Int J Biol Med Res. 2010; 1(3): 88-89.

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com

Case Study

Coexistence of conventional renal cell carcinoma with gastrointestinal stromal tumor

Anil Malleshi Betigeri [a,*], Palanisamy Pasupathi[b], Govindaswamy Bakthavathsalam[c] , Balakrishnan Pugazhenthi[d]

[a,*] *Department of Pathology &* [b] *Department of Clinical Biochemistry, K.G. Hospital and Post ,Graduate Medical Institute, Coimbatore-641 018, Tamil Nadu, India*
[c] *Department of Surgery &* [d] *Department of Radiology, K.G. Hospital and Post Graduate , Medical Institute, Coimbatore-641 018, Tamil Nadu, India*

ARTICLE INFO

Keywords:
Gastrintestinal stromal tumors (GIST)
Papillary renal cell carcinoma
Conventional renal cell carcinoma
Cancer registry
Oncogenes

ABSTRACT

Gastrointestinal stromal tumors (GISTs) constitute an important group of mesenchymal tumors of gastrointestinal tract. Sporadic coexistence of papillary renal cell carcinoma and gastrointestinal stromal tumor is known. Mutation in proto-oncogenes, related to tyrosine kinase receptor molecules are involved in both tumors. We here in present a case of conventional clear cell renal cell carcinoma in a patient diagnosed to have gastrointestinal stromal tumor on endoscopic biopsy, stomach. It would be interesting to verify our case with findings of larger cancer registries. The repeated associations of specific tumors often serve as pointers to novel oncogene defects. Such germ line mutations are rarely found in sporadic cases such as ours.

1. Introduction

Gastrointestinal tumors are subset of mesenchymal tumors that are different from neoplasm of neurogenic or smooth muscle origin. Gastrointestinal tumors constitute approximately 3.6% of all gastric tumors [1]. Approximately 95% of GISTs have gain of function mutations of the KIT gene and immuno positive for CD117. The most common mutations (in-frame deletion, point mutations, duplications, and insertions) are at the juxta-membrane domain (exon 11). Less commonly, mutations occur at the extracellular domain (exon 9) or at exon 13 and 17. Most of the remaining 5% of GISTs have mutation of the platelet derived growth factor alpha (PDGFRA) gene (juxtamembrane exon 12 or tyrosinase kinase domain at 18 or 14). A very small number of tumors have no detectable mutation (wild type) [2].

Detecting individual mutations is valuable in predicting the prognosis of a GIST and determining whether it will respond to imatinib therapy. Some authors blame imatinib mesylate (Gleevac), which is traditionally used in gastrointestinal stromal therapy, as etiological factor in certain secondary tumors, especially papillary renal cell cancer [3]. C-MET protooncogene also encodes protein belonging to the tyrosine kinase receptor family, and some cases of papillary renal cell carcinoma (RCC) have been found to be associated with germline mutations of the c-MET oncogene [4]. The repeated associations of specific tumors often serve as pointers to novel oncogene defects.

The frequent co-expression of c-MET and c-KIT in solid tumors suggests the existence of common co-regulatory mechanisms. We present here a case of clear cell RCC and GIST.

2. Case Report

This patient was admitted with history of melena, dyspepsia since three days. He complained of giddiness since 2 days. On endoscopy a growth in the cardia with partial stenosis of lower gastroesopahgeal junction was noted. CT abdomen revealed mass right kidney with adherence to liver. Subsequently he was offered a choice of surgical treatment. He was taken for elective surgery. Laprotomy/ upper gastrectomy [Figure 1.(b)] with distal esophagectomy done. Right radical nephrectomy [Figure 1.(a)] and spleenectomy was also performed in the same setting.

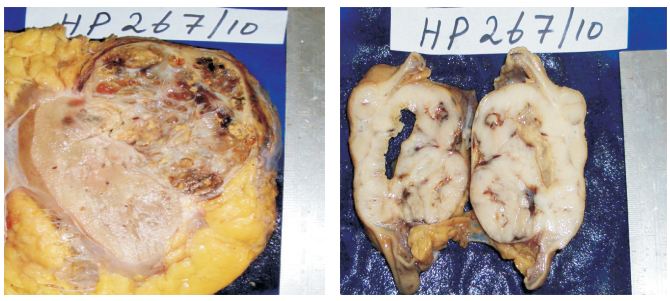
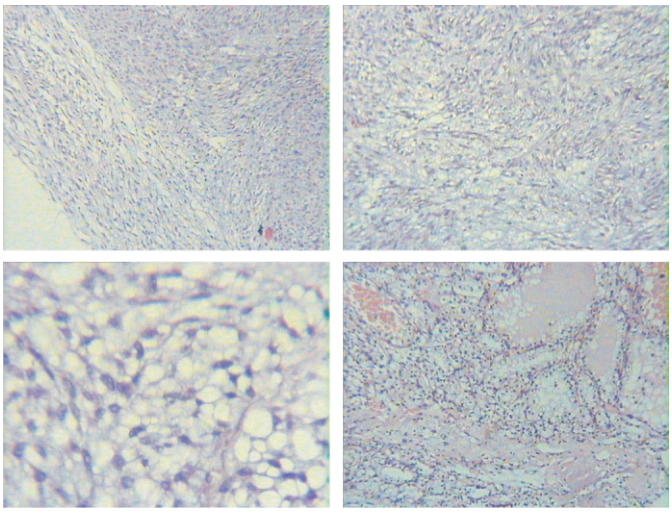


Figure 1. (a) Gross photograph of right kidney tumor (Cut surface). (b) Cut surface showing of gastrointestinal stromal tumor (Stomach – Coronal section).

* Corresponding Author : Dr. Anil Malleshi Betigeri M.D.,
Department of Pathology,
K.G. Hospital and Post Graduate Medical Institute, Coimbatore.
Tel: +91 422 2201201, Fax: +91 422 2211212, E-mail: pathneel@gmail.com

Histopathology revealed a spindle cell tumor [Fig2(a)] below the gastric mucosa. Sarcomatoid & epitheliod cells were noted with clear cell change [Figure 2.(c)]. Areas of necrosis noted with myxoid change [Figure 2. (b)]. Immuno histochemistry showed diffuse C-Kit positivity. Focal CD34 & S-100 positivity was noted. SMA & Colponin were negative. Sections from the nephrectomy showed conventional clear cell carcinoma [Figure 2. (d)]. Fuhrman nuclear grade was 1.



3. Discussion

GISTs arise from any portion of the gastrointestinal tract, most commonly from the stomach (39%), small intestine (32%), and colorectal regions (15%). The average age of patients presenting with the tumor is between 40-60 years. Eight different histological subtypes (four spindle cell types and four epitheliod types) of GIST have been described. Familial GIST cases have germ line mutations of KIT or PDGFRA. These patients develop multiple tumors that may eventually behave in a malignant fashion. Two major factors enter into the determination of malignant potential: gross size, and mitotic activity per 50 high-power fields (hpf) [5]. Our patient had no family history and no cutaneous pigmentation or mastocytosis. Predicting the biological behavior was not easy.

Surgical resection is the mainstay of treatment for patients with operable tumors and was the only effective intervention prior to the introduction of imatinib. The drug imiatinib has revolutionized the treatment and prognosis of metastatic malignant GISTs. Generally, tumors that are CD117-positive by IHC will respond to imatinib, but the extent of clinical response will vary with the exact KIT or PDGFRA mutation present.

The receptor tyrosine kinase family is rather large and any given agent would most likely only function as an antagonist against a subset of these critical receptors. Of greater concern would be potential activation of a subgroup of these receptors, which could predispose to secondary malignancies [6,7]. Reports from Sweden and New York reported an increased incidence of second tumors in patients with PRCC, but not in those with other RCC histology[8]. Coexisting papillary RCC & GIST have been described in literature; but not with conventional clear cell RCC. Our case showed conventional clear cell RCC, histologically.

Both PRCC and GIST may occur as recurrent familial tumors, related to mutations in the proto-oncogenes c-MET and c-KIT. These are both receptor tyrosine kinase (RTK) molecules. Such germ line mutations are rarely found in sporadic cases such as ours. Clinically tyrosine kinase inhibitors (e.g. imitinib mesylate) that is effective against several RTK proto-oncogenes.

It would be interesting to verify our novel association with the findings of larger cancer registries.

4. References

[1] Mignon F, Julie C, Izzillo R, Luciani A, Guichoux F, Mesurolle B, El Hajam M, Qanadli SD, Chagnon S, Lacombe P. Imaging features of gastric stromal tumors: radiological correlation. Report of 4 cases. J Radiol. 2000; 81: 874-881.

[2] Miettinen M, Lasota J. Gastrointestinal stromal tumors: review on morphology, molecular pathology, prognosis and differential diagnosis. Arch Pathol Lab Med. 2006; 130: 1466-1478.

[3] Berkan R, Sumer B, Mustafa R, Duygu K, Berna S. Coexistance of papillary renal cell carcinoma and gastro intestinal stromal tumor in a case Turk J Gastroenterol. 2007; 18: 47-49.

[4] Schmidt L, Duh FM, Chen F, Kishida T, Glenn G, Choyke P, Scherer SW, Zhuang Z, Lubensky I, Dean M, Allikmets R, Chidambaram A, Bergerheim UR, Feltis JT, Casadevall C, Zamarron A, Bernues M, Richard S, Lips CJ, Walther MM, Tsui LC, Geil L, Orcutt ML, Stackhouse T, Lipan J, Slife L, Brauch H, Decker J, Niehans G, Hughson MD, Moch H, Storkel S, Lerman MI, Linehan WM, Zbar B. Germline andsomatic mutations in the tyrosine Kinase domain of the MET proto-oncogene in papillary renal carcinomas. Nat Genet. 1997; 16: 68-73.

[5] David A, Owen. Sternberg's Diagnostic surgical pathology. 5th ed. Stacey E. Mills et.al: 2010 Lippincott Williams & Wilkins. Pp 1304-1306.

[6] Benjamin RS, Blanke CD, Blay JY, Bonvalot S, Eisenberg B. The management of gastrointestinal stromal tumors in the imatinib era: selected case studies. Oncologist 2006; 11; 9-20.

[7] Rygaard K, Nakamura T, Spang-Thomsen M. Expression of protooncogenes c-met and c-kit and their ligands. Br J Cancer. 1993; 67: 37-46.

[8] Au WY, Ho KM, Shek TW. Papillary renal cell carcinoma and gastrointestinal stromal tumor: a unique association. Ann Oncol. 2004; 15: 843-844.