

PUSHPA I have no conflicts of interest to disclose. Today I am representing the multidisciplinary pediatric thyroid center.

VISWANATHAN: I'm giving this talk on behalf of our team. And we'll talk about thyroid diseases. If you are not aware, January is the Thyroid Disease Awareness month, so time selected for this presentation is perfect.

By way of overview, these are the learning objectives. I would like to give an update about pediatric thyroid cancer and American Thyroid Association pediatric guidelines on the management of thyroid nodules and differentiated thyroid cancer in children. I'm excited to share our collaborative efforts and multidisciplinary approach to the care of children with pediatric thyroid diseases. Towards the end I'll spend the bulk of the time describing two cases and thereby discuss the various treatment options.

Thyroid nodules and thyroid cancer are more common in children than previously appreciated. Older studies report a prevalence of about 2%, but these studies reported their findings mainly based on palpation and clinical examination. Recent studies are coming out reporting a higher rate because of the use of ultrasounds. Thyroid nodules are rare in children compared to adults, however about 25% of these nodules in children are malignant compared to only 5% to 10% in adults. That is thyroid nodules in children are five times more likely to be malignant than nodules in others.

So incidence of pediatric thyroid cancer is increasing. How are they picked up? Usually presents as an asymptomatic neck mass picked up by medical providers or the patients themselves or picked up incidentally when they go for other procedures like ultrasounds or CT scans for non-relevant or evaluation of other diagnoses. Occasionally cancer gets picked up in a metastatic cervical lymphadenopathy. Although very rare in children, 10% to 20% present with pulmonary mets at presentation.

So before moving forward some reported facts about thyroid cancer in the United States according to the CR data, new cases of thyroid cancer, in general, across all age groups seems to be increasing. However, the good news is that the mortality rate continues to be low without any change. So how about in pediatric population? The incidence again appears to be increasing. This could very well be because of increased detection due to increased use of technology and medicine.

New cases in thyroid cancer in people less than 20 years of age-- it represents about 1.8% of all thyroid cancers diagnosed. In the 15 to 19-year-olds, it's the eighth most frequently diagnosed cancer and the second most common cancer among girls. What else do we know? More likely to be diagnosed in adolescence than younger children and five times more likely to occur in adolescent girls than boys. Most common presentation of thyroid cancer in children is a thyroid nodule, and it's thyroid nodules are more prevalent in preexisting thyroid disease like autoimmune thyroiditis.

More facts, pediatric thyroid cancer, main types are differentiated thyroid cancer, which includes papillary, thyroid carcinoma, and follicular and their variants. Undifferentiated thyroid cancer is medullary, anaplastic and other variants. Medullary thyroid cancer is rare in childhood and the other forms are even rarer. From now on when I refer to thyroid cancer I usually am trying to refer to differentiated thyroid cancer and the management of differentiated thyroid cancer.

Just some historical background-- until recently, both in children and adults we followed a similar protocol. Once a diagnosis of thyroid cancer was made, everyone underwent total thyroidectomy and were started on thyroxin replacement. About four to six weeks later, thyroxin replacement was stopped. This is aiming to stimulate the remnant thyroid tissue in the body and make the tissue more sensitive to the radioiodine. Everyone undergoes a diagnostic whole body scanning to see if they have any mets. And regardless of the cancer staging, everybody got radioactive iodine ablation, either remnant ablation or higher doses based on local or distant mets.

This approach, however, led to a high rate of cure, but the problem is every children needed to undergo the same treatment, including thyroidectomy and radioactive iodine ablation regardless of the staging. Subsequently pediatric guidelines were published for the first time in 2015, which we'll review briefly. Very busy slide, but it's very important. This gives a gist of all what I'm going to say.

Let's review in some detail as to how the pediatric thyroid nodules and thyroid cancer is different and what created the need for these specific guidelines. There's a major difference even with the clinical presentation in children compared to us. As we have seen, thyroid nodules are uncommon in children. Although uncommon, it's five times more likely to be malignant. Again the number is 25% of the nodules in children are likely to be malignant compared to 5% to 10% in adults.

Adults may present as a lump in the thyroid or thyroid nodule. Children may have that, but at the same time have multiple cervical metastases at presentation. Many children present with primary metastasis. So despite these extensive disease at presentation, the children are less likely to die from this disease. And even the children who present with pulmonary metastases, they develop a persistent but stable disease. So a more favorable progression-free survival compared to adults who have persistent thyroid cancer.

There are many molecular and pathological differences in children. In adults, point mutations in BRAF and RAS genes are common. However, in papillary thyroid carcinoma in children, there's a higher prevalence of gene rearrangements like RET PTC. This might be one of the reasons as to why children respond much better to radioactive iodine than kids.

As pediatricians, we always worry about the long-term health of our patients. There's an apparent increase in the risk of second malignancies in childhood cancer survivors who were treated with radiation so this has led to some rethinking of the earlier concept as to whether all the thyroid cancers need to be treated the same. So we could use radioactive iodine therapy when warranted, but limit overtreatment to those children who are unlikely to benefit. So if it's a minimal neck disease limited to the thyroid, might just need thyroidectomy without any radiation. So that is what the new guidelines are more heading to.

So the pediatric guidelines goes over evaluation of thyroid nodules including the role of ultrasound and ultrasound-guided fine needle aspiration, goes over the pre and postoperative cancers staging. It's very imperative that you stage the cancer as much as possible preoperatively and then again postoperatively to help categorize the risk recurrence. Guidelines again emphasize the selective use of radioactive iodine. And I won't go through it in detail. We'll just review some of these briefly.

Let's see the guidelines regarding evaluation for thyroid nodules. There are several risk factors that predispose to a development of thyroid nodules in children including iodine deficiency, prior radiation exposure, history of preexisting thyroid disease like autoimmune thyroiditis and several genetic syndromes. Childhood cancer survivors, especially survivors of Hodgkin's lymphoma, leukemia, sinus tumors, they have a higher incidence of thyroid nodules. The peak incidence is, however, about 15 to 25 years after the radiation exposure. So children who received radiation at a younger age, and those who received radiation doses up to 20 to 29 gray, they are at a higher risk.

There are several genetic syndromes and disorders that predispose to thyroid nodules and thyroid cancer. There's a big list down here. I'm not going to go through all of them, but APC mutations associated with familial adenomatous polyposis causes a higher prevalence of papillary thyroid carcinoma. Carney complex is an autosomal dominant disease. The condition is associated with nodules in different organs including thyroid. PTEN gene mutations predispose to the development of thyroid cancer, but here follicular cancer is reported more. And children who have family history of non-medullary thyroid cancer seems to have a predisposition to thyroid nodules.

So regardless of whether we found a nodule in a high risk patient or your regular child when you found a nodule during evaluation, how do you evaluate them further? Who needs sampling? Which nodules need sampling? In pediatrics, we cannot just go by the size criteria alone. We need to consider aspiration for nodules if there is an increased suspicion based on certain ultrasound characteristics and if there are any additional clinical features as listed. And if suspicious, further evaluation is scheduled including fine needle aspiration and biopsy.

So the report that's given by the pathologist is usually categorized based on the Bethesda classification. If the report comes back in the category two, which is benign, or category six, malignant, the further treatment planning is comparatively easier. However, if it comes in the category three, four, or five, then it falls in the category of indeterminate nodules. The guidelines do not give clear cut recommendations regarding evaluation of indeterminate nodules. However our center we are developing evidence regarding use of molecular genetic studies, which we will see soon.

So in the evaluation of a thyroid nodule, a high resolution thyroid ultrasound is the imaging method of choice. And we are looking for certain radiology features that clue us in sending the patients for a fine needle aspiration and biopsy. So as I said earlier, more than the size criteria we are going for the ultrasound characteristics.

What do we look for? If the nodule is hypoechoic, has irregular margins, or the presence of these microcalcification or increased intranodal blood flow. Presence of abnormal lymph nodes is an indicator as well. So what is the abnormality in the lymph nodes? Lymph nodes are usually oval in shape and has a characteristic hilum limb in the center. When they are positive for malignant, the lymph nodes become more rounded and they lose the hilum in the center.

Two key points here. Guidelines do not recommend FNA for a hot nodule or functioning nodule. That's where the TSH is suppressed and there is increased thyroid hormones. In pediatrics there are published studies which report pyloric carcinoma with hot nodules, but here the assumption is that these nodules would be surgically removed and available for pathology so we don't need to do an FNA. If a fine needle aspiration is needed in a child, ultrasound-guided FNA is highly recommended.

So to recap from this part of the talk, differentiated thyroid cancers are mainly papillary and follicular. Papillary thyroid carcinoma is the most common type of thyroid malignancy. It's often associated with somatic mutations in the RET proto-oncogene, which is activated by rearrangement. RET PTC rearrangement is the most frequent molecular change noted in children. 70% of the children with PTC have lymph node metastasis and 15% with DTC have lung metastases. Of course we know to ask about family history in case of medullary thyroid cancers, however 5% of patients with non-medullary thyroid cancer have family history of non-medullary thyroid cancers.

Guidelines are very detailed, but some take home points from the guidelines-- as we discussed before, ultrasound-guided fine needle aspiration is highly recommended. All pediatric patients should be managed at a multidisciplinary center and surgery should be performed by a high volume surgeon. Extreme importance is given for pre and postoperative staging to classify the risk for persistent disease and recurrence. Of course, not everybody needs radioactive iodine therapy, and we need to be selective.

We all know guidelines are always a good start. It's not the final answer. Treatment needs to be tailored for each patient. At Children's, we were able to identify these issues before the guidelines were published and multiple departments collaborate in providing excellent care to our patients with thyroid diseases. The multidisciplinary center has an integrated team approach for the evaluation of thyroid diseases in children. And as you see, selected members from multiple departments are involved in the center.

To highlight some points that set us apart is that we have a very committed team of interventional radiologist and cytopathologist. The cytopathologist is always present at the time of fine needle aspiration to make sure that the sample collected is optimal for interpretation. We are one of the very few centers where we use molecular genetic testing in the case of indeterminate nodules. That is the Bethesda Category three, four, and five. All our surgeries for thyroid cancer are performed by our identified two thyroid surgeons. And we meet on a monthly basis and make case-based decisions.

Let me introduce the role of each member of our team. So patients identified with goiter or thyroid nodule are referred to endocrinology. endocrinologists evaluate the patient initially. Occasionally they end up in the office of our surgeons or oncologist, but we work as a team so patients get referred back to endocrine. And as we discussed, a preoperative evaluation is extremely important in the case of nodules just in case the nodule turns out to be malignant. The endocrine team members are also involved in the acute postop care and long-term care and surveillance. Our interventional radiologist and cytopathologist work together. A very important part in thyroid FNA is to ensure the adequacy of the sample.

If the initial cytopathology is indeterminate, reflex molecular testing is being done. This is not done in many centers. UPMC is one of the very few institutions where we are very advanced in this area of thyroid, cytopathology. Why is this important? If FNA report comes back as indeterminate, they could go for a repeat FNA, but if the repeated result is indeterminate they might end up getting a lobectomy. If the pathology report comes back as malignant, then that calls for a completion thyroidectomy. So now this involves a second surgery. If we end up doing a molecular genetic study, it could guide us to the potential malignancy risk. If any of the thyroid cancer causing mutations are identified, then the child could go for an initial complete thyroidectomy and then avoid a second surgery and then later complications.

In the ATA guidelines there are no clear cut recommendations. What we have learned from our practice is that molecular genetic testing is very helpful in deciding the treatment plan especially for the indeterminate FNA pathology. We've published preliminary studies and we are planning to get the data out in a large group. The pathologist in the team also evaluate the specimen after thyroidectomy and also the lymph nodes that are removed for a final diagnosis and postoperative staging.

Guidelines for the management of thyroid cancer in children specifically discusses that the treatment should be in a specialized center and surgeries to be performed by a high-volume surgeon. The complications after thyroidectomy, mainly hypoparathyroidism and recurrent laryngeal nerve damage, are much lower in the hands of surgeons dedicated to thyroid surgeries.

So we have identified two surgeons in our team who perform all the thyroidectomies for children with thyroid cancer. In case of extensive disease or complicated surgeries, the additional advantage is that they work in consultation with the head and neck colleagues and endocrine surgeons at UPMC. Our radiology and nuclear medicine physicians provide help with pre and postoperative imaging. The nuclear medicine team takes care of the diagnostic whole body scans and plan the radioactive iodine therapy for children who have extensive disease. We are helped by our oncology team members for appropriate counseling for patients and families. They assist us with the management of recurrent and metastatic cancer. Oncology team members also play a key role in surveillance for thyroid cancer in their cancer survivor population and help with the treatment of secondary cancer.

So highlights from this part of the talk is that having such a center with members from multiple departments working together has certainly improved patient care. We plan to develop the unique strength of this team by continuing our efforts in developing molecular genetic markers for thyroid cancer prediction in pediatric population.

So now I choose to present two cases managed by our team members. The first child presented with an extensive disease and it shows the effort put in by all the different team members. Second case is an example where proper screening and early detection of the disease is emphasized.

So patient is a 12-year-old male who presented to endocrine clinic from the primary care physician with a thyroid enlargement. In lieu of symptoms, only complaints he had was a harder time getting up in the mornings, more aches after soccer games, but he did not have any change in his voice, no difficulty swallowing, no painful swallowing, no weight loss, weight gain, and no history of radiation in the past and no family history of thyroid cancer.

As you see, maternal great-grandmother and mother with hypothyroidism. On examination, he just had an asymmetric enlargement of the left lobe of the thyroid and clinically no lymph nodes were palpable. So initial labs consistent with autoimmune thyroiditis. As you see, the thyroid antibodies were significantly elevated, and hypothyroidism with elevated TSH and low free T4. So he was started on levothyroxine replacement and he underwent a thyroid ultrasound.

So a large heterogeneous mass occupying the left lobe was noted. To orient you, this is the trachea. The carotids are on the sides. And this is the area of thyroid with the right lobe and a part of the left lobe. You see this large mass extending to the isthmus and you see the microcalcification along the border. So a detailed lymph node mapping of the neck was performed. And although clinically not palpable, there were abnormal prominent lymph nodes and some of them even had calcifications.

So as we discussed earlier preoperative staging is critical in the evaluation of any newly diagnosed thyroid cancer. Given the higher rate of cervical metastasis, all regions of the neck should be evaluated for abnormal lymph nodes. If suspicious or abnormal lymph nodes are detected, fine needle aspiration of the lymph nodes should be performed in addition to the aspiration of the thyroid nodule.

Usually CT or MR of the neck is not needed. However, if there's a bulky fixed mass, that could be considered. Same thing with routine chest CT, not recommended in the guidelines, but like our patient if it presented with an extensive neck disease, a routine-- not routine, a chest CT should be considered.

So the diagram here represents the levels of the neck that are usually evaluated for the lymph nodes. If lymph nodes are present in level six, which are positive for malignancy, the patient usually goes for a central neck dissection and lymph node dissection along with total thyroidectomy. but if they're positive lymph nodes, the lateral neck, especially levels four, levels five, and that calls for extensive surgery, including bilateral lateral neck dissections for lymph nodes, a central neck dissection, and thyroidectomy.

So in our patients, the FNA result came back positive for thyroid carcinoma with positive lymph nodes for metastatic cancer. So it's concerning that he had positive lateral neck nodes. So it suggests a very extensive disease way preoperatively. So a chest CT was performed in this case and it did not show any pulmonary metastasis. I have the cytopathology slides, and Dr. Monaco, our cytopathologist is here. She will help us guide through the path slides.

**SARAH
MONACO:**

So we did FNA of the thyroid in this patient and the suspicious lymph nodes that were seen radiologically. And so when we're there on site we do a rapid Diff-Quik stain, so this is sort of a high power image of that stain. Basically you can see sort of these cohesive clusters of cells. And they're sort of-- architecturally they're crowded and overlapping. And what catches my eye at this power is that you have these concentrically laminated areas, which are psammoma bodies, and we typically don't see psammoma bodies outside of papillary thyroid carcinoma, so that would be a very concerning feature for me.

Let's see more there. His lymph nodes were also aspirated and what you can see here are nice discohesive lymphocytes saying that we are in the lymph node. And within this sea of lymphocytes you also see these clusters of cells, which again show abnormalities in terms of architecture. And also you start to see some more of the oval nuclei that correspond to grooves. It's hard to actually see good nuclear detail in this rapid stain, so I have to go more by architecture and morphology of the nuclei not so much the chromatin pattern.

And we also have some immuno stains that can help us, so if we see a lymph node FNA and we're going percutaneously, we really shouldn't see any cytokeratin positive cells, so the presence of clusters that are cytokeratin positive would suggest that you are dealing with a metastatic carcinoma. And then TTF-1 is a good marker we use for thyroid.

So this case actually was positive for papillary thyroid carcinoma in the thyroid and the lymph nodes. And he was actually found to have a RET/PTC gene re-arrangement on molecular testing. So we basically diagnose all of our thyroid cytology using the new Bethesda classification system for thyroid reporting. And as we reviewed before, these are the diagnostic categories. We do collect for molecular testing preoperatively on all of these cases so every FNA that walks through radiology will get molecular testing collected, but we only send it on the indeterminate nodules.

PUSHPA Thank you, Sarah. So our patient underwent total thyroidectomy, with central and bilateral lateral neck lymph node dissection. So when you plan surgery for thyroid cancer in kids, there are several issues including determining the extent of surgery.

How can you ensure a complete surgery the first time? So we have brought our thyroid surgeons right here. I would like them to comment briefly on these surgical issues.

SPEAKER 1: Well, thank you, Pushpa, very much for that great overview of thyroid nodules and cancer in children and talking about our center. There's enough to talk about in terms of surgical issues, we could spend the whole hour just discussing these things. But we'll do it in a couple of minutes instead.

Pushpa already emphasized that there's an importance of having high-volume thyroid surgeons doing thyroid surgery. Thyroid surgery is relatively uncommon in children, compared to adults. So at our center, we've decided to have two surgeons, myself from pediatric otolaryngology, and Dr. Mollen from pediatric surgery, that do all the thyroid surgery. And that lets us have enough volume that we can really focus and maintain our outcomes.

The other thing that's important to do, to take care of children with thyroid nodules and thyroid cancer in a multi-institutional center. What was happening, when the guidelines came out in 2015, kids were going a lot to community hospitals and having their thyroid cancer taken care of by adult surgeons that would take care of thyroid nodules in adults, which are much more common.

And the outcomes were found to be much better in major centers. So there are isolated centers through the country that tend to be multi-disciplinary. And they have been found to take better care of children. And we're really proud of the center that we've developed here over the past five or 10 years.

So there's two of us that are doing all the thyroid surgery, and we work very closely with the rest of the team. In terms of extent of surgery, Pushpa mentioned a few things that come up. We, first of all, need to decide when to do compartmental neck dissection for lymph nodes versus just doing the thyroid.

And the other thing that we have to discuss is whether to do a thyroid lobectomy versus a total thyroidectomy. Traditionally, every patient with thyroid cancer would undergo a total thyroidectomy. And even the current guidelines for pathology cancer in children, which are from 2015, suggests that all patients-- all children with pediatric thyroid cancer-- should undergo a total thyroidectomy.

The reality is that some of those children are probably being overtreated. And some of them would probably benefit from a lobectomy alone, which has less risk, and a little bit less morbidity potentially. So one of our challenges is to figure out which children can undergo a lobectomy only versus needing a total thyroidectomy. But still the majority of children with thyroid cancer undergo a total thyroidectomy.

Another thing that comes up is whether to monitor the recurrent laryngeal nerve during surgery. There's a way we can monitor the nerve with electrodes that go in the endotracheal tube. And that's controversial.

Some of us-- I monitor the nerves always. I don't know that Dr. Mollen does. I don't know that there's good studies that show that the outcomes are better one way or the other. But that's a surgical issue that always comes up.

And when I did my training, there was no monitoring of laryngeal nerves. That's something that has come up since I trained, but has become more popular recently.

DR. MOLLEN: Yeah, I would just make a couple of comments on the coordination of care, which is incredibly important in these patients. Preoperative, where this comes into play really, not only in our work up of the thyroid nodule itself, which includes fine-needle aspiration and molecular testing, which may actually contribute to our decisions about extent of surgery.

There may be patients who would benefit from an upfront total thyroidectomy, with the goal of limiting the number of operations for these patients. And this also applies very heavily with work up of lymph nodes. Again, this is a morbid procedure, potentially morbid procedure. So you really want to limit the extent of your dissection as much as possible.

However, we know that there is a benefit to lymph node dissection with positive nodes in terms of disease-free survival. So the pre-operative work-up always involves ultrasound-guided lymph node mapping, FNA of suspicious nodes. And then of course, molecular testing factors in this decision to pursue lymph node dissection or not. It's not something we venture into. It's something we go into carefully.

And then in terms of our post-operative care, again coordination of care comes into play. We work very closely with the endocrinologists. These patients all may have transient hypocalcemia, which needs to be monitored. In addition to usually overnight monitoring, looking for potential surgical complications of disease.

PUSHPA Thank you. Back to a patient. Surgical pathology report came back consistent with multi-focal papillary thyroid
VISWANATHAN: carcinoma with greater than 40 lymph nodes that were positive for PTC. And it also is indicating extracapsular invasion of the tumor.

So definitely extensive disease, and we plan to treat him with radioactive iodine therapy. So initially he goes for a diagnostic whole-body scan. Thyroxin replacement was topped to stimulate any remnant tissue that's left in the body. And that's why you see the TSH high. We stopped the thyroxin treatment for two to three weeks. And his thyroglobulin level were detectable at 3.1.

Whole-body scan only showed uptake in the area of thyroid, with no distant metastasis. So he underwent radioactive iodine ablation with 50 millicuries of iodine 131. So he followed him with seeded ultrasounds. So repeat ultrasound, and a recent spec CT scan that was done in February was very reassuring. There was no abnormal focus of uptake, either at the thyroidectomy bed or we couldn't identify any distendments.

So the goal of radioactive iodine treatment is to decrease that thyroid cancer recurrence and to improve mortality. As the guidelines suggest and we discussed earlier, minimal disease limited to thyroid do not need radioactive iodine treatment.

If lymph nodes are positive for malignancy, the preferred treatment is surgical removal. But if lymph nodes are present in areas that are not amenable to surgery, or if they have extensive neck disease like our patient, or they have distant metastasis, then of course radioactive iodine treatment is indicated.

During the iodine ablation, we need to make sure that the TSH is at least about 30. This is to facilitate the radioactive iodine uptake, and then the treatment is complete. Post-treatment whole-body scan is recommended after therapy. So it could be done about a year after therapy, and that could be monitored.

There are short-term and long-term risks with radioactive iodine treatment. Most common side effects of this is nausea. Our nuclear medicine team had success with prophylaxis with anti-nausea medications.

Most of the other short-term side effects is mainly from accumulation of radioactive iodine in various glands, including the salivary glands. So you usually see dry mouth, rarely sialadenitis. Our nuclear medicine team again prepares them well with advice for good hydration and recommends sour candy to keep stimulating salivary secretion.

As pediatricians, we worry about the long-term risks. Permanent salivary gland dysfunction is possible, but it's extremely rare. If a child needs repeated radioactive iodine dosing for pulmonary metastasis, there is increased risk for pulmonary fibrosis.

Worry about the gonad effects and increased risk of secondary malignancies. More than me, our nuclear medicine physician, Dr. Judith Joyce is right here. I'll let her comment on these long-term risks.

DR. JOYCE:

Thank you. This is an excellent group of people that we're working with here. So it's been a pleasure being involved with all of you. With the radioactive iodine, I tell the patients and the family, it's been around over 70 years. So we have a lot of experience with it.

And of course, it used to be that everybody got radioactive iodine. So fortunately, I'm glad that the guidelines have come out. And our attitudes have changed. So why have they changed?

Well, one of the big concerns is the long-term effects of radiation. And in the old days, we didn't really think about that. But as you know, even with x-rays, we're now really thinking about, what are we doing? And so with radioactive iodine, the proof is not really out there distinctively, but it's looking like there is a slight increased chance of other cancers, leukemia, lymphoma, down the road.

So because of that-- and we're living longer, and we're talking about children here, we've really pulled back on whether we give radioactive iodine. So each patient-- we all discuss exhaustively to determine, does this patient need it, deserve it? You know, what would be the long-term implications.

So because of that, the things we think about are other malignancies. And we don't know, maybe they're genetically prone to these malignancies. But because of that-- you brought out hydration. So I always tell the patients, hydration. Drink, drink, drink, drink. And go to the bathroom very frequently. Because it's just sitting in the bladder until you get rid of it.

Our surgeons are excellent, so most of the disease, or even residual thyroid is gone in the neck. And so when we quantitatively look at the neck, it's about 1% uptake in the neck or so. So plus 90% goes out through the bladder, especially in the first 24 hours.

So we recommend hydration and going to the bathroom very frequently. And also keeping the bowels moving. So I think that potentially could help the long-term effects.

The other thing is gonadal effects, which especially when you're talking in children, and you're sitting there with their parents, they're very concerned about this, rightfully so. But the proof on the gonadal effects is also looking at-- let's say, for example, miscarriage.

They did find over 100 millicuries, that in the first year, there might be a slight increase in miscarriage. But you know, maybe that's related to dysregulation of the thyroid hormone. But after that, they didn't find increased infertility, miscarriage, congenital defects over the regular population.

So the gonadal effects, especially when I'm talking about the females, I'm not as concerned about. In the males actually, there has been concern, especially if we get up to a cumulative effect of 400 millicuries or more.

So as you can see, our patient here got 50 millicuries. So it would take a while-- you know, that would be multiple doses before we get up to the 400 millicurie. But when we start getting more and more doses, we do need to think about sperm banking. So that's something you always want to keep in the back of your mind that that may be necessary down the road. So, thank you.

PUSHPA Thank you, Judy. Back to our patient. He's doing very well. When we follow patients with thyroid cancer, the goal
VISWANATHAN: of treatment is threefold. One, we need to make sure that they are on adequate doses Tyroxin replacement to keep the THS suppressed. This is to ensure that there's no stimulation of any thyroid tissue, if there is remnant.

And thyroid globulin is monitored as a tumor marker. We need to make sure that thyroid globulin levels have remained undetectable. And also follow them serially to make sure it's not increasing, suggesting tumor recurrence. And third is to monitor for acute post-op complications, as well as long-term complications, including persistent disease, or risk of recurrent tumor.

OK, this will be brief. My second patient. Now this patient is a 12-year-old female with Gardner Syndrome, status post proctal colectomy in 2010. Just to recap, Gardner syndrome is a subset of familial adenomatous polyposis [INAUDIBLE]. Which causes tumors in different organs.

This is a condition caused by APC gene mutation. There's a higher risk for colorectal cancer and papillary thyroid carcinoma. So her endocrinologist got a screening ultrasound, because of suspicion for a thyroid nodule, and he knew about the increased risk of thyroid cancer, and rightfully referred her to endocrinology.

Thyroid ultrasound revealed a small nodule, limited to the upper pole of the right thyroid lobe. Lymph node mapping of the neck was done. No pathological nodes were identified. Due to the increased risk, because of her underlying diagnosis of Gardner's syndrome, and the ultrasound features that we discussed earlier, she underwent a fine-needle aspiration.

If final report was positive for papillary thyroid carcinoma. We have the pathology slides. And I'm indicating the intra-nuclear inclusions. And I'm being told that this beta catenin stain is very important in Gardner Syndrome because it moves inside the nucleus. Right, Sarah? And that is a characteristic of Gardner Syndrome, this particular stain.

So here we could argue the tumor is extremely small. She could-- we could argue that she could get a lobectomy, and then that would be the treatment. So we had discussions in our meetings to determine the extent of surgery.

And then we decided to let her go for a total thyroidectomy, because of the concerns that patients with Gardner Syndrome might be at an increased risk of multifocality and recurrence. So she underwent surgery, and post-operatively, she's doing well.

To conclude, I would like to point out incidence of pediatric thyroid cancer is increasing. Thyroid nodules in children are more likely to be malignant than thyroid nodules in adults. Early detection and treatment of thyroid cancer in children is associated with a very favorable outcome.

Proper management of children with thyroid nodules and thyroid cancer requires a multi-disciplinary approach. I can say for sure that having such a center with multiple team members has definitely improved communication, enhanced research, and most importantly, optimized care of patients with thyroid disease.

I would like to thank all my team members. My co-director, Dr. Witchel our surgeons, Dr. Simons and Dr. Mollen Our cytopathologist, Dr. Monaco. Our intervention radiologist, Dr. Escobar and Dr. Crowley. Our oncology team member, Dr. Randy Windreich and Dr. Judith Joyce from nuclear medicine. And thanks for supporting me and helping me present the hard work and efforts of everyone on the team. And thank you all for listening.