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COMMENTARY

Colorectal Cancer in Young Adults: An 'Issue Screaming for Action'

John L. Marshall, MD; Thomas Weber, MD | January 30, 2017

Editor's Note: *Conferences on early-age-onset colorectal cancer will be held in March and September 2017 at the NYU Langone Medical Center in New York, New York. Dr Thomas Weber, who is interviewed here by Dr John Marshall, is chair of the EAO-CRCSummit, which convenes international researchers, clinicians, and patients to examine the emerging data on this distinct form of colorectal cancer presenting in young adults.*

John L. Marshall, MD: Hello. I'm John Marshall, Director of the Ruesch Center for the Cure of Gastrointestinal Cancers at Georgetown Lombardi Comprehensive Cancer Center in Washington, DC. I want to welcome you back to the 2016 Ruesch Center Symposium.

I want to focus on the incidence of colorectal cancer in young people. I did not sign up to be a doctor for young people. I wanted old people with cancer. All of a sudden, I have a bunch of young people, young adults in my clinic with colon cancer, many of them with metastatic colon cancer. I am so lucky to have as a friend and partner Dr Thomas Weber, who is an academic professor of surgery at the State University of New York Downstate Medical Center in Brooklyn, New York. For the second year in a row, Tom has been a part of our symposium and an expert in the realm of young people with colorectal cancer. This is not on many people's radars. Give us the big picture of where this is. Thank you for joining us, but go right to work. Give us the big picture.

Thomas Weber, MD: Thank you, Dr Marshall. Yes, it is a bit of a surprise because, when you take a 30,000-foot view, colorectal cancer incidence in the United States is actually decreasing quite dramatically for people older than 50 years of age as a result of our successful population-based screening programs. However, for people younger than 50 years, over the past two to three decades there has been a very dramatic increase in incidence: 2%-3% increases per year, largely driven by left-sided cancers and especially rectal cancer. What we see is that the result is often delayed and there is late-stage diagnosis because both the patients and providers are not anticipating a cancer diagnosis.

Dr Marshall: They're literally sitting on it.

Dr Weber: Tragically, yes. That is a major issue. This is a major focus for us.

Dr Marshall: Do you think we are just picking it up more, or is this really an increased number of young people getting this disease?

Dr Weber: Sometimes people offer that hypothesis, but this is based on SEER data and our best cancer center data information. There is no question that the incidence is increasing dramatically. Sometimes people will say that when you look at the actual numbers, it is an order of magnitude less than what we see for people older than 50. The reality is that it is 10%-12% of all cases in the United States. We have approximately 140,000 cases in the US. That 10%-12% is 14,000 individuals, 14,000 cases per year. That exceeds the total number of acute lymphocytic leukemia, Hodgkin's lymphoma, and even cervical cancer. Of course, if you are the person diagnosed, it is not a trivial number.

Dr Marshall: Washington, DC, is a very young town with a lot of young people. I can go through a full day of clinic and make it until 11:00 PM without seeing somebody over the age of 50. In my world, it's getting to feel like almost half of my patient

population is middle-aged and younger instead of middle-aged and older. It's really a big deal.

It's a situation that is really screaming for some action.

Dr Weber: It's a situation that is really screaming for some action. The way we have tried to approach the problem is to look at presymptomatic or prediagnosis strategies and then try to improve the timeline for diagnosis when people are symptomatic, because that is a big deal.

How do you identify people who are at risk? You have spoken to experts about the hereditary colorectal cancer components. Interestingly, less than 20% of these cases of people younger than 50 are associated with a known hereditary syndrome.

Dr Marshall: You would expect it to be a higher proportion, but it isn't.

Dr Weber: However, there is risk stratification. Going back to Medical School 101, take that family history and see if there are people who have been affected. That is very important, as well as other potential risk factors such as diet, weight, and diabetes. These are all potential risk factors.

Risk stratification is #1, but #2 is responding and reacting in a timely manner to people who are symptomatic. For people who have had prolonged rectal bleeding with any other abdominal complaints, if you link that to any physical sign such as anemia, the probability that there is a cancer goes up dramatically. It deserves action.

Dr Marshall: If you are a 60-year-old with some bleeding, you get your scope. If you are a 35-year-old woman with some bleeding who has had two babies, it might take 6 months for somebody to be willing to do a colonoscopy on you.

Dr Weber: You're exactly right. It's 6 months. That can be a very costly delay.

Dr Marshall: I don't think there is much of a barrier at the insurance level. This seems to be more our own reflex response to a young person who may have a colon cancer symptom. Is that right?

Dr Weber: The experiential model we often refer to is the excellent work done by Dr Barbara Goff, a gynecologic-oncologist who did an enormous amount of work looking at ovarian cancer. For many, many decades, ovarian cancer was the silent killer. Women with vague abdominal complaints were not taken seriously, which translated into late-stage diagnosis. She surveyed a large population, she identified the key abdominal complaints, and she was able to produce a study that showed that if you had those complaints over a prolonged period of time, the likelihood of ovarian cancer went up dramatically.[1,2]

We feel that the situation is very similar for young people, especially with rectal cancer. If you have rectal bleeding that is prolonged and you have any other symptoms, it deserves evaluation.

Dr Marshall: I know you're going to talk a lot in your session about many topics, but I'm really trying to understand why this is happening. Is there something we can do? I know about some of the genetics and molecular profiling, right- versus left-sidedness of tumor location,[3] but what's going on? One of the theories, which I can't wait for one of our speakers to teach us about, is the [role played by] the microbiome. This generation is not really feeding their microbiome.

When I was a kid, I was told to go out and play in the yard, make a mud pie, and eat it. That's what we did. I don't know how much of this is that we have whitewashed our microbiome and somehow that is affecting it.

Dr Weber: I think you're exactly right. It's very important to keep in mind that it's unlikely for the human genome to have that kind of plasticity. It has not changed that much over this period of time. I think it's definitely some sort of environmental interaction. Diet is an extremely important possibility. How it impacts the biome is extremely important.

There has been some exciting comparative work by Dr O'Keefe at the University of Pittsburgh that looked at diet among native Africans and African Americans, and demonstrated changes in the microbiome that actually influenced the chemical composition.[4] Of course, with the American diet, there was a much higher ratio of chemicals that are proinflammatory and procarcinogenic.

The positive message out of all of this is that if we increase our understanding of these phenomena, we can improve the situation. We can have an impact. We can make it better. If we improve our diets, if we do risk-stratification, if we educate our

providers and consumers about what the symptoms and signs are, we can save a lot of lives.

Dr Marshall: We have to focus on this. You and I have been involved in a project with Medscape around awareness and creating a video documentary for both patients and medical folks alike. I know that this is something you and I both care a lot about. Hopefully, in the next few years we can have some significant positives to push out to others to change this story.

Dr Thomas Weber, thank you so much for coming down to Washington, DC, and being a part of our Ruesch Center Symposium for yet another year.

Dr Weber: Thank you.

View the new Medscape TV series *Not on Anyone's Radar: Colorectal Cancer in Young Adults.*

References

1. Goff BA, Mandel L, Muntz HG, Melancon CH. Ovarian carcinoma diagnosis. Cancer. 2000;89:2068-2075. Abstract
2. Goff BA, Mandel LS, Melancon CH, Muntz HG. Frequency of symptoms of ovarian cancer in women presenting to primary care clinics. JAMA. 2004;291:2705-2712. Abstract
3. Venook AP, Niedzwiecki D, Innocenti F, et al. Impact of primary (1º) tumor location on overall survival (OS) and progression free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC) analysis of CALGB/SWOG 80405 (Alliance). Program and abstracts of the 2016 American Society of Clinical Oncology Annual Meeting; June 3-7, 2016; Chicago, Illinois. Abstract 3504.
4. Ou J, Carbonero F, Zoetendal EG, eg al. Diet, microbiota, and microbial metabolites in colon cancer risk in rural Africans and African Americans. Am J Clin Nutr. 2013;98:111-120. Abstract

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