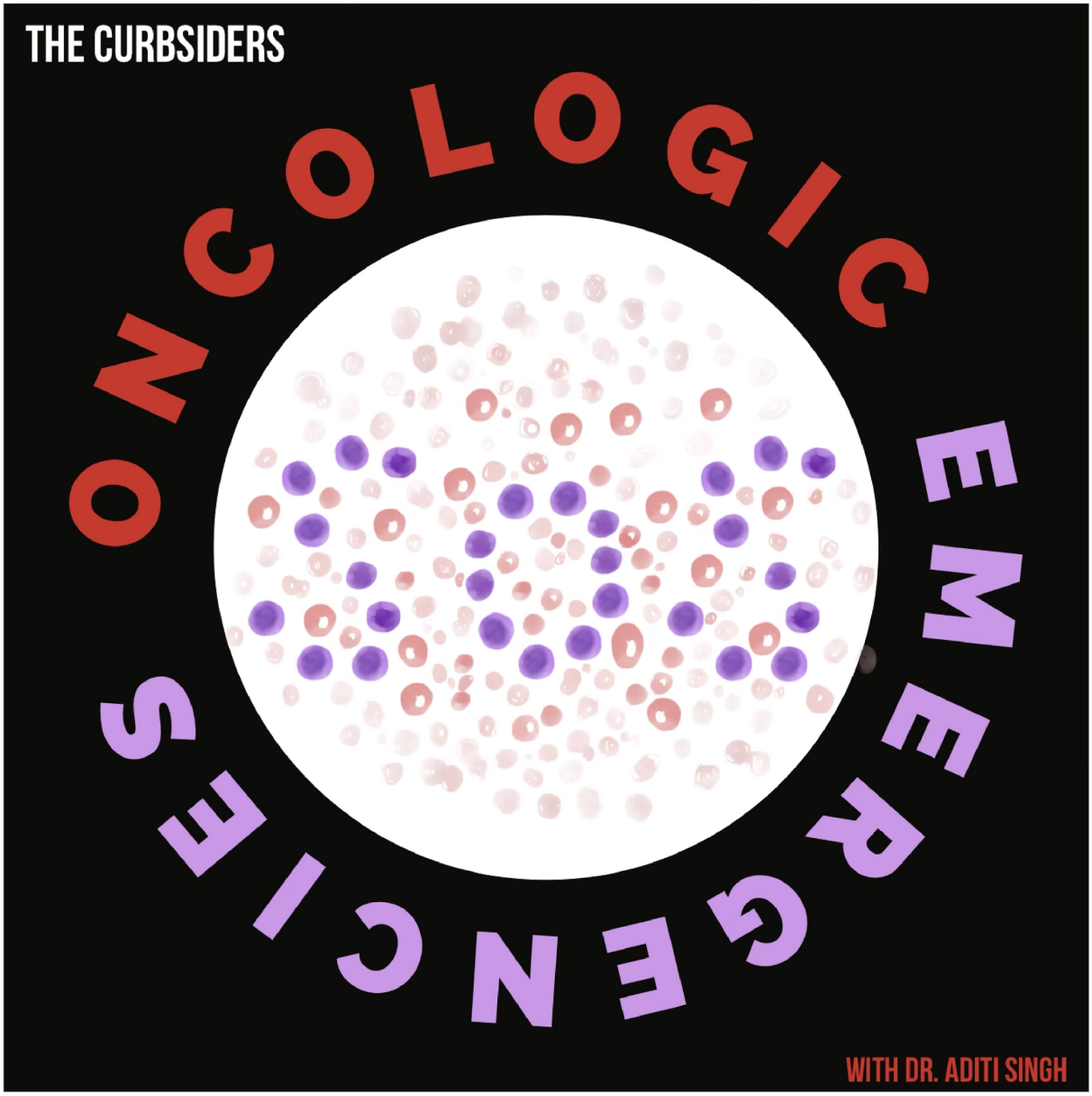
#358 Oncologic Emergencies with Dr. Aditi Singh



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[The Curbsiders Podcast theme]

Monee: And welcome back to Curbsiders. I am not Matthew Frank Watto, I'm Monee Amin, and I'm joined by my cohost, Meredith Elizabeth Trubitt. How are you this evening?

Meredith: Doing well. How are you?

Monee: I can't complain, but it's been a long night so we will keep on. So, on tonight's show, we discuss oncologic emergencies with our guest Dr. Aditi Singh. In a minute Meredith is going to tell you a little bit more about her. But first, will you please tell the good people in the audience what it is we do on this show?

Meredith: Sure, Monee. We are The Internal Medicine Podcast. We use expert interviews to bring your clinical pearls and practice-changing knowledge. So, tonight we have an awesome conversation with our guest Dr. Aditi Singh. She is medical oncologist at the Abramson Cancer Center at the University of Pennsylvania in Philadelphia. She specializes in the treatment of patients with lung and head and neck cancers with a special focus on neuroendocrine tumors of the lung. She spends several weeks during the year on the inpatient oncology service and is very passionate about teaching internal medicine residents. Her other interests include optimizing clinician efficiency by harnessing the power of the electronic health record. And when she's not working, she loves spending time with her husband, two daughters, and dog Bilbo. So, before we get started, I just wanted to check in with you, Monee.

Monee: Oh, no.

Meredith: And just see have you been on call recently?

Monee: Oh, God. No, I have not.

Meredith: So, you wouldn't call yourself an oncologist?

[laughter]

Monee: This is what happens when we go rogue without Matt and Paul.

Meredith: Monee looks so mad. [laughs] We can go ahead and jump in, I hope we don't have too much of a blast talking about all these crises.

Monee: You went there, you had to do that. You had to do that. Okay. All right. Let's get this started.

A reminder that this and most episodes will be available for free CME credit for all healthcare professionals through VCU Health at *curbsiders.vcuhealth.org*.

Hey, Aditi, thanks for coming on the show, we're really excited to have you. We're going to start with some rapid-fire questions. So, let's just start off with your one-liner, if you will.

Aditi: Sure. I'm a medical oncologist in Philadelphia. I work at the Abramson Cancer Center at the University of Pennsylvania. I specialize in the care of patients with lung and head and neck cancers. And I'm a mom of two toddlers and a fluffy golden doodle.

Meredith: Awesome. What's the golden doodle's name?

Aditi: Bilbo, [Meredith laughs] like the hobbit. Eats a lot, scruffy.

Meredith: It's the best name. Okay, I think we'll go ahead and jump in. What is a recent book, movie, show, album, culture item that you would recommend to people right now that you've gotten some enjoyment out of?

Aditi: The book I was recently reading and absolutely loved was Suzanne Koven's *Letter to a Young Female Physician.* Really, really brilliantly written and very relatable.

Meredith: Cool, I think that's actually been recommended before.

Monee: Yeah, I think so.

Aditi: Highly recommend reading it, if you haven't.

Monee: Definitely need to read it.

Meredith: On this current, three-female podcast. I think on that realm, is there any meaningful advice or feedback then that you've gone throughout your career that you would want to share with young learners or young attendings?

Aditi: Yeah, I'll give you two. One is, which I'm really working on still. But really, imperfect action is better than perfect inaction. And I say that as a recovering perfectionist myself. I think this piece of advice will help you in a lot of-- any kind of project, honestly, whether it's research or otherwise. And then something more related to patients, I was once told that really listen to your patients. It sounds very cornier obvious, but really actually sit down and listen to your patients. And I know a lot of times we tend to dismiss symptoms that don't sound like they're a big deal. And it may not be a big deal, but actually making them feel heard and actually following through on what you say you will do for them, I think it makes a huge difference.

Monee: No, I think those are both really good things to keep in mind, because especially early in your career, it's really easy to sort of get bogged down by the man if you will.

Aditi: Yes.

Monee: And so, just getting in there and doing it and then, I think sometimes when you have so many patients to see you get anxious, and maybe don't spend as much time listening as you should. So those are really good reminders. And that's really great advice, but we're going to change gears entirely. Meredith, please give us your pick of the week.

Meredith: I've been going back and forth on what it should be. I think I'm going to go with maybe a more traditional pick of the week.

Monee: You keep doing this to me, girl.

Meredith: No, you know this one, but it's going to be Phil Rosenthal on a block for all of his things. So that I can't keep recommending his stuff over and over. But he has his Netflix show, *Somebody Feed Phil*. And before that one, *I'll Have What Phil's Having*, which is also on Netflix. And he just came out with his new podcast called Naked Lunch. And I guess the theme of all of his shows and stuff is just like, how the better you travel or try different things and try different pieces of other people's culture, the better you're going to like understand each other and brings about a lot of ideas of acceptance and stuff. But he does it in a humorous way. He's the creator and our producer for *Everybody Loves*

Raymond is kind of what he's best known for. But in his later years, he's done all these shows. They bring me infinite joy, got me through the pandemic, continued to get me through my day-to-day.

Monee: Yeah, every time you say Phil, I get confused.

Meredith: I mean, I'm essentially married to the same one, so it's fine.

Monee: [chuckles] Yeah, it can get very confused every time I hear you talk about Phil because I'm not sure which one you're referring to. So, my pick of the week is really this playlist I've been working on for the greater part of the last six months. I decided I wanted to create a playlist that's basically every song I've ever liked ever. And I mean, right now it's a 28 hour, so we'll see where it stops. But it's pretty random. And I'm pretty excited to one day finish it, or really, I think this is one that just will be evolving. It's called the Vault if you will. Keeping it classy. Meredith, will you please take us to our first case from Kashlak?

Meredith: Yeah, I will preface this episode, we got a lot of cases and a lot of different topics we're going to try to cover. So, jumping into our first case, we got Mr. Brown, he's an 80-year-old male with past medical history, significant for prostate cancer, hypertension diabetes, he presents to the emergency room with a three-day history of progressively worsening lower extremity weakness as well as low back pain. His vitals are stable. His exams notable for four out of five lower extremity weakness bilaterally, about five out of five than his upper extremity strength. His sensations grossly intact. His labs have been unrevealing, MRI of his L spine done in the ER show, bony metastatic lesion at L3 with evidence of cord compression between L3 and L4. I think that often we get these reads from their imaging from the ER and then it's sort of passed off to the hospitalist as to what to do next. And often when I get a cord compression call, after hyperventilating, I'm like, "Well, who all do I need to really call in this case? So, Aditi, what's our first step of who we should get involved?

Aditi: Great question. I will say the absolute first thing to do is actually get on your computer and order them steroids. So, before you call anybody else, you want to order steroids. And there's no magic number in a lot of studies that could support this number, but that's what is has been traditionally used for several years. But we basically start with IV steroids, so dexamethasone 10 milligrams right away, and then you can put standing orders to continue that four milligrams every six hours. And the reason is that this is really, really a true oncologic emergency, and you might be saving someone's ability to walk. And right, it's time is of the essence. By giving them steroids, you're essentially reducing some of the edema that's happening, that's resulting in that cord compression. So, it takes the edge off and as you go to your next step.

The next step, once you've put in those orders and told the nurses that we will need to get this in stat, is that you essentially end up calling neurosurgery and then followed by radiation oncology, both.
And the reason is that not everyone is going to be a surgical candidate. There's no way that you as a hospitalist is expected to know who will go to surgery, who will not, unless there's someone this was who was clearly not a surgical candidate in terms of their systemic-- how they're doing otherwise, and if they have major cardiac issues and such. So those are the two specialties that you will call pretty much right away after you order steroids.

Monee: Thank you for giving us permission to not ask permission for steroids. Hallelujah.

Meredith: Yeah.

Aditi: That's right.

Meredith: When you call those specialists is there other information they're going to ask you right away that you'd want to make sure you know at that point?

Aditi: Yeah. So, they will want to know, obviously what type of cancer this patient has. And something that you might have to decipher from oncologist notes which I know are not easy. But at some point, might be useful to involve the oncology consult team or the patient's outpatient oncologist to figure out where they are in their cancer journey. So very different if this is a young patient with breast cancer, who has endless options and has several years life expectancy, versus someone who has metastatic lung cancer is now on their third, fourth line of therapy and is really has only a few months to live. So, they would want to know that what is the oncologic status.

One of the ways they assess the surgical candidacy of patients is a framework called NOMS, N-O-M-S, which stands for Neurologic Oncologic Mechanical and Systemic status. So, you don't have to remember that, but it's just helpful to know what they're thinking. They're thinking of what is the neurologic status? Is this a high-grade obstruction? Or, is this a low-grade obstruction where the tumor might be abutting the spinal cord? And you'll see these on radiology reports that it's kind of abutting the cord, but it's not causing complete compression, you still need to act, because you don't want to wait for the cord to get compressed.

Then they'll want to know what kind of oncologic? What is the type of cancer, not only where they are in their cancer journey, but also, is this a cancer that is radiosensitive? Will it respond to radiation? And then they want to know the mechanical stability of the spine, if the spine is unstable, they might have to rush the patient into surgery anyway. And then if there's just too many vertebrae that are involved, they may not be able to take out that entire part. And they still need to have somewhat normal spine above and below. So that's another thing to consider. And then their systemic status, what is their cardiac status? What is their life expectancy? Those kinds of things. So, they're going to be hinting at all of those things as they ask you more questions about the patient.

Meredith: And this is, I guess, just something I've heard talked about because the effect of a cord compression would be so severe to someone's quality of life, that sometimes the person who for a different type of surgery, you may not think of as a surgical candidate, we might be more aggressive because it will have such a profound impact. Is that an accurate statement or--?

Aditi: I think so, at least for all practical purposes, it means you should call neurosurgery, regardless. Even if you think like, "Ah, I don't really think this is a great surgical candidate from my medicine expertise, I don't think this person is going to survive a major surgery." It's still good form, no one will ever fault you for asking neurosurgery. And they can very quickly say, "Well, no." And then that's that. and you've still called radiation oncology, because radiation oncology techniques and radiation techniques have also improved a lot over the years. They can quickly do a simulation, even on a weaken when simulation is essentially a radiation planning session, they can do the simulation and treat the patient in the same day, anywhere between one to five fractions, meaning how many days they're actually getting radiation. And it can provide quick symptom control in terms of pain and actually achieve good outcomes for people who are not operable or are not surgical candidates.

Meredith: Okay.

Monee: One of the things I was wondering about with rad onc surgery, that sort of stuff. Is there a sort of a cut-off for rad onc like, how many lesions can they sort of tackle versus not? I feel you mentioned with surgery there needs to be good spine above and below. But does the same sort of thing hold true for radiation?

Aditi: Theoretically, yes, because they have to limit the dose of radiation that's hitting the spinal cord. But it's very rare to have multiple sites where the cord is being impinged. It's usually one or two or three levels. But they are able to do, depending on the technique of radiation, they are able to cover a lot. And the other thing is, even for people who do get surgery, most of them will still end up getting radiation after surgery. Radiation oncology is usually playing a role regardless, it's whether they're going first or after.

Meredith: So, I think that's a good segue to-- so then now let's say Mr. Brown got surgery and radiation. What do we do with the steroids in the meantime? Does he stay on that for as long as this specialist say or is there actually a timeline we should think about?

Aditi: Yeah, I would say, it's good to ask the specialists because sometimes they forget to give you clear instructions, and it's really not something that you should be managing. So, it's perfectly fine to ask radiation oncology because sometimes we'll continue it for, during the time of the radiation and a few days after because there is a lot of inflammation from radiation itself. And you want the steroids on board for some time. And it really depends on the radiation oncologist. There's no prospective trial saying, "How long should you continue this at what dose?" But depending on how much inflammation there is, how much radiation the patient is getting. And other factors if they have terrible diabetes and they're hypoglycemic now because of the steroids, they might want to quickly taper.

Obviously, remember, this is typically not issue with tapering. We can taper pretty quickly. It's not like they've been on it for weeks and weeks and weeks that we need to worry about, like other things, like adrenal insufficiency and such. So, once radiation oncology gives us the clear, they should tell us how to taper off the steroids quickly.

Meredith: Okay. And then I think the last question I had on this one is, it seems to me at least from this conversation so far, that the main players during cord compression are going to be rad onc and neurosurgery. Is there any role that systemic chemotherapy or other therapies from a medical oncologist would come into play during the situation?

Aditi: Usually, I think medical oncologists end up getting involved anyway because we're internists and that's what we do. We're either giving people information on, "Well, what is the oncologic status?" Or, "Where do we go next?"

Usually, we don't, unless this is a highly, highly, chemosensitive tumor, like small cell lung cancer or lymphoma, with some kind of soft tissue in the back that's causing the compression. We don't always start chemotherapy while we're doing. Obviously, not during surgery, and oftentimes with high dose radiation that is given, we don't really start systemic therapy during it. But definitely, medical oncology should be on board if this is a new patient. But again, as hospitalists, you just can't possibly keep up with what type of cancer this is, and whether we would want to actually do something. I would say more often than not, we're not doing systemic therapy while they're in the hospital, but doesn't hurt to ask.

And then one other thing I'll say, which is not completely related, but I always tell people to be aware of the trap of the red flags and cauda equina syndrome. I see a lot of trainees tell me, "Well, it's not cord compression, because they didn't have saddle anesthesia and urinary retention. And we didn't get those three, the triad for cauda equina. Remember, you're only going to get that if you have tumor at the level of the cauda equina. And most commonly, cord compressions really occur at the level of the thoracic spine, followed by the lumbar spine, then lower down and cervical spines. So most likely the most common symptom is going to be back pain. And depending on where the enrollment is, it could be some paraesthesia in the arm or a lot of shooting pain in the leg. And if it's impending cord compression, it could just be some paresthesia because the nerve roots are getting compressed and

not the cord itself. It's just a caution to everybody that just because you don't have those classic three symptoms doesn't mean that they don't have cord compression.

Monee: Are there some cancers that are predisposed to cord compression than others?

Aditi: Yes. Most commonly we see it in prostate cancer, any cancer basically that causes bony involvement. So, prostate is a big one, lung, breast cancer, myeloma because it can cause those lesions in the bone and then a soft tissue component can poke the spinal cord, essentially. But yes, those are the most common places where we see cord compression. I would say any patient that has a diagnosis of cancers coming in with back pain and vague neurologic symptoms, you should really just be ruling it out.

Meredith: Okay. I think we can just briefly summarize because we got a lot of cases and just to keep everyone straight. So, it seems like I would say generally speaking, broad take-home point from cord compression starts steroids before you think twice about anything else. Go ahead and call all of your sub-specialists who would include neurosurgery, radiation oncology, and probably medical oncology, because, well, I'm not confident without medical oncology on board personally. So, I would include them. And then otherwise, it's going to largely be up to that multidisciplinary team to determine whether this patient would be a candidate for whatever intervention and whatever is best for him or her.

Monee: And I think one of the points that this will probably come up several times during this episode, which is, we have all these multidisciplinary approaches to pretty much all these emergencies. And our job as a hospitalist really isn't obviously, to know the nuance of the decisions that are made, but just being aware enough of the process to be able to provide our patients with anticipatory guidance essentially. So, I think that's probably a point we're probably going to make a few times but I think we should start early.

Aditi: Absolutely.

Monee: Okay. We'll move on to our next case. Ms. Goff, she's 67. She's got a past medical history of stage four lung adenocarcinoma, COPD and hypertension, who presents the emergency department with two weeks of worsening left arm swelling and cough. In the past two days, she's noticed that her voice has been getting hoarse, and she's mildly short of breath. Her husband says her face has become more red and more round than usual.

Initial vitals notable for mild tachycardia and hypertension, but she's otherwise stable. Her physical exam is essentially what her husband has described. And her labs are also pretty normal. I have not yet seen SVC syndrome in my career, but this really does seem like it. [chuckles] So, first things first, how do we prove it like imaging-wise?

Aditi: Yeah, so the best test, as long as your patient is not allergic to contrast or anything, would be a CT scan of the neck with IV contrast that can really show whether there's compression and show you what level the compression is at? Whether there's an associated thrombus or clots? And the status of the disease, what really is it that is pushing up on that SVC.

Meredith: And if a CT isn't an option?

Aditi: Yeah, and then you can discuss with radiology, and these things may not be available everywhere, but you can get an MR venography, and then go from there. There's also the gold standard, which is a CT venogram and such, which can be done, but I would move if there's a contrast allergy, I would go to an MR.

Monee: Okay, so, got the imaging, lo and behold, we confirm this is SVC syndrome. So, what's my first step as internist taking care of this patient in certain terms of medical management?

Aditi: The first step is just knowing, do they have a known cancer diagnosis or is this new? This case we know that this patient has lung adenocarcinoma or non-small cell lung cancer. But there are patients that this is their first presentation for their cancer, and we don't know what it is. And we need to know that SVC syndrome is certainly an urgency. But it's not a true emergency, unless there is a central airway obstruction or altered mental status from cerebral edema, or there's laryngeal edema, or compression of the heart causing arrhythmias and such. So obviously, it is devastating for patients to be, their face is swollen and their hands are swollen, and it may look scary. But as long as their vitals are okay, and they're breathing comfortably, it's not an emergency in the sense. If they don't have a histologic diagnosis yet, we do need to establish that first. It's not that we can just throw empiric radiation or empiric chemotherapy without knowing what cancer it is because just the treatments are so, so different. We first need to establish a diagnosis.

And in that case, if this is a brand-new cancer diagnosis, I would definitely involve medical oncology, and as with the previous case, everything is going to be multidisciplinary which is great, because you'll have a team that's thinking about the patient. And then you will figure out what we can biopsy. If this is a lung mass, then you might be calling interventional pulmonary for bronchoscopy or you might be calling interventional radiology if there's a more peripheral area that we need to get. Basically, we established diagnosis first, that way we can tailor the treatment to the type of cancer that is causing the SVC syndrome.

Now, if we know what type of cancer it is, it's just like in this case, or if it is an emergency where the patient does have impending airway obstruction or some kind of hemodynamic instability, you will stabilize them, whether it's in the ICU, or you need to intubate, you'll do all of those general things stabilizing the patient. But then you will most likely call interventional radiology or vascular, really, because the first step, in that case, might be a stent and endovascular stent that is deployed, which has become more and more common over radiation therapy, but you will start there, you might end up calling radiation oncology as well because again, there are certain tumors that are very radiosensitive, non-small cell lung cancer, it's moderately radiation sensitive. So, this patient, if we need a quick, fast response, we might do a stent first, sometimes we do both. So, that's what I will start that even though, might look scary, don't need to panic. We do have usually some time to establish your diagnosis or call the relevant consults and then kind of go from there.

Monee: Well, you told me not to panic. I feel like I'll probably be mentally hyperventilating regardless. [Aditi chuckles] But kind of like we were talking about the last time, are there any cancers that are predisposed to this more than others? Obviously, chest, probably plays a big role, but are there other ones maybe that we need to keep in mind?

Aditi: Yeah, absolutely. So, like you said, most commonly, lung cancers, but then also lymphomas, particularly non-Hodgkin lymphomas. And then think of things that happen in the mediastinum. So thymic cancers or germ cell tumors, or mesothelioma, or sometimes breast cancers that might have bulky, adenopathy that might cause SVC obstruction, but most commonly, it's usually long, or lymphoma.

Meredith: I had another question from what you just said to. You differentiated that there's this timeframe where it's more of like an oncologic urgent problem versus oncologic emergency. In my head, I'm thinking maybe in that urgent time that's when they have early signs and symptoms and may

come in for evaluation. Is there a timeframe that we would typically expect before that becomes an emergency? For example, if they only just noticed it.

Aditi: Yeah, not always, because it again, depends on the type of cancer, how fast it is growing. So, lung cancer, non-small cell lung cancer, it's not going to be growing that quickly, small cell lung cancer lymphomas might be growing much more rapidly. So, it's a discussion with radiology, getting on the phone with them and seeing, "Okay, how bad is this? How critical is it? Is there any impending airway compromise?" And they'll usually mention that in reports to, like, "Okay, this is compressing the atrium or the trachea is narrow." So those kinds of things, if it's not mentioned on your report, then clarifying with radiology is always helpful.

And then, besides stenting and radiation, another thing might be chemotherapy. If this is something like small cell lung cancer or lymphomas that really melt away with chemo, then that might be something that we start. We will not have to do stenting or radiation. Depending on whether there's a clot there, sometimes there are associated clots. So, if there's a thrombus there, then there might be a case to anticoagulant the patient as well. So that might be something to do if they're very sick. And there's again, airway compromised hemodynamic instability, and they have a clot. This might involve the vascular group or IR actually doing some kind of a thrombolysis, before putting a stent in. So those are things to keep in mind as well.

Monee: I never thought of, sort of, to do the double whammy, if you will, of mechanical plus, endovascular, in the vessel.

Aditi: Yeah.

Monee: Okay. I think it's probably a good point to summarize for our SVC syndrome. What I'm hearing is, you come in, you see it with a patient that has what looks like SVC syndrome. The first thing to do is get a CT, contrasted CT of the neck. Once you do that and confirm that diagnosis, the most important thing is to figure out why, so which cancer is causing it, because pretty much everything falls into place after that. So, you can treat the etiology of it as opposed to just trying to, I guess, move it out of the way if you will. And then in terms of cancers, obviously, things that reside in the chest would be common, but then in addition to that lymphomas are a good thing to keep in mind, specifically you said non-Hodgkin's lymphoma are correct.

Aditi: Right.

Meredith: Okay, so moving on to, I guess the next case, we've got Mr. Terrence. He's a 70-year-old man with a history of metastatic adenocarcinoma of the small intestine who presented with worsening abdominal pain, nausea, vomiting, which is really gradually worsened over the last couple of days. He's not been able to take any of his home meds or keep any oral intake down. On arrival, he's tachycardic hypotensive but afebrile. His exams notable for cachectic appearing male and moderate distress after an episode of emesis. His abdomen is firm, distended and tender to palpation, with high pitch bowel sounds diffusely. He has low potassium, he's a little bit of creatinine bump. And the ER gets an abdominal X-ray, which shows dilated loops of bowel and air-fluid levels consistent with a bowel obstruction. So, thinking about him, is there anything else that you'd really want to know on, like history, physical labs or imaging at this point?

Aditi: So, let's start with history. Again, here, I would want to know, what is the cancer status. I always say, what treatment are they on? There's chemotherapy drugs like irinotecan, that actually can cause a pseudo-obstruction type picture because they can slow down gastrointestinal motility a lot. What are they really taking? And then again, what line of therapy is this? Is this someone who's just started

treatment and hasn't really had a chance to see what cancer-directed therapy can do? Or this is someone who's had multiple different therapies and had unfortunate progression of disease despite those? And then when was the last tumor assessment? So, when was the last CT scan and what did it say? Did the patient have stable disease? Were they progressing? Or they actually responding to the treatment that they were getting? So those kinds of things are important to know from a cancer standpoint.

And then also just things that we would ask any patient, regardless of cancer histories, whether they've had prior abdominal surgeries or radiation. Yeah, I would start there, In terms of history. In labs, I would add-- we usually will also have an albumin because a lot of times we're getting a full chemistry. And that just gives us a little bit picture into what their general nutritional status and overall health is. Obviously, you said this patient was cachectic, so that's obviously pretty telling. And then also getting a lactate in case there is some mesenteric bowel ischemia. So that would be helpful as well.

This patient has had an X-ray, which is often the first thing we do. But then when there is really a real suspicion for bowel obstruction, I would get a CT scan of the abdomen. And this will not only tell us whether there's an obstruction or not, it can give us a better sense of where's the transition point? What is the grade? Is this a high-grade obstruction or a low-grade obstruction, partial or complete, and whether there's any bowel ischemia that we can see it.

Meredith: I think one of the things that's been very telling so far is actually how much the oncologic history plays into some of the decision0making, which I think is just helpful for all of us to think about. This patient has a known GI cancer. Are there other malignancies that we should be thinking about, that are commonly associated with malignant obstructions?

Aditi: Yeah, so I would say, besides GI cancer, colorectal cancer, gastric cancers, the next most common one would probably be ovarian cancers. And really any cancer that has peritoneal involvement, that can be breast or lung or melanoma even. And that's why it circles back to, again, their oncologic history and status because it's very different to have metastatic cancer where you have one single met in the bone versus metastatic cancer where you have known peritoneal carcinomatosis and things like that. So those are things I would keep in mind.

And then I guess one other thing I would say, besides cancer, someone can have cancer, but this may not be cancer that's causing the obstruction, they actually could have additions from a prior surgery, maybe a cancer surgery. And then pelvic radiation is another big one. So, there's no active cancer there, but pelvic radiation can cause scarring and fibrosis can then has a late complication result in obstruction.

Meredith: I guess the other thing that I have seen sometimes, and I actually just don't know what to do with this information often is. There's a million reasons someone might have a little bit of ascites, and so one of the questions is that ascites contributing to the obstruction? But I often feel like paralyzed because I'm afraid to put a needle into like an area that might have cancer growing. Is there any guidance for what to do in that situation?

Aditi: Yeah. I think this is not a decision that you should be making by yourself. This is really involving your GI surgeons or colorectal surgery and asking them. Just like any other patient again, even with the previous case, you may think that this may not be a candidate for surgery, but I think just getting their input on things like whether they really think ascites could be causing it. But in that case, you wouldn't necessarily see the same pattern on a CT scan. And if there is malignant ascites, which is kind of contributing to more of a pseudo-obstruction kind of picture, then we would recommend doing a paracentesis and people get it all the time that people that do have malignant ascites, and they may

have even a peritoneal catheter that is in place. So, I don't think there's nothing wrong in doing that, but it should be driven by a discussion with surgery as well. And talking about pseudo-obstruction, another thing to keep in mind is also, a lot of our patients are on opioids. And so that's another thing to think about, which is a catch-22 situation because they're in a lot of pain and you want to help them in the treatment that might actually be more opioids, but it's just discerning what's causing the obstruction. It's just helpful to keep that in mind as well.

Meredith: And you mentioned, like getting surgery involved, like medical oncology, is there anyone else to consider in these patients?

Aditi: I think palliative care can be really helpful in helping with symptom management, especially if this patient who looks emaciated. He's clearly not doing well overall big picture. The emaciation didn't happen overnight from the obstruction. So that can be a really helpful resource to both, the patient and the medical team to just help with symptom management. And then discussion of obviously helping facilitate goals of care discussions.

Meredith: Let's say before you've had a chance to call everyone or maybe not everyone seen the patient yet, are there things that as a hospitalist you should be doing right away, same as the steroids right away for the cord compression?

Aditi: I think basic management of bowel obstructions, so decompressing with an NG tube to suction, fluids to maintain hydration, and you mentioned this patient had a little bit of an AKI and was tachycardic and hypotensive. So, fluids, pain control, I would use, appropriate pain management I wouldn't hold opioids in this setting, you have to get the patient comfortable. That's what I would start with. And then as we get more input on whether this patient is going to be a surgical candidate or not, which is again, dependent on the rate of obstruction and whether there are surgical candidates in terms of life expectancy, and what other medical comorbidities they have that might preclude them from actually getting a surgery.

Then there's other measures that can be taken like somatostatin analogs like octreotide that can reduce, it can really help with pain control, and also nausea and vomiting that occur by just reducing the gastrointestinal and pancreatic secretions. And also, just reducing motility and that cramping pain that they might have. We tend to use octreotide. But other options are also some anticholinergics like scopolamine or hyoscine. Some people talk about steroids and there's not great data to support routine use of steroids, but it can be a helpful adjunct to the antiemetic regimen. And then so that's another component, so getting their nausea under control. You can use Lodoz, Haldol, you can use Metoclopramide, or Reglan. And that's really not to be used if there's complete obstruction, only if there's partial obstruction because it can cause severe cramping. It's going to increase motility prokinetic agent. But basically, fluids decompressing them from above, pain control, nausea control as you figure out the next step.

Meredith: Since you just said it, so then those are a lot of symptom control. So, what is the next step big picture for the patient?

Aditi: Yeah, so obviously, if they're surgical candidates, and there's a transition point and they go to surgery, and then are managed based on whatever surgery they got. This patient looks like is overall not doing well and may not be a candidate for surgery. And we don't recommend that for people who have very limited lifespans. Sometimes if they're coming in, they might get a venting G tube as another form of decompression. The other thing that comes up very commonly on whether we should be starting them on TPN. And I think again, this really, really, really depends on where they are in their cancer journey. If this is a mechanical obstruction and someone who has many different lines of therapy

that can be used, then in the short term as a bridge, TPN is absolutely fine. But if this is someone who has had several lines of treatment and is not doing well, and is only few months to live, then most of us believe that TPN just prolongs suffering. And there's data to show that there's no improved survival with kind of artificial nutrition at that time.

And then that's where palliative care can really help, and the discussions with outpatient oncology can really help the primary oncologist because, I think you probably have heard this many times, but for family members, specially, it's just very, very hard to wrap their minds around the concept that their loved one is starving or not able to eat.

Meredith: Yeah, I think that's one of the more difficult conversations.

Meredith: Yeah, no, I think the conversation that frequently is had is when you start broaching sort of food for comfort, as opposed to for nutrition, I think-

Aditi: Right.

Monee: -that's really just a very-- one, it's conversation that needs to be had, and two, it's definitely hard for families to grasp it. But it is something I think we should definitely talk about.

Aditi: Yeah. And don't hesitate to and have the primary oncologist involved here, because it's a lot for them to hear it from you. And it's a lot on you to say to them, and so they need to hear it from the oncology team that, "Listen, we don't think this is going to help you, big picture." And then kind of getting in, that's where palliative care can really help facilitate these discussions.

Monee: One of the things I'm always puzzled by is with a venting PEG. I feel there's like locations that if the mass happens to be, that's not an option. Can you talk a little bit about that? Obviously it's going to be under the guidance of the surgeon, but in my head just like to know coming into it. if that's something that's going to come up.

Aditi: I guess if the obstruction is proximal, then I guess venting G Tube is not helpful. There are sometimes stents that are put in as well. And it's definitely a nuanced discussion because there's a whole bunch of complications that can occur with those as well. But if the obstruction is distal, there might still be benefit for the venting G tube.

Meredith: To summarize this case on malignant obstruction, it seems the most important things that we really have to determine are where the patient is, like you keep saying during their cancer journey, is this someone who's going to be able to tolerate maybe more aggressive therapy with surgery and other specialists or more going down maybe a palliative route. And some of that can be decided by additional lab work or things like that. But for the most part, it will be based on a lot of information that they've gotten potentially from their outpatient oncologist to drive that. And then otherwise, the management and everything is largely how we would think about an obstruction in any other situation with decompressing and treating them conservatively that way until surgery decides whether this patient's a surgical candidate or not.

Aditi: Right, and then I'll say one thing, in addition, is that it may not be something that we know, the day of it may not be immediate. So, a lot of times surgery will say, "Let's start with conservative measures and see what happens." And then they might do a gastral graphing challenge in a day or two and see if they're passing. And sometimes, if there's a partial obstruction, people might, that obstruction might get relieved, and they might actually those-- it may not be that you're in that place of having goals of care discussions or anything, because with conservative management, they did resolve.

It's not uncommon to then have the same patient get admitted multiple times for the same type of obstruction, where we start thinking more of a venting G tube and such more to also just provide comfort. And that's where some of those more long-term discussions come into picture unless the patient in front of you is just looking really, really sick. And you don't think that they have very much time to live, this might be an ongoing discussion over several weeks or even longer.

Monee: Great. Okay, so I think we've dealt with some of the more mechanical pathologies for onc emergencies pretty well. So. we're going to kind of slowly shift gears now. One of the things that always seems to come up for onc emergencies is hypercalcemia. But you wonderful, dedicated Curbsiders listeners probably know that there's already a Curbsiders episode on hypercalcemia. And if you're not sure, it's Episode 281 from June of 2021. So, if you want a full download on hypercalcemia, I would go there. But in the meantime, Aditi, could you maybe give us a couple clinical pearls that are more specific to onc-related hypercalcemia?

Aditi: Absolutely. So, I'll start with what are the common cancers that actually result in hypercalcemia of malignancy. And the most common ones would be squamous cell, cancers of the lung or head or neck, lung just being way more common. But it's the squamous cell histology that's notorious for causing hypercalcemia. And then we can see it in breast cancer most commonly. Surprisingly, not so much with prostate cancer, even though there is bony involvement there. Both in squamous cell cancers, and with breast, the mechanism can be that PTHR, so PTH-related peptide, we don't necessarily need to test it. If you have a diagnosis of squamous cell carcinoma of the lung and they have hypercalcemia, you don't have to send a complete workup on why this is.

And then other things to think about as patients that do have lytic lesions in their bones, like multiple myeloma, or patients that have lymphoma where the mechanism is that, and I'm sure you talked about this before, but the vitamin D activation within the tumor cells. I would say, big picture again, you can do all the temporary measures like fluids and bisphosphonates and or RANK ligand inhibitors and such. But really, it's going to come down to fixing the underlying problem, which is the cancer. So, a lot of times, I do get patients where the first thing that I'll notice about their cancer starting to grow or progress again, is a spike in their calcium. And it's kind of like an, "Oh, boy," moment where we're like, okay, clearly, there's cancer that's starting to grow. And then we do everything that we have to do to stabilize the patient and get the calcium down. But usually, it's temporary unless we can get cancer-directed therapy in them to actually help them feel better.

And then the only other thing that you might have discussed before is that I will say is someone has hypercalcemia, you really need to get it down. At that point, we're not worried about dental clearances and such, the risk of osteonecrosis of the jaw is very low, and it's more cumulative risk over years. So, I would just keep that in mind because sometimes people get hung up on getting an urgent dental consult before treating the calcium.

Monee: Yeah. That's literally the only thing I remember about zoledronic acid for medical school is osteonecrosis of the jaw. So, thank you for pointing that out.

Aditi: Yeah, I mean, when it happens it's really devastating and bad. So, I get the worry but this is an urgent situation.

Monee: Great, those are some really good pearls. Thanks, Aditi. All right, we've gone through the obstructive processes, we touched briefly on hypercalcemia, I strongly encourage you to check out the other hypercalcemia episode. And now we're going to go full-blown heme malignancy. Meredith, can you take us in?

Meredith: We've got Ms. Greenfield, she's a 73-year-old female with past medical history of hypertension, diabetes and huff puff. And she just was recently diagnosed with Burkitt's lymphoma. And she presents to her oncology clinic for her first scheduled chemotherapy infusion. And she's complaining of some generalized weakness, fatigue, nausea, some muscle cramps. She reports having some increasing symptoms over the last several days, but because she had this appointment already scheduled, she's like, "I'll just wait till my appointment." Her vitals are stable. And labs prior to chemo are notable for elevated potassium and phosphorus. A low calcium in a high uric acid. And her crown ends up a little bit from her baseline. But the remainder of her labs are pretty much stable from her priors. Her oncologist calls the hospital for direct admission for concern for TLS. So, we know right now that we're talking about TLS. But I think the best place to start for TLS because it at least helps me is just thinking about the pathophysiology of what's going on. So, could you walk us through that, Aditi?

Monee: And I'm commencing just pain, thinking about pathophys.

Aditi: This one is simple. Tumor lysis syndrome or TLS, literally, the tumor cells are lysing, either spontaneously because the turnover is the tumor cells are growing so rapidly, they eventually outgrown their blood supply and then they die. So, it can happen even without any chemotherapy that's given, it's just happening spontaneously, like a bunch of cells just outgrow their supply, they die a whole bunch more grow. So, just basically any tumor that causes high cell turnover, this can happen. And because there's lysis of the cells, whatever's inside comes out, and when it's built in the blood, those are the criteria for tumor lysis syndrome. So, some of the ions that are inside are intracellular and now once the cell lysis come out potassium, phosphorus, uric acid goes up, because you have a combusting cell and your nucleic acids are expelled, and they get broken down into hypoxanthine and xanthine, and then uric acid.

And so, the diagnosis of tumor lysis syndrome is essentially based on this seminal paper that defines the Cairo-Bishop criteria for TLS, where you need to have any two of these lab abnormalities which include hyperkalemia. So, K over six, hyperphosphatemia with a phosphorus over 4.5 milligrams per deciliter, or a uric acid more than eight milligrams per deciliter. Or a calcium that is actually low, less than seven milligrams per deciliter. And the reason the calcium is actually low is because when there's excess phosphorus, it binds to calcium and then precipitates, and so your calcium is driven on the lower side.

So, any two of these criteria within the same 24-hour period, either before or after chemotherapy or cancer-directed therapy is diagnostic of lab-defined, TLS. And if they have these lab criteria, in addition to certain clinical criteria, which includes renal insufficiency, so same diagnostic criteria any acute kidney injury with an increase in 0.3 milligrams per deciliter, or they have arrhythmias because of their electrolyte abnormalities or tetany, in other criteria is death, but well, and that is called Clinical TLS. So that's really the most important things to know about the pathophysio.

Meredith: Great.

Monee: Great.

Meredith: Okay. So, I think then that answered the next question that often comes up is, when I have learners like, you're going off of labs only essentially, typically, there's not going to be something that you specifically asked the patients outside of maybe palpitations or muscle kind of symptoms or things like that.

Aditi: Exactly, all the symptoms are typically related to either their tumor burden, or the electrolyte abnormalities. So, getting an EKG and those kinds of things if the potassium is very high.

Meredith: I think my only other question with the definition for it is they have to have a known cancer, if they came in with those lab abnormalities, but didn't have that known cancer, are you going to go and search for them? Search of a new cancer?

Aditi: Well, most of the times it's usually obvious if it's a heme malignancy, usually you will be also getting a CBC, so we'll see something there or if it's a lymphoma, they might actually have palpable adenopathy, or they might have had imaging that's kind of showing where the cancer is coming from. But, yeah, people can present with spontaneous TLS, especially people with Burkitt lymphoma, which is one of the most notorious for causing TLS. It's just very, very rapid doubling time. And the one thing I'll mention here is the role of LDH. So, as you notice, it's not part of the criteria for defining TLS. But it is a marker of high cell turnover. And when we check TLS labs, it is often included. And with Burkitt, you will see rapid doubling of LDH. Like you'll see something going from like 5000 to 10,000. The next day, it's pretty dramatic. But that's where we are worried about. We usually have other indicators of the tumor.

Monee: Yeah, so you mentioned Burkitt lymphoma as particularly high turnover cancer and heme malignancies in general. I know this is [unintelligible [00:54:18] heme breakdown, but are there any solid tumors we should be thinking about? You mentioned that there might be some, so I was curious if you could maybe tell us a few of those.

Aditi: Yeah. So, let's say in addition to Burkitt the most common heme malignancies first would be diffuse large B cell ALL, those are some of the other heme malignancies where you need to be mindful of. Sometimes it can happen even in CLL patients with very, very high white cell counts, particularly when we're treating with this agent called Venetoclax, which is usually when that's happening, people are being admitted electively to monitor for TLS. It's usually hopefully not on a medical floor, or at least hopefully, there's heavy involvement of the oncology team there. For solid tumors, not very common, but some of the more common ones would be with small cell lung cancer. I routinely treat patients that have pretty bulky disease with small cell. We treated outpatient majority of the time unless they're very sick and need to be inpatient. So not very common, but can happen with that. There's been reported cases even in colon cancer, but just very rare.

Monee: And you mentioned, maybe these patients don't need to be on the floor, which I think we all as hospitalists, our blood pressure, heart rate all kind of go up when we start thinking about tumor lysis patients. But I was wondering if the severity of the TLS plays any role in where they should go, and if that's, like, I guess how to characterize the severity.

Aditi: The most important thing will be how risky is it or what is the risk of their particular cancer and disease burden in causing TLS. So, if they have it, or whether they're at high risk for it, so this person with Burkitt, they clearly have TLS, they have AKI. This basically requires frequent monitoring of labs. So, they're going to be getting bloodwork every four hours at minimum. So, it might depend. If that's the only reason for monitoring, so it just depends on the kind of resources you have. So, if they can get bloodwork quickly, every four hours on the floor, then it might be someone who can be managed on the floor, step down unit, some places that might not be possible, and that might require ICU for just close monitoring.

Same thing, if they have arrhythmias if their potassium is really, really high, those kinds of things are obviously where they need to be on a cardiac monitor, those kinds of things. So again, not necessarily

particular to TLS. But clinically, if you think that there's other reasons for them to have just closer monitoring in an ICU setting or a step-down setting, then that would be appropriate.

Meredith: Cool. Now thinking about assuming we've triaged Ms. Greenfield to her right place, and it sounds like from her case, probably okay for the four. What's kind of that initial management for the hospitalist to be ordering?

Aditi: Fluids, definitely. Now this patient you mentioned has a history of heart failure, so obviously, we're cautious about it. But in general, we say this is a real hydration, this is not the baby gentle hydration, we give heart failure patients like we're really giving, pushing the fluids 150 to 200 CCs or 250 CCs an hour really monitoring their urine output, emphasizing to nursing staff that this is someone we really need to make sure is, we're flushing out their kidneys really well. So, fluids, fluids, fluids, is the first step that you would start. Then we start coming down to, obviously, if this is someone that has not gotten treatment yet, obviously oncology is going to be heavily involved in actually starting treatments and such. And then we come down to more specific treatments to really drive down like the uric acid level, and so on and so forth.

Meredith: Before we get into the specific ones, is there any limitation? So, for example, if someone has spontaneous tumor lysis syndrome versus-- does that change whether you can start the chemotherapy? Or do you have to start treating the TLS first, or how do you prioritize that?

Aditi: I would say with these levels, especially the potassium and such, I would say can happen pretty close together, but I would get them stabilized from a TLS standpoint, and the medications we have now are so good, and so effective and quick-acting that hopefully the treatment is not delayed, and we can start pretty quickly.

Meredith: So, you can go ahead, I think, and tell us what those medications are instead of leaving us on the cliffhanger. [laughs]

Aditi: [chuckles] Obviously, the medicine that we've used for a long, long time in driving down uric acid level is allopurinol. And that is a xanthine oxidase inhibitor. So, it's blocking that step where uric acid is being produced. So, it's really blocking the production of uric acid. So, it's preventing the conversion of xanthine to uric acid. In the process, it does result in accumulation of xanthine, which is also nephrotoxic at high levels.

And the second issue is that it takes some time to act. The third issue is, it does not do anything for the uric that's already floating around in the blood because it's preventing more being formed, but it's not doing anything with what's already there. We still need to start that because we do need to drive down the production of uric acid, so we would start allopurinol for everybody. Remember, this is a renally dosed medications. If they do have AKI, you want to make sure that you're dosing this appropriately.

And then the second thing that we do is rasburicase, which is a recombinant urate oxidase enzyme. So, it actually breaks down uric acid into this water-soluble compound called allantoin. Which obviously you don't need to remember, but just remember it like combust the uric acids that that's there. And it's pretty dramatic. If you've ever given rasburicase, you give it one day, and then uric acid goes from like 11 to like undetectable the next day. So, it's very quick. And the thing to know about rasburicase is, you technically have to check G6PD levels, which I don't know what hospital we can get that stat before. And it doesn't really change your management in the moment. But technically, if someone does have G6PD deficiency, it can precipitate a hemolytic crisis in them. I've never seen it and it's never come back on time, but we do send it. And usually, for the most part, you don't need to reduce the respiratory

case, because it's just very, very effective. So, depending on the level of uric acid, especially if the uric acid level is pretty high, I will just do that along with your fluids and allopurinol.

Meredith: Real quick, going back to the allopurinol, if you're not concerned about having to renally dosage, do you just do like the 100-milligram dosing? Or would you go higher during the TLS?

Aditi: Usually, we use the 300-milligram dose.

Meredith: Okay.

Aditi: Oh, sorry, one more thing.

Meredith: Go for it.

Aditi: We should talk about calcium.

Meredith: Okay, let's talk about calcium.

Aditi: Okay. [chuckles]

Monee: Calcium in the context of TLS.

Aditi: I will add that, when you're monitoring TLS labs, two things I would not overreact to. One is calcium. So, if you see a very low calcium, resist the urge to replete it, because what that will do is just bind more to phosphorus and precipitate as calcium phosphate crystals and damage the kidneys. So that is one of the reasons why they get kidney injury and renal failure. Instead of replacing the calcium, put them on phos binders. So here if you know need to talk to pharmacy or renal, it's a good idea, but just resist the urge to replace the calcium immediately unless they're very, very symptomatic from their low calcium levels.

And then the other thing I will say is LDH, because we do certainly get calls from people saying, "Well, their LDH was 2500 and now it's 5000, what do I do?" Well, it's kind of expected, we know that will happen. And that does happen even when we have a high-risk patient who's not in TLS, but we're monitoring for TLS because we're starting treatment. As long as they're not meeting other lab criteria for TLS, their electrolytes are okay. LDH by itself going up, it's very much expected, it's not dangerous. It's just a marker of now this tumor cells are getting killed.

Meredith: That was helpful. I definitely don't know the calcium bit to think about and definitely would be the one who's reacting to that.

Monee: Yeah, now you're just giving me lots of ammo to educate my learners. I'm very excited about this.

Meredith: Cool. So, I think we can go ahead and summarize the case just to keep all of us in line. So, it sounds like then so tumor lysis syndrome or the tumor cells all break down, we get this influx of potassium, phosphorus, uric acid, and then dropping their calcium. We can use this Cairo-Bishop criteria in order to determine if they have the two criteria to meet lab diagnosis of TLS. And it seems like the mainstays for treatment really are going to be lots and lots of fluids, don't be shy about them. And then the allopurinol and/or rasburicase for your patients. I think the other key point or pearl that you provided all of us is to not treat their low calcium that we all 100% I think would want to, anything else?

Monee: And then start checking those I Cals, you know how it goes.

Meredith: [chuckles] Yes.

Monee: Well, I think we're ready for our next case. Mr. Chang, he's 62. And as a history of CML, chronic low back pain and hypertension, came to the ER just not feeling great. He's been picking up extra shifts at work, and he'd run out of his Imatinib for approximately two weeks. It's not the first time this has happened to him either. At his last oncology appointment about a month ago, his white cell count was 12, while he was taking his Imatinib, and at this point, he's noting some generalized fatigue but last few days he's been having some fevers and night sweats.

His vitals on arrival to the emergency room are notable for being afebrile and otherwise hemodynamically stable. His exam is largely unrevealing. And in the ER, he has a CBC, which shows a white blood cell count of 160,000, blasts of 21% on the differential. He has mild anemia and thrombocytopenia as well. So, I guess this is hyperleukocytosis, yeah?

Aditi: Yes.

Monee: Can you define that a little better for all of us?

Aditi: Yeah. So, hyperleukocytosis is a white blood cell count of more than 100,000. By itself, shockingly a high white blood cell count does not necessarily mean badness or doesn't necessarily cause problems. We have patients with CLL and CML, who are sitting with white count of 200,000, 300,000, virtually no symptoms, it's really just a lab abnormality for them.

Most of the time, when we do run into trouble with hyperleukocytosis is in patients with AML. So acute myeloid leukemia, where it does need urgent management, or sometimes, as this unfortunate case, where they actually have CML, which is now in blast crisis. Clearly related to them not taking their highly effective medication.

Usually, CML is seen in chronic phase. So counts that are not this high, blast count that is not this high. So over 20% blast is what we define as blast crisis. Our medications, the tyrosine kinase inhibitors, or TKIs for CML are excellent, when they're taken appropriately. So, we don't see blast crisis as much as we used to in the past before these TKIs. Here, clearly, he stopped taking it, and so now it seems like he does have a blast crisis, which is what we worry about.

Monee: So, the definition, I think, honestly, I'm not sure I'd ever made that distinction between hyperleukocytosis and badness. So that's helpful to know. Other than his labs, is there anything imaging exam, other labs you might want that would be helpful in this situation?

Aditi: Yeah. I would always say a peripheral smear, ask a hematologist. That's the first thing we want for everything. But it matters because you're confirming whether they're in myeloid blast crisis versus not, or if this is a new diagnosis of leukemia, we want to see what type of blasts these are not all blasts are equal. These myeloid blasts that are seen in AML and blast crisis of CML are the sticky ones that cause issues.

And you also want to rule out another-- I would say oncologic emergency, which is APML, or acute promyelocytic leukemia, so you want to really rule that out. So, you definitely want a peripheral smear and your oncologist is definitely involved here, especially in someone who does not have a known diagnosis of leukemia. In addition to that, I would also get set up coag, because one of the

complications that can occur with hyperleukocytosis is DIC. So, you would want to know what their PTT fibrinogen is as well.

Monee: Okay. And so let's just jump right into treatment, I guess, after we've sort of established the diagnosis and the situation with a patient who's got 21% blasts?

Aditi: Yeah, so it really depends on what type of leukemia this is. If it's AML, you really need to treat the leukemia. Sometimes to just rapidly get their white count down, the oncologists might recommend hydroxyurea as a cytoreductive agent. And that's given every institution has hopefully a separate pathway on how to do this. But it could be as something like starting Hydrea three grams, and then dosing it every few hours.

And in some cases, it might be appropriate to actually start them on chemotherapy that is going to treat their AML. So, we usually call it our induction therapy, or seven plus three, which is heavy-duty chemotherapy, it's cytarabine and daunorubicin. At that point, they are definitely, not being managed by medicine. This is what their cancer therapy is. And in this case, where they're just not taking their [unintelligible [01:09:41] we would start them back on their TKI. So, this would be how to start. You wouldn't hear also be concerned about TLS because again, the counts or the disease burden is very, very high. So, here you might start them again on allopurinol.

Things to be careful about is, there is a theoretical risk of precipitating leukostasis, if you give them blood transfusions. So again, be careful with their anemia, make sure you run it by the oncologist before giving them pack red blood cells, because the problem with hyperleukocytosis when it is badness is because like I said with myeloblasts, which are sticky. So, one issue that happens is, it's just a viscosity issue, too many cells, clogging up the microvasculature.

The second issue is these sticky myeloblasts actually adhere to the endothelium. And then cause a loss of vascular integrity. So, there's basically leaky capillaries and they enter organs and cause direct injury in that way as well. So, because of this, once you start getting into the realm of leukostasis, which again, hyperleukocytosis is just a number, very high white count leukostasis when these sticky myeloblasts start causing organ injury, and plugging up microvasculature. So, if you are really concerned about that, one of the other treatments, and this is controversial, might include leukapheresis, where you're physically removing the layer of these mononuclear cells from the body.

I will say this is also very, very dependent on institution policy. Most of the time, it's either hematology or your pathology or transfusion medicine department that's arranging this. There's never been any good, large prospective studies looking at it, it's usually been case theories from different institutions. A big meta-analysis that was done of all these studies actually did not show a survival or mortality benefit of leukapheresis. But if someone is very, very sick, that might be something you're thinking about as well.

Meredith: So, while we're on the topic, can you just speak to how common is the leukostasis? How common does that actually happen?

Aditi: I will say not very common, but it is still particularly-- when we're looking at AML and when we're looking at blast crisis of CML, which itself is not very common. You can get into trouble with leukostasis, which depending on the organ that's being affected can present as shortness of breath. Or they might be confused, or have a headache, or just basically be an encephalopathy, or might have changes in their vision. It's board questions talking about priapism technically, I've never seen a case with that. But I don't think we see a lot, but we certainly do get into trouble from time to time.

Meredith: Okay, so sounds like not super common, but you also wouldn't want to miss it. So, to be thinking about it, if you had someone come in with those labs.

Aditi: Absolutely, this could kill a patient. So always very, very concerned when you start hearing some of these symptoms. And it's hard because pneumonia could present similar way.

Meredith: Yeah, for sure. So, can we go back also to what you were saying for the leukapheresis? So, in that same realm, it sounds like even though there's not necessarily a mortality benefit, are there other treatment options that you would be considering? Or is that kind of the only option you would have, and so therefore, if someone's sick enough, that's what you go with?

Aditi: Well, besides Hydrea or chemotherapy, there's other chemotherapeutic agents that can be used, cyclophosphamide, it's just like, nuke everything, it basically kills things and can significantly drop the white count quickly. There's other newer medications that are coming up certain monoclonal antibodies that have been used, that can actually be helpful. So again, that's very much driven by oncology and whether they think treatments that they have can they lower the counts rapidly enough for the symptomatic patient. But if someone is very, very sick, and you don't have time because it will take about 48 hours for even Hydrea to work, and you really need something immediate than you might not have any other option but to do apheresis, which is not easy because you need a big apheresis catheter, you need to make sure their coags are okay. And you definitely don't want to do it if someone has APML because that can worsen DIC and just make everything worse. So, this is really for non-APL cases, with very, very close consideration with your oncologists and transfusion medicine doctors.

Meredith: Yeah, I think that's what I was going to say is the main takeaway. It seems that this is pretty nuanced, and probably as the hospitalist, you are not the one making most of these decisions, you just need to be aware of that the diagnosis is out there and to have it on your radar.

Aditi: Absolutely, you actually can have leukostasis with a count of more than 50,000 inpatients with myeloid blasts. So even if their account is over 50,000, not quite above that 100,000 level and if they're symptomatic, you still should be considering leukostasis as a real possibility.

Meredith: And is that for all myeloid lineage like AML and CML?

Aditi: Yeah, and CML again, it's not chronic phase, and that's one of the reasons of doing involving hematology-oncology and looking at the peripheral smear, because you're ruling out chronic phase, CML versus blast crisis where there's actually these blasts that are circulating more than 20%.

Monee: We've put Mr. Chang through the wringer, I think we should sort of summarize this section, this case. First and foremost, hyperleukocytosis, man, it's just a number. And it's important to remember that you would need at least 20% blasts to make this a blast crisis. Just because someone's white cell count is 200,000, doesn't necessarily mean they have a crisis that needs immediate attention.

And then, the other thing to keep in mind when they're coming in is to make sure that you check labs, such as coags to make sure that they're not in some sort of DIC type picture. And the last piece to keep in mind is, if someone starts developing shortness of breath, altered mental status, potentially even priapism, you might start thinking this has progressed into some sort of leukostasis hyperviscosity state. And in that case, we don't have a lot of great treatment options. But obviously, as with all of these cases, involving the oncology team, early and often is the best way to go. So, you can provide, the right plan of care for the patient.

Aditi: And I'll say that we've seen patients who are on a ventilator get quickly off within four to six hours with the right treatment, which cytoreduction even by itself, so these treatments are highly effective, and just recognizing it and involving the specialists is key here.

Monee: So, I think we've covered a lot of ground. And so, I think it's a good time for, Aditi, can you give us a few take-home points?

Aditi: Yeah, I will say, first of all, don't ever be shy to involve your friendly oncologist. No matter how grumpy we sound, this is our job, these are our patients, and we are here to help and facilitate their care in the hospital. Secondly, I'll say as you see the common theme has been a multidisciplinary approach. So, you might be calling various consults, who might be putting their heads together to come up with the best plan for the patient. And then I would say the other common theme has been really finding out what the oncologic status is for the patient. I know it's very hard to decipher our notes sometimes and their oncology histories are very long, and you have a lot of patients, but even if it's a quick understanding from the primary oncologist on where this patient is at, whether they're new to treatment, whether there are several lines into treatment, what the patient's understanding is of their cancer, I think are all very good to keep in mind.

[Curbsiders theme]

Meredith: So, this has been another episode of the Curbsiders bringing you a little knowledge food for your brain hole.

Monee: Yummy.

Meredith: Get show notes at *thecurbsiders.com* and sign up for our mailing list to get our weekly show notes in your inbox. Plus, twice each month you'll get our Curbsiders digest, recapping the latest practice-changing articles, guidelines and news in internal medicine.

Monee: And remember, we're committed to high-value practice changing knowledge. And to do that, we need your feedback. So please subscribe, rate and review the show on Apple Podcast or Spotify, or email us at *thecurbsiders@gmail.com*. A reminder that this and most episodes are available for free CME credit for all healthcare professionals through VCU Health at *curbsiders.vcuhealth.org*. A special thanks to our guest Aditi Singh, to my effervescent cohost, Meredith Elizabeth Trubitt, and to our whole team. The Curbsiders is produced and edited by the team at Pod Paste, Elizabeth Proto runs our social media and Stuart Brigham composed our theme music. Until next time, I've been Dr. Monee [unintelligible [01:19:53] Amin.

Meredith: And I've been Meredith Elizabeth Trubitt. Thank you and goodnight.

[Curbsiders theme music]

[Transcript provided by SpeechDocs Podcast Transcription]