به نام تو ای بهترین سر آغاز

15th Asia-Pacific Biotechnology Congress

July 20-22, 2017 Melbourne Australia

Novotel Melbourne St Kilda -16 The Esplanade -St Kilda VIC 3182, Australia

Histopathology criteria suggesting Microsatellite instability in colorectal cancer in Iranian patients

Soraya Siabani , MD PhD

Kermanshah University of Medical Sciences

The University of Technology Sydney

ssia5034@uni.Sydney.edu.au

Research team

Dr. Sarah Siahbani - Clinical and anatomical pathology resident- Medical School Shahid Beheshti Medical University, Tehran, Iran

Dr.Abdolali Ebrahimi Associate professor- Medical School- Shahid Beheshti Medical University, Tehran, Iran

Dr. Soraya Siabani* Assistant professor -Public Health School - Kermanshah University of Medical Sciences (KUMS), Iran & Registered External Supervisor at the University Technology Sydney(UTS) Australia

Headings

- ✓ Introduction
- ✓ Importance and the rational of the current research: What known before the study?
- ✓ Aim and objectives
- ✓ Methods & materials
- ✓ Results
- ✓ Conclusion

Introduction

Colorectal cancer (CC) is a cancer that starts in the colon or the rectum. Colorectal cancer is the third most common cancer that along with breast and lung cancers contribute more than 43% of all cancers and fourth cause of cancer death worldwide, third in western countries. Adenocarcinomas make up more than 95% of colorectal cancers. These cancers could be familial or non-familial which could be polyposis or non polyposis(Hereditary non-polyposis colorectal cancer)

Introduction

MICROSATELLITE INSTABILITY (MSI): MSI means mutation in a set of genes(DNAs), normally responsible for repairing DNA, and it occurs in different organs cancers, specially in colorectal cancers. MSI mostly is a characteristic feature of HNPCC.

PREVALENCE:MSI occurs in about 15% of colorectal cancers and 100% of Hereditary non-polyposis colorectal cancer (HNPCC) which is about 10 % of all CC.

Importance

MSI should be recognised because:

- Helps to predict the prognosis,
- Helps to select drugs of choice
- Helps to ask for genetic consultation for family resulted in cancer prevention.
- Helps doctors to search for the related cancer in other organs(e.g. ovaries)
- Help to understand cell/DNA patterns in tumors, better in order to fight against cancer, in the future

Importance

Discovery of MSI has clarified the diversity of colorectal cancers and implications for specialized management of patients.

- The CC associated with MSI have a better prognosis in compare with those without MSI, but do not have the same response to some of chemotherapeutics(such as 5-FU)
- According previous studies, colorectal tumors with MSI have distinctive histopatologic features, including a tendency to the **proximal colon**, **lymphocytic infiltration**, and a **poorly differentiated, medullary, mucinous** or **signet ring appearance**
- **However,** In Iran there was a few studies in this regard.

Importance

- MSI can be diagnosed using molecular studies on tumor cells(e.g., PCR) and recently by immunohistochemistry(IHC) methods
- Performing of these complex and expensive methods routinely, for all patients are not cost benefit, especially in developing countries. Hence researchers are looking for another ways including histopathology features, clinical and personal characteristics predicting MSI, for diagnosing/finding patients who likely are at risk for MSI

Aim

The Aim of this study was *to investigate the histopathology features of colorectal carcinoma suggesting MSI, based on revised Bethesda guideline among Iranian patients.*

Material & Methods

- In this analytical cross-sectional study, the medical records of 250 patients with colorectal cancer, registered at Imam Hossein hospital in Tehran, from April 2010 to March 2016, were evaluated.

Material & Methods

- After Ethical approval the study by research committee at KUMS, data including personal, clinical and histopathology, using three checklists and by a professional pathologist was collected. 20 cases that did not have appropriate tissues sample, or complete personal information were excluded from the study. As a result, 230 patients were participated.

Material & Methods

The tumor tissue samples were explored, by a skillful pathologist, for the histopathology predictors of MSI (2016 CAP protocol) including “tumour infiltrating lymphocyte”, “crohn’s like lymphocytic reaction”, “mucinous differentiation”, “signet ring cell differentiation” and “medullary growth pattern”.

Material & Methods

- The relationship between those histopathology variables and variables of sex, age, tumor site, tumor size, regional lymph nodes, lack of dirty necrosis, Intratumoral heterogeneity, Lymphovascular invasion, perineural invasion, microscopic tumor extension (pT), Grade and stage were analysed using SPSS and applying biostatistic tests including Chi-squair and t-test.

Results

- The mean age of patients was 60.72± 15.01 years
- Among 230 eligible cases, 141 patients(61.3%) were male
- The mean size of tumors was 4.5 ± 2.19 cm
- Marked lymphocytic infiltration in 58.3 % of tumors were seen
- Marked crohn like lymphocytic reaction in 12.2 % of tumors were seen

Results

- About 13.4 of tumors were high grade
- The most common tumor stage : stage II
- The most common tumor site : rectum
- The most common tumor microscopic extension : pT3
- Tumor heterogeneity was seen in 4.3%

Results

- Medullary growth pattern in 0.9 % of tumors were seen
- Mucinous carcinoma in 11.7 % of tumors were seen although about 31.3% of all tumors had shown different degrees of mucinous differentiation
- Signet ring carcinoma in 3% of tumors were seen although about 3.5 % of all tumors had shown different degrees of Signet ring cell differentiation and all of them had mucinous differentiation ,too.
- Most of the adenocarcinomas had shown moderate glandular differentiation
- Dirty necrosis was seen in 62.6% of tumors and 37.4 % lack this characteristic feature
- Perineural invasion was seen in 18.7% of tumors
- Lymphovascular invasion was seen in 27% ot tumors
- Regional lymph node involvement was not seen in 58.3 % of tumors and 41.7% had shown at least one involved lymph node.

Limitation

- Since this study was a retrospective one , the most important limitation that we faced was unavailable adequate information about patients' therapeutic process(neoadjuvant and adjuvant chemotherapies), existence of distant metastasis and medical family histories, that could be helpful in regard with analysing their association and outcome variable(based on revised Bethesda guidline)

Conclusion

- 174 out of 230 tumors have at least one of 5 previously mentioned histologic criteria suggestive for MSI but if we limited these criteria to the age between 50 to 60 years old and then add all the patients who are younger than 50 years old,there are just 86 out of 230 patients who are candidate for undergoing molecular studies.

Conclusion

- The findings indicated that:

  - the most common histopathologic feature suggesting MSI in Iranian patients is tumor infiltrating lymphocytes.

Conclusion

- The results showed that there is significant relationship between these features and

1. Patient age (age <50 years)
2. (Larger)tumor size
3. Absence of perineural invasion
4. Histological differentiationof adenocarcinoma, (poorly diff)
5. High grade histology

Conclusion

- But we did not find any significant relationship between these features and

1. Sex
2. Tumor site
3. Tumor heterogeneity
4. Tumor stage
5. Tumor microscopic extension(pT)
6. Intratumoral lymphovascular invasion
7. Regional lymph node involvement
8. Lack of dirty necrosis
9. Specific type of polypoid lesion (even exist)

Recommendation

- Concerning the limitations of the study further studies, cohort and registry studies, in particular would be recommended

References

1. Rosai J. Rosai and Ackerman's surgical pathology: Elsevier Health Sciences; 2011.
2. Setaffy L, Langner C. Microsatellite instability in colorectal cancer: clinicopathological significance. Polish journal of pathology: official journal of the Polish Society of Pathologists. 2015;66(3):203-18.
3. Kloor M. [Pathogenesis of microsatellite-unstable colorectal cancer. Evaluation of new diagnostic and therapeutic options]. Der Pathologe. 2013;34:277-81.
4. Geiersbach KB, Samowitz WS. Microsatellite instability and colorectal cancer. Archives of pathology & laboratory medicine. 2011;135(10):1269-77.
5. Lynch HT, de la Chapelle A. Hereditary colorectal cancer. New England Journal of Medicine. 2003;348(10):919-32.
6. Umar A, Boland CR, Terdiman JP, Syngal S, de la Chapelle A, Rüschoff J, et al. Revised Bethesda Guidelines for hereditary nonpolyposis colorectal cancer (Lynch syndrome) and microsatellite instability. Journal of the National Cancer Institute. 2004;96(4):261-8.
7. Kurzawski G, Suchy J, Debniak T, Kladny J, Lubinski J. Importance of microsatellite instability (MSI) in colorectal cancer: MSI as a diagnostic tool. Ann Oncol. 2004;15(Suppl IV):283-4.

References

- 8. Kazama Y, Watanabe T, Kanazawa T, Tada T, Tanaka J, Nagawa H. Mucinous carcinomas of the colon and rectum show higher rates of microsatellite instability and lower rates of chromosomal instability. Cancer. 2005;103(10):2023-9.
- 9. Connelly JH, Robey-Cafferty S, El-Naggar A, Cleary K. Exophytic signet-ring cell carcinoma of the colorectum. Archives of pathology & laboratory medicine. 1991;115(2):134-6.
- 10. Desselle F, Verset G, Polus M, Louis E, Van Daele D. [Lynch syndrome and microsatellite instability: a review]. Revue medicale de Liege. 2012;67(12):638-43.
- 11. Yamamoto H, Imai K. Microsatellite instability: an update. Archives of toxicology. 2015;89(6):899-921.
- 12. Odze RD, Goldblum JR. Surgical pathology of the GI tract, liver, biliary tract, and pancreas: Elsevier Health Sciences; 2009.
- 13. Washington MK, Berlin J, Branton P, Burgart LJ, Carter DK, Fitzgibbons PL, et al. Protocol for the examination of specimens from patients with primary carcinoma of the colon and rectum. Archives of pathology & laboratory medicine. 2009;133(10):1539-51.
- 14. Boland CR, Goel A. Microsatellite Instability in Colorectal Cancer. Gastroenterology. 2010;138(6):2073-87.e3.

Question?

Thank you for your attention

شناخت انواع مولکولهای سرطانی انسانی نشان دهندهی آینده شخصی انکولوژی است و میتواند تکامل دارویی و استراتژی دارای ویژگی های فنوتیپی متفاوتی است همچنین و BRAFهای مربوط به آن را هدایت کند. سرطان کلورکتال با در برابر جهش MSIویژگیهای علت شناسی متفاوتی نیز دارد که شامل غیر فعال شدن اپی MLH1جهشهای سوماتیکی های جرم لاین در ژنهای به MMRژنتیکی که باعث شکل گیری سندروم لینچ میشود. ، در بررسیهای انجام شده نشانههایی است که مبنی بر هتروژن MSIهمراه جهشهای ثانویه بودن مولکولی در تومورهای ای است که در ژنهایی که تنوع بیولوژیکی فرآیندها را تنظیم به طور کلی میتوان MSIمیکند رخ میدهد. درمقایسه با سرطانهای که ریزماهوارههای پایدار گفت، نشانهها حاکی از آن است که تومورهای عمدتا دارای رفتارهای کلینیکی متفاوتی دارند یا همان سرطان پاسخ (MSS) microsatellite-stableهستند و به داروهای ضد ، MSIمیدهند. 5 با پیش بینی بیماری مرتبط هستند ودراین زمینه کاردبرد دارند ولی به داروی هرچند که پیش بینی MMRبرای داروهای اگزالوپلاتین و یا Fuتومورهای - مقاوم هستند اثر ، و نسبت به آن پاسخ منفی میدهند

- در MSIاز مواردی است که هنوز در حال بررسی و مطالعه میباشد (Sinicrope and irinotecan Sargent 2012). LH1 ,MSH2 , MSH6 , PMS2تومورهای