PROGRANULIN LEVELS ARE SIGNIFICANTLY ELEVATED IN PLASMA AND WOUND FLUID FOR TWO WEEKS AFTER COLORECTAL CANCER RESECTION

SAGES 2024
Abstract ID: 133470
Poster Number: P257

HMC Shantha Kumara[1], Anuj R Sharma[1], Neil Mitra,[1] Aashutosh Sah[1], Pablo Palacios[1],Xiaohong Yan,[1] Vesna Cekic[1],Richard L Whelan[1,2,3]

1.Northwell, New Hyde Park, NY 10042-1069 USA, 2. Division of Colon and Rectal Surgery, Department of Surgery, Lenox Hill Hospital, Northwell Health, 1421 Third Avenue - Suite PH, New York, NY 10028, USA ,3. Donald and Barbara Zucker School of Medicine at Hofstra/Northwell 500 Hofstra Blvd, Hempstead, NY 11549, USA

Introduction

Progranulin (PGRN), also known as Precursor Cell-Derived Growth Factor (PCDGF), is a widely expressed and secreted glycoprotein (1,3). PGRN acts primarily through the mitogen activated protein kinase (MAPK) and phosphatidylinositol 3-kinase (PI3K) pathways, stimulating mutagenesis and progression through the cell cycle. It has an essential function in the orchestration of cell proliferation, differentiation, and in the occurrence of pathological processes (4,5,6). As a growth factor, PGRN activates the PI3k and ERK pathways, enhancing the expression of cyclin D1 and cyclin B that foster the growth and longevity of mesenchymal and epithelial cells(7,8). Overproduction of PGRN is noticeable in several types of cancers, including breast (8), ovarian (9), and renal(10). Notably, PGRN incites VEGF expression in breast cancer cells in vitro (11). As a crucial agent in wound healing and tissue repair, PGRN instigates inflammation, accumulation of fibroblasts, and angiogenesis, all being crucial to wound healing (12). This study's purpose was to compare perioperative PGRN levels in plasma and wound fluid (WF) in colorectal cancer (CRC) patients (pts) undergoing colorectal resection.

Methods

Consenting CRC patients undergoing elective surgery enrolled in an IRB approved tissue/data bank for whom adequate volumes of plasma and wound fluid (Wound fluid, from intra-abdominal Jackson Pratt drains) were available made up the study group. Demographic, clinical and pathologic data were reviewed. Preoperative (preop) and post-operative (postop) blood and postop wound fluid samples were simultaneously obtained on postop day (POD) 1, POD3 and, a time point between POD 7-13; the latter were bundled and considered as a single time point . Late postop samples were obtained at the time of post discharge office appointments or during follow-up visits (provided the JP drain remained). Plasma were collected from blood via centrifugation at 450 G, and clear wound fluid collected via centrifugation at 16,000G for 10 min at 6^0C. centrifuged samples were stored at -80^0C. PGRN levels (ng/ml) were assessed in duplicate via ELISA, and the Wilcoxon and Mann-Whitney tests were employed for statistical analysis (significance p<0.05).

Parameter	Result
Demographic & Operative Data	N =29 patients
Age, years (mean ± SD)	66.1± 12.3
Sex: Male	12 (41.0%)
Female	17 (59.0%)
Incision size :cm (mean ±SD)	
LAP Assisted procedure Hand assisted procedure Open procedures	8.3 ±3.5 11.5±3.6 23.8±7.8
Surgery time, min (mean ± SD)	459.8± 108.1
Length of stay, days (mean ± SD)	9.6± 6.3

Figure 1: Progranulin levels in preop and post op Plasma vs. postop Wound fluids

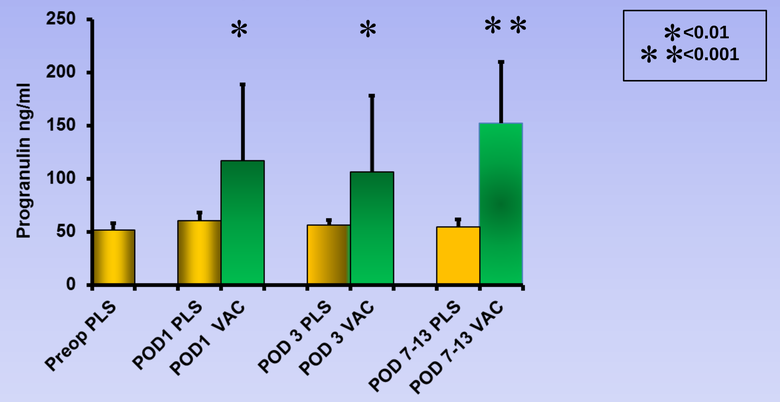


Figure 1: Surgical procedure

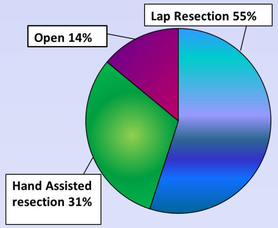
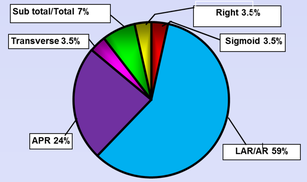


Figure 2: Types of Resection



Results

The study included 29 CRC pts (12 males, 17 females; 5 colon and 24 rectal cancers; mean age 66.10± 12.28 years) whose plasma and WF were studied. Minimally invasive colorectal resection (MICR) was done in 25 patients (Laparoscopic; 16 pts (mean incision length: 8.3±3.5 cm), hand assisted; 8 pts (mean incision length: 11.5±3.6 cm) and open surgery in 4 pts (mean IL 23.8±7.8 cm). The mean length of stay was 9.6 ± 6.3 days. There was a significant increase in plasma PGRN levels on POD 1, 3, and 7-13 (to P<0.01 to P= 0.03) compared to preop levels. WF PGRN levels were significantly higher than the corresponding plasma levels at all postop points (P<0.001 to P<0.01). Progranulin levels are expressed as median and 75% quartile range (Figure 1).

Conclusion

Wound PGRN levels were notably higher at all postop time points. PGRN in the wound likely plays a key role in the healing process. The significant rise in plasma levels after surgery may be related to PGRN diffusion from the wounds. Increased plasma PGRN might stimulate the growth of residual tumor deposits post-surgery.

References

1. Liu CJ, Bosch X. Pharmacol Ther. 2012 Jan;133(1):124-32.
2. Daniel R, He Z, Carmichael KP, Halper J et al. J Histochem Cytochem. 2000;48(7):999–1009
3. Liu Y et al BMC Cancer. 2007 29;7:22
4. Sell C, Dumenil G, Deveaud C et al. Mol Cell Biol. 1994;14(6):3604–3612
5.Zanocco-Marani T et al Cancer Res. 1999;59(20):5331–5340
6. Ong CH and, Bateman A. Histol Histopathol. 2003 18(4):1275-88
7.He, Z. & Bateman, J Mol Med (Berl) 2003;81, 600–12
8. Lu R, Serrero G Proc Natl Acad Sci U S A. 2000;97(8):3993–3998
9. Kamrava M, Simpkins F, Alejandro E et al. Oncogene. 2005;24(47):7084–7093
10.Nicoletto BB and Canani LH,Bmc 2015 Dec;doi: 10.1186/s13098-015-0112-6
11.Perrot-Applanat M and Di Benedetto M Cell Adh Migr. 2012 ; 6(6): 547–553.
12. He Z et al 2003 Nat. Med. 9, 225–229