NETWise - EP 52: Why Is Neuroendocrine Cancer on the Rise?

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Over the past several decades, the number of people diagnosed with neuroendocrine cancer has increased significantly — in the United States and around the world. So the question is: Why? Are neuroendocrine cancers truly becoming more common? Or are we simply getting better at finding them?

I'm Jessica Thomas, Director of Patient Education at NETRF, and you're listening to NETWise, the podcast designed to inform, empower and guide patients and caregivers through the world of neuroendocrine cancer.

To understand the rise, we first have to understand how these tumors are defined. Dr. Ulrich-Frank Pape, a specialist in gastroenterological endocrinology and oncology at Asklepios Klinik St. Georg in Hamburg, Germany, explains how changes in classification have shaped what we're seeing in the data today.

Ulrich-Frank Pape, MD, Gastroenterologist, Asklepios Klinik St. Georg, Hamburg, Germany

In the statistics that we are evaluating, we see a rise in neuroendocrine neoplasia incidence, and this is already the first point we need to talk about neuroendocrine neoplasia as the super group, and we have neuroendocrine tumors and neuroendocrine carcinomas, according to WHO these days. But neuroendocrine neoplasia have come a long way along classifications, and they've been very, very variable over the years and decades, actually. And the reason for the changes in classification has been that we've been learning so much about it, and that the understanding has led to reformation of classifications. And these classifications have led to confusion in patients, but as also, and more, at least as importantly, in the experts. So the experts shouldn't be confused. But oncologists, surgeons, gastroenterologists, all have been confused, even pathologists, over over the decades, and fortunately, we have the WHO classification, which now assumes neuroendocrine neoplasia with neuroendocrine tumors and neuroendocrine cancers.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Classification matters. As our understanding evolves, definitions evolve. And when definitions change, statistics can shift.

Dr. Nancy Joseph, Professor of Pathology at the University of California, San Francisco, explains how improved knowledge has reshaped diagnosis.

Nancy Joseph, MD, PhD, University of California, San Francisco

Neuroendocrine cancers have definitely been misclassified in the past. I mean when I say misclassified, that's because we've learned more information. They're misclassified to no one's fault. In the past, we've just learned more and updated the classification system.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

So part of the rise may reflect something simple — we are now calling these tumors what they truly are. But beyond classification changes, what does the long-term data show?

Dr. Arvind Dasari, Professor of Gastrointestinal Medical Oncology and Director of Clinical Research at MD Anderson Cancer Center, walks us through what decades of epidemiologic information in the SEER database reveals. The SEER database is a nationwide cancer registry that has tracked cancer diagnoses and outcomes in the U.S. for decades, helping researchers understand trends and improve care.

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

So the main source for figuring out these large-scale epidemiological trends is in the United States, the SEER database. So what we saw kind of looking at the trends from the 1970s up until more recently, is that the incidence of neuroendocrine tumors has been steadily rising. So from the 1970s up until now, depending on which study you look at and which time period you look at, it's anywhere from five to six fold increase in the incidence. And by the way, incidence, the definition is the number of new cases per year, and prevalence is the number of people who've been affected by that diagnosis and are still alive at a certain time point. Based on the trends that we're seeing, this rise in incidence largely seems to be driven by early-stage, low-grade neuroendocrine tumors, suggesting that these tumors were probably detected when patients were getting tests for other reasons.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

A five- to six-fold increase. Much of that rise is in early-stage, low-grade tumors — often found not because someone felt sick… but because something else triggered a closer look. Sometimes, it’s an accident… And, sometimes, it’s a routine blood test. For Jessica Ochoa, it was exactly that.

Jessica Ochoa, Person Living with Neuroendocrine Cancer

I officially got the diagnosis of pancreatic neuroendocrine tumor. It was metastatic, with lesions in my liver, no, no symptoms before, nothing. So the only way it came up was only my elevated calcium levels in my blood test I would do regular your your regular screening, your regular blood screen that you go to the doctor. She had seen my trends. If I had to get it, that's what she explained it to me.

She goes, hey, something's not right. I didn't think much of it, because I felt just fine. I didn't really understand what she was trying to tell me, when she said, let's get additional test, until I went to go get the test, and are like, oh, yeah, this is a breast cancer. This is a test to see if you have breast cancer. This is a test for bone cancer. I was like, Oh, we're testing me for cancer.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

What started as a routine lab result quickly became something much bigger… and far more confusing.

Jessica Ochoa, Person Living with Neuroendocrine Cancer

All they knew at the moment was that I had a pretty large tumor in my pancreas. The medical professionals tend to gravitate at that point to that it was pancreatic cancer. That's probably what they thought I had just from the original ultrasound and X-ray when they did the biopsy and I got the results, they did not know I had lesions in my liver until the doctor, he's the one that actually said, Hey, I also found some lesions in your liver, and it seemed to be the same. So I took samples of that as well, and then when the result came back, that's when I discovered they just explain it to you, like, Oh, this is a neuroendocrine tumor. And I'm like, Okay, what does that mean?

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Jessica's story reflects something researchers are seeing across the country — tumors discovered not because they caused symptoms, but because medicine is looking more closely than ever before. Dr. Dasari explains.

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

Increasingly, we do colonoscopies or screening and tests for colon cancer, and we're seeing a rise in rectal neuroendocrine tumors, likely because we're detecting more of these patients. Patients, increasingly are getting more and more scans when they're in the ER for other reasons, or ordered by their providers for other reasons, and they may pick up small neuroendocrine tumors in the small bowel and the appendix and the lung that may be kind of adding on to this numbers as well.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

More colonoscopies. More CT scans. More imaging overall. Dr. Neil Renwick, Associate Professor in the Department of Pathology and Molecular Medicine at Queen's University, says better detection explains much of the rise … but he cautions that researchers must also consider deeper biological and environmental factors.

Neil Renwick, MD, PhD, FRCPC, Queen's University

So the question is, are neuroendocrine cancers on the rise. And if so, why? So? There's some really great epidemiology studies that are coming out from many, many different countries. And it seems to be that neuroendocrine tumors are on the rise in the US and in Canada, and actually globally. So the question is, why, I think a large part of this is just better detection, so we have better imaging and, you know, then lumps and bumps are found. And there's sort of they wouldn't have been found previously, but now the imaging technologies are better. But the other thing that's kind of fascinating is, you know, could there be a causative agent? You know, is there an infection that's driving something? Is there something in diets, you know? So I think from a research perspective, we always have an eye on this to see if that increase in numbers is actually due to something that's maybe in the environment. There are a couple of neuroendocrine tumors that are related to viruses. So Merkel cell carcinoma of the skin is related to a polyomavirus, and we're still finding out a lot more about how widely that's spread in the community. And actually, some of the neuroendocrine tumors in gynecology, and gynecological neuroendocrine tumors are related to human papillomavirus, and so, you know, maybe it's related to that even so, I think we always have to keep an eye on things, but I'd say it's mostly better detection.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Better imaging explains much of the rise. But Dr. Renwick also raises an important question: Could there be other factors? Diet… Environment… Viruses… For patients, those questions don't feel abstract… They feel personal.

Jessica Ochoa, Person Living with Neuroendocrine Cancer

If I look back, I reflected and said, Okay, I wasn't eating well. So... and mine is, we don't know if the cancer is causing my diabetes or the diabetes cause a cancer. I don't know, but I do believe that now my eating did have an influence on me having this cancer now, now started to take it a little bit more seriously and really take care of it. Now I'm actually like working out, which I've never worked out in many, many different years, many years. And now I'm like eating healthier, being more conscious about my lifestyle and teaching it to my kids.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Jessica's questions are the same ones researchers are still trying to answer. How much of this rise is detection? How much could be environmental? And does the pattern look the same everywhere in the world? To understand that, Dr. Pape gives us a better look from a global perspective.

Ulrich-Frank Pape, MD, Gastroenterologist, Asklepios Klinik St. Georg, Hamburg, Germany

In the statistics that we are evaluating, we see a rise in neuroendocrine neoplasia incidence. And the more often you apply the appropriate diagnostics, the more often you diagnose these entities. And then, obviously the statistics will be more will show a rise in incidence. There are differences by region, which also depends on the population, so the people who live there and where they come from. So we know that in eastern Asia we have certain subgroups of neuroendocrine tumors more prevalent than, let's say, in the Western world, like rectal neuroendocrine tumors, for example, are more more prevalent in South Korea and Japan and other data from from southeast or Eastern Asia. And so there is a difference there, but the overall incidence is very similar throughout the world.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Greater diagnostic awareness leads to greater recognition — worldwide. But incidence numbers tell only part of the story — a point Dr. Dasari highlights in his research.

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

There are racial differences in the incidence and outcomes of neuroendocrine tumors. And the challenging part there to that we are unable to really tease out would be how much of these differences are related to true biologic differences based on race versus other factors that are often associated, such as access to care and how close are they to kind of the best possible treatments and other health conditions that may be affecting their outcomes as well. So bottom line is, yes, there are racial differences. What we don't know is how much of that is social, cultural versus truly biological.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Access to care, referral patterns, and social determinants of health may all influence outcomes. And as detection increases, so do new clinical questions.

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

So the big question would be, is all of this being driven by just increased detection, versus are there other causes that could be contributing that are potentially modifiable? If there were a contributing factor, we would expect to see somewhat of a proportional increase across all the different stages, like early stage, kind of more advanced cancers, which we're really not seeing, which makes me think that the majority, if not all of it, is just being driven by increased detection. So that's question number one. Question number two is, what are the clinical implications of this finding. Well, the big question would be, well, so if we have somebody with a diagnosis of a very small, say, appendix tumor or a rectal tumor, how aggressive do we need to be in terms of managing those tumors? Because every treatment we do, every test we do, comes at a cost, comes at a quick risk, potential complications and inconvenience for patients and their families, and that, I would say, is a bit of an unanswered question.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Earlier detection is powerful — but it also raises important questions about what we're really seeing. From his work in pathology, Dr. Renwick argues that neuroendocrine tumors may be more common than we think.

Neil Renwick, MD, PhD, FRCPC, Queen's University

But interestingly, there's quite a lot of research work on neuroendocrine tumors in autopsy patients. And it brings up the question of, are neuroendocrine tumors actually rare or not? And if you ask a lot of clinical people, they'll say, yeah, absolutely, it's rare. If you ask an autopsy pathologist, they're going to say, actually, no, it's not rare. It's way more common than people think, and maybe even 10 times more common than people think. And the reason is, a lot of these tumors are sub-clinical, so they really don't come to attention. It's the serious ones that come to clinical attention. But actually, in our practice, we can see fairly benign types of tumors that are just discovered incidentally.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Many tumors may never cause symptoms. They remain hidden unless found by chance. So what does that mean for screening? Dr. Dasari helps put that into perspective.

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

The question of whether we need to screen for neuroendocrine tumors, I think is a really hard one to answer, because it needs to make sense at a population level, and so I think we still do not have concrete data suggesting that if we screen lots of patients when your endocrine tumors, will improve outcomes for the entire population. We don't have that information yet.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Population-level screening remains uncertain. But when it comes to individual patients, Dr. Pape makes clear that early detection still matters.

Ulrich-Frank Pape, MD, Gastroenterologist, Asklepios Klinik St. Georg, Hamburg, Germany

Early detections, as in any neoplastic or cancerous disease matters because early detections allows for complete removal before the cancer becomes the true cancer, invasive, metastatic and ultimately life threatening.

Nancy Joseph, MD, PhD, University of California, San Francisco

Early detection is huge. It's really important because no matter how high grade a cancer you have, if you catch it early enough before it's spread into other sites. That's why we care about early detection. You can cut it out and you're done with it.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Some tumors signal their presence through symptoms. Others remain silent until they're found unexpectedly. Dr. Joseph breaks down how those two pathways to diagnosis differ.

Nancy Joseph, MD, PhD, University of California, San Francisco

The ones, I think the neuroendocrine cancers that get detected early now probably fall into two main groups. It's the ones that are producing that we call functional neuroendocrine tumors that produce hormones like insulin or glucagon or somatostatin, and these hormones actually give the patient symptoms, you know, like carcinoid syndrome. So if you have a tumor that's producing hormones, you're going to get symptoms early, when it's still small, and then they'll do imaging. They'll find it while it's still small. The other way is incidental detection, like, you know you just happen to be getting imaging for different reasons.

Ulrich-Frank Pape, MD, Gastroenterologist, Asklepios Klinik St. Georg, Hamburg, Germany

So, it is important to recognize these entities early and to remove them as completely as possible, and to understand if there is a risk of recurrence or if these were spontaneous once in a lifetime, events that that might not need any further follow-up. But here's the conjunctive you really we have to consider neuroendocrine neoplasias for any time point along the lifeline or the along an individual lifetime. So once one has been removed, some kind of follow up is usually justified with maybe the exemption of appendiceal neuroendocrine tumors.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Improved imaging doesn't just find tumors — it helps doctors understand exactly what they're dealing with. Dr. Pape outlines how these advances are reshaping care for patients.

Ulrich-Frank Pape, MD, Gastroenterologist, Asklepios Klinik St. Georg, Hamburg, Germany

I'm a gastroenterologist, so we've we've seen a lot of improvement with improving endoscopy techniques for early neuroendocrine tumors of organs that we can access through endoscopy. But we also have so these are usually early stage tumors which can be resected easily via endoscopy, and therefore patients can be cured in a large proportion of patients. But we also have modern techniques like the DOTATOC PET/CT using gallium as a radionuclide that kind of labels the tumors very, very specifically, not 100% specifically, but very specifically. And therefore identity, identification of these neuroendocrine tumors is- is possible with the PET scan in combination with cross-sectional imaging, usually a CAT scan, but could be an MRI as well, but that's very advanced technology, only available in few centers.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

With more advanced imaging, small lesions and other discoveries are made that may not pose an immediate risk. Dr. Dasari explains what that means in clinical care.

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

Now rectal neuroendocrine tumors, they're more readily accessible to do local treatments through colonoscopy and things like that, but say when patients are getting scans for lung screening, that is increasingly becoming a mainstay of kind of screening for lung cancer if we diagnose lung carcinoids, because that is a more involved surgery and more involved treatment. And similarly, when patients are, say, getting abdominal scans for unrelated reasons, we often see small lesions in the pancreas. These are for the most part, if they're less than two centimeters, should not be causing any issues in terms of risk of spread.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
More scans… More visibility… More early findings. If we're finding these tumors earlier, how do we provide the right treatment?

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

So we published the most recent iteration just last year. The big takeaways are neuroendocrine tumors are continuing to increase in incidence, and the incidence is largely for early-stage, low-grade tumors and the unanswered question is, how do we best take care of these patients, so that we address the diagnosis, but not over-treat the patients and cause them inconvenience.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
To understand this better, researchers rely on strong data — not just from the United States, but from around the world.

Ulrich-Frank Pape, MD, Gastroenterologist, Asklepios Klinik St. Georg, Hamburg, Germany

Because until the work of the ENETs registry, only large-scale data were available from the US, where the Surveillance Epidemiology and End Results Registry, the SEER registry, provides very good information, which is being being worked up every couple of years, and has just been worked up last year by a group and from MD Anderson and and so the ENETS registry has so contributed to the worldwide understanding, because it has made available large scale European data of more than 12,000 patients.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
That international collaboration has transformed what we know about neuroendocrine cancer — making this a truly global effort.

Ulrich-Frank Pape, MD, Gastroenterologist, Asklepios Klinik St. Georg, Hamburg, Germany

Yeah, the ENETS registry is really a multinational, multicentric registry which has collected a very large cohort of patients with proven neuroendocrine neoplasias

Jessica Thomas, LCSW, Director of Patient Education at NETRF
As the data grows, so does the understanding that these tumors are complex. They require experience — and teamwork.

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

One piece of advice that I'd like to reiterate is that for any rare tumor, please consider partnering with somebody who has expertise and experience in taking care of patients with that diagnosis, because there are a lot of nuances that go into taking care of these patients, and that expertise is not an individual-based. What I mean by that is, when a patient comes to an institution like MD Anderson, where I work, it is the collective expertise and experience ranging from the pathologist, the radiologist, the medical oncologist, the surgical oncologist, the nuclear medicine folks, social workers, genetic counselors, a huge network that can provide that collective expertise that would benefit patients.

Jessica Thomas, LCSW, Director of Patient Education at NETRF
While the numbers may appear to be rising, there’s an important distinction to make. This isn’t necessarily more cancer. In many cases, it’s more recognition — more precision.

Ulrich-Frank Pape, MD, Gastroenterologist, Asklepios Klinik St. Georg, Hamburg, Germany

Doctors and healthcare systems look more deeply into the patients and into possible neuroendocrine tumor disease, so it's recognized more readily, and therefore it can be approached more specifically and more effectively by that so that's actually good news, because the overall cancer incidence, which has been nicely shown from the U.S. data, is not rising. So it's just we are recognizing more cancers as neuroendocrine and therefore we can treat them more specifically.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Earlier recognition… More precise diagnosis… More specific treatment. That’s the promise of progress. But for patients diagnosed before that progress reaches them — the experience can feel very different.

Jessica Ochoa, Person Living with Neuroendocrine Cancer

My tumor is way too big, unfortunately for mine, I got diagnosed way too late because I didn't show symptoms. So hopefully, by raising awareness, people can potentially– me telling my story and say, hey, this is what I was feeling with the hopes that more people can get diagnosed earlier and that they can get it addressed and hopefully live many, many years stable.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

Jessica’s hope is simple: earlier detection, earlier answers, better outcomes. And that hope is shared across the neuroendocrine cancer community — by clinicians, researchers, and patients alike.

Progress in detection… Progress in understanding… Progress that only happens when clinicians, researchers, patients, and advocates work together, all pushing toward better answers.

Arvind Dasari, MD, Gastrointestinal Medical Oncologist, MD Anderson Cancer Center

I just want to thank NETRF for the incredible work that they're doing and kind of education, patient advocacy and supporting and promoting research. So really, really grateful for the incredible work that's being done, and really honored to be part of the NET community.

Jessica Thomas, LCSW, Director of Patient Education at NETRF

The rise in neuroendocrine cancer reflects improved detection, refined classification, global collaboration, and continued research.

What remains unanswered are the deeper biological questions — and how best to balance early detection with thoughtful management, and that is why NETRF is here.

Thank you for listening to NETWise. I'm Jessica Thomas, Director of Patient Education at NETRF, and you're listening to NETWise, the podcast designed to inform, empower, and guide patients and caregivers through the world of neuroendocrine cancer. This episode was brought to you in part by the generous support of Boehringer Ingelheim and ITM.

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