sarcomatoid carcinoma of colon: extremely poor prognosis. J Korean Surg Soc 2011;80:S26-30.
3. Shim HJ, Hong YK, Kim SJ, et al. Carcinosarcoma on ascending colon found by bowel perforation: a case report. J Korean Soc Coloproctol 2010;26:368-72.
4. Diamond M. Adenoma of the rectum in children: report of a case in a thirty month old girl. Am J Dis Child 1939;360-7.
5. Chow E, Macrae F. A review of juvenile polyposis syndrome. J Gastroenterol Hepatol 2005;20:1634-40.
6. Wei C, Dayong W, Liqun J, et al. Colorectal polyps in children: a retrospective study of clinical features and the value of ultrasonography in their diagnosis. J Pediatr Surg 2012;47:1853-8.
7. Stojcev Z, Borun P, Hermann J, et al. Hamartomatous polyposis syndromes. Hered Cancer Clin Pract 2013;11:4.
8. Brosens LA, van Hattem A, Hylind LM, et al. Risk of colorectal cancer in juvenile polyposis. Gut 2007;56:965-7.
9. Tsekouras DK, Katsaragakis S, Theodorou D, et al. Rectal carcinosarcoma: a case report and review of literature. World J Gastroenterol 2006;12:1481-4.
10. Jeong YJ, Lee MR, Kim JC, et al. Carcinosarcoma of the rectosigmoid colon in a 13-year-old girl. Pathol Int 2008;58:445-50.
11. Ryu Y, Kim A, Kim H, et al. Carcinosarcoma in the cecum. Gut Liver 2012;6:395-8.
12. Khuu HM, Crisco CP, Kilgore L, et al. Carcinosarcoma of the uterus associated with a nongestational choriocarcinoma. South Med J 2009;93:226-8.
13. Armah HB, Parwani AV. Sarcomatoid urothelial carcinoma with choriocarcinomatous features: first report of an unusual case. Urology 2007;70:e11-e4.
14. Ulbright TM. Germ cell tumors of the gonads: a selective review emphasizing problems in differential diagnosis, newly appreciated, and controversial issues. Mod Pathol 2005;18:561-79.
15. Semczuk A, Zakrzewski PK, Forma E, et al. TGFβ-pathway is down-regulated in a uterine carcinosarcoma: a case study. Pathol Res Pract 2013;209:740-4.
16. Li Y, Xu Q, Zhang Z, et al. The impact of TGF-β1 on the mRNA expression of TβR I, TβR II, Smad4 and the invasiveness of the JEG-3 placental choriocarcinoma cell line. Oncol Lett 2012;4:1344-8.
17. Bouras M, Tabone E, Bertholon J, et al. A novel SMAD4 gene mutation in seminoma germ cell tumors. Cancer Res 2000;60:922-8.
18. Davison JM, Hartman DA, Singhi AD, et al. Loss of SMAD4 protein expression is associated with high tumor grade and poor prognosis in disseminated appendiceal mucinous neoplasms. Am J Surg Pathol 2014;38:583-92.
19. Liu NN, Xi Y, Callaghan MU, et al. SMAD4 is a potential prognostic marker in human breast carcinomas. Tumour Biol 2014;35:641-50.