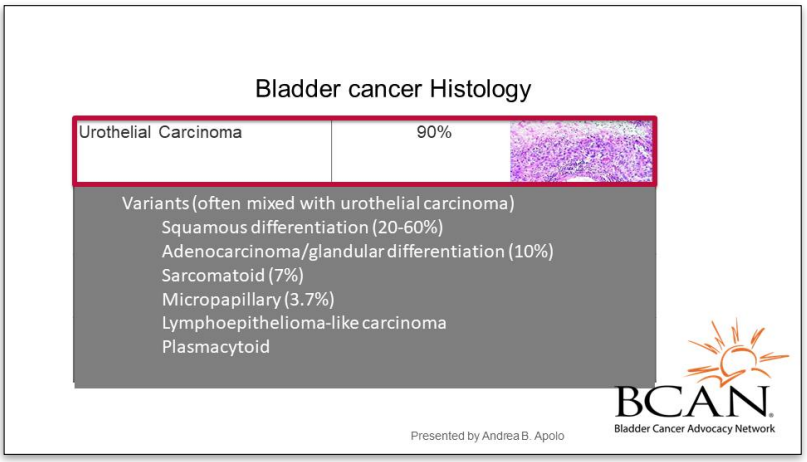
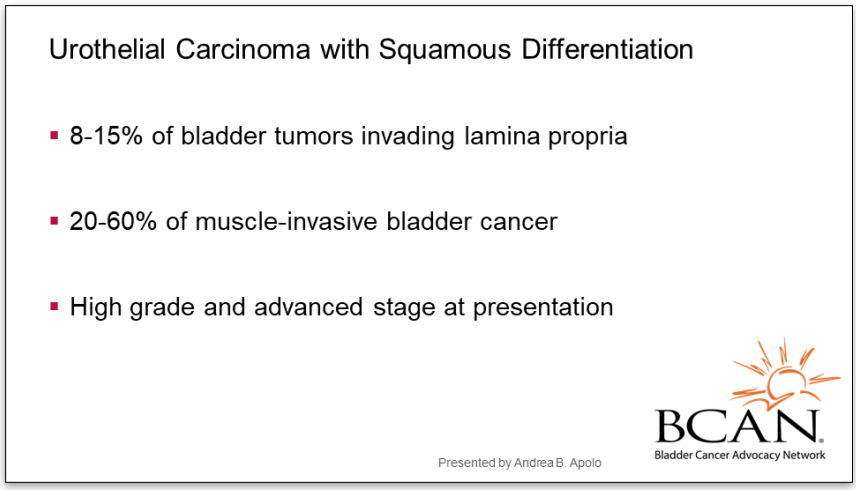
Rare Forms of Bladder Cancer: Urothelial Carcinoma Variants

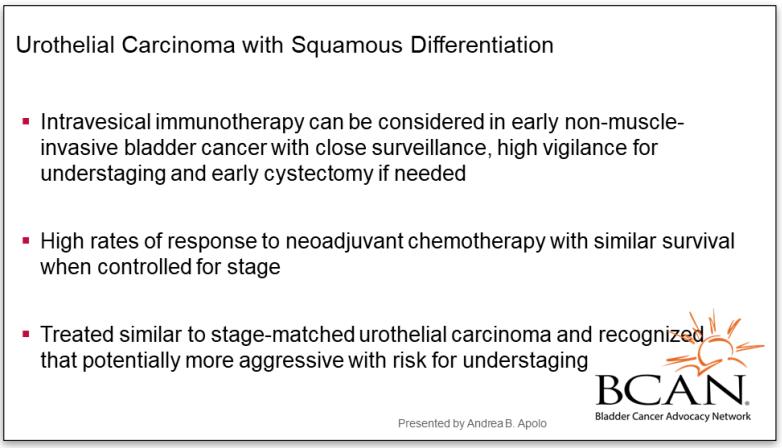


Dr. Apolo: So now I want to talk about urothelial carcinoma tumors that have a variant histology, and there's a lot of different types of variants. And I just listed the most common rare variants. These include squamous differentiation, adenocarcinoma/glandular differentiation, sarcomatoid, micropapillary, lymphoepithelioma-like carcinoma, and plasmacytoid. So, for urothelial carcinoma variants, similar to rare bladder tumors, it's difficult to diagnose. And the optimal treatment for these variants is unclear because we don't have randomized data. Most of the data that we have are from a single institution experience. And again, some of these are super rare.

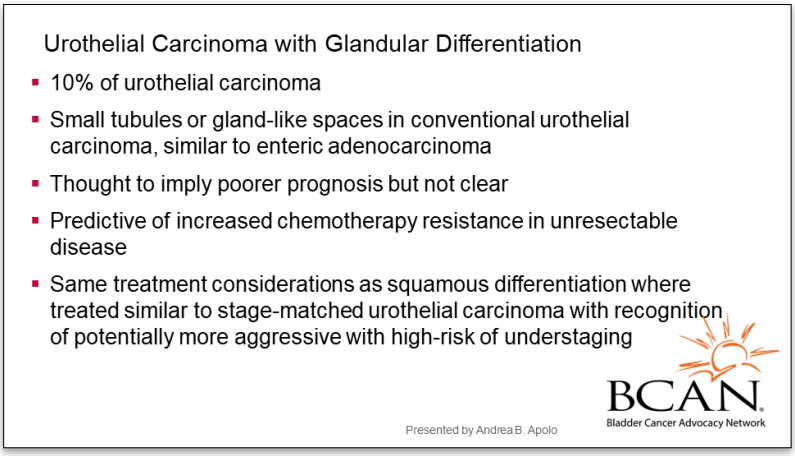


So I'll start off with urothelial carcinoma with squamous differentiation, and this is different than pure squamous cell carcinoma. Squamous differentiation within urothelial carcinoma is actually not too uncommon. We do see it in T1 tumors. These are non-muscle-invasive tumors occurring about 8 to 15% of the time. And we see it actually pretty commonly in muscle-invasive tumors, occurring about 20 to 60% of the time, depending on which surgical theories do you look at. These are high-grade and usually advanced stage at presentation. Next slide.

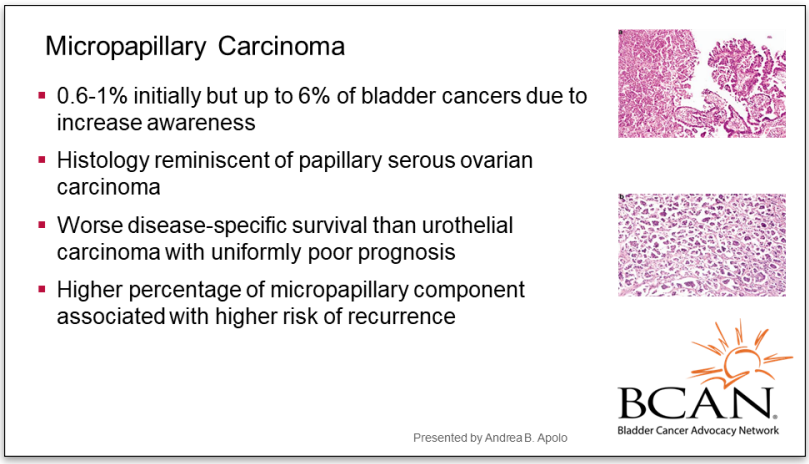
So, in terms of giving intravesical therapy for non-muscle-invasive disease, this is reasonable and this is okay to do as long as there's close surveillance with high vigilance for understaging and early cystectomy if the patient has recurrent. In terms of responding to chemotherapy, these tumors do respond. Remember, these are urothelial carcinoma with squamous differentiation. And they actually have a really good response to chemotherapy. Similar stage-matched to urothelial carcinoma in terms of their outcome, although some studies have suggested that these are potentially more aggressive, and there's more risk of understaging. Next slide.



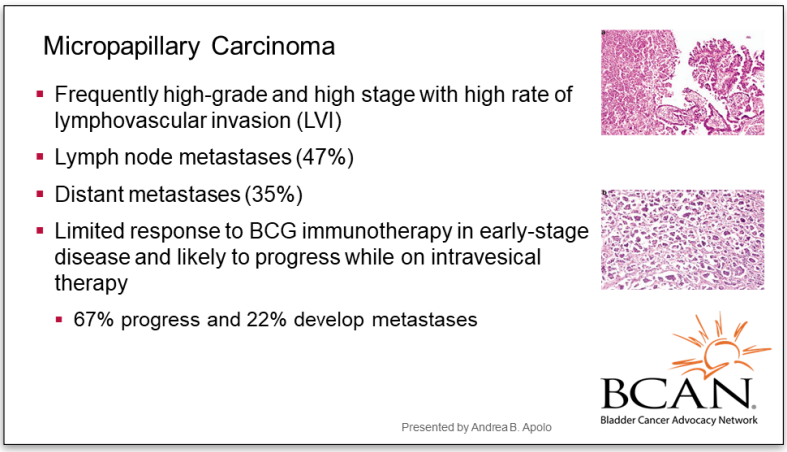
So, moving onto urothelial carcinoma with glandular differentiation. These kind of look a little bit like the adenocarcinomas, but just a little spot of them have adenocarcinoma, and the rest of them are urothelial carcinoma. These occur in about 10% of urothelial carcinoma. You see small tubules or gland-like spaces in conventional urothelial carcinoma histology, similar to enteric adenocarcinoma. It's thought that these possibly have a poor prognosis, but it's not clear. In terms of the response to chemotherapy, there's a theory that these may be more resistant to chemotherapy, but this has not been shown consistently in trials. Some trials have actually shown that they're just as responsive to chemotherapy, and the treatment is the same. Similar to squamous cell differentiation, you treat it the same,



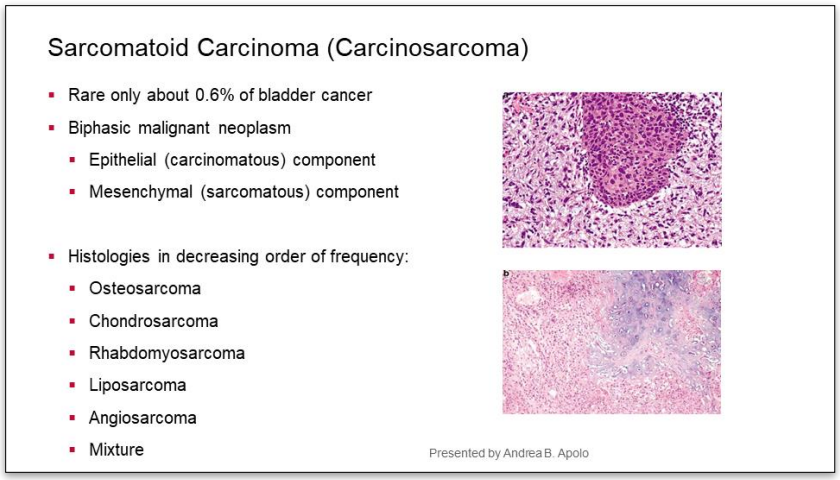
again, recognizing that these may be more aggressive, and again, a high risk of understaging.



So, micropapillary carcinoma. These are really rare. These are urothelial carcinoma with micropapillary in them. Initially they were about .6 to 1% of all urothelial carcinomas, but they're actually being found more now as pathologists learn how to find these. Histologically they look like a papillary serous ovarian carcinoma, but these are urothelial carcinoma. They just look like that under the microscope. They do have a worse disease-specific survival than urothelial carcinoma, with a poor prognosis. And actually, the higher the component of micropapillary within the specimen, then the more aggressive the tumor is. So, the more percentage of the tumor that has micropapillary features, the worse the outcome seems to be.

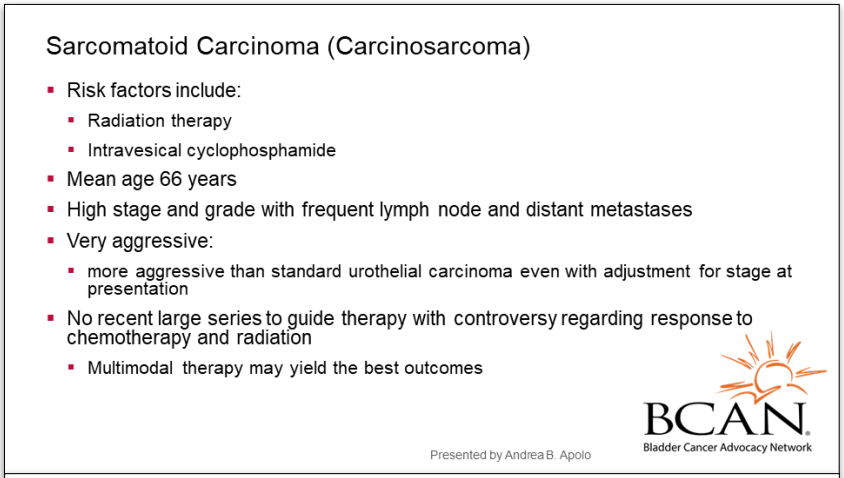


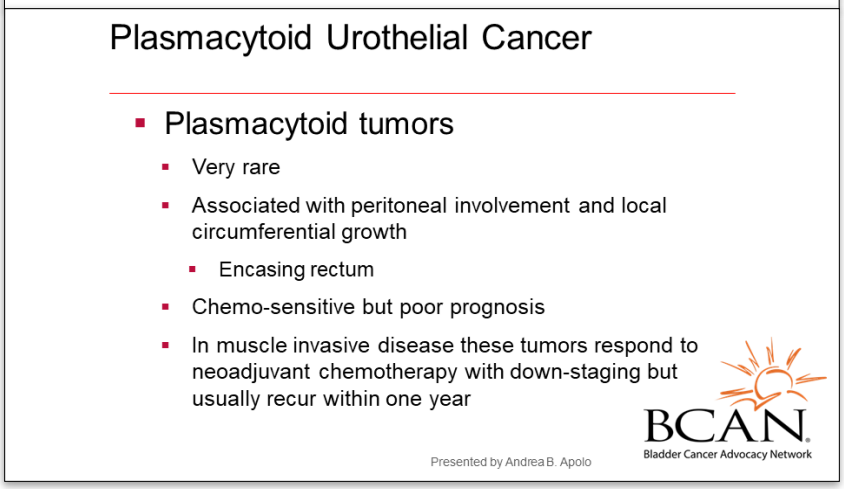
So, frequently these are high-grade, higher stage with lymphovascular invasion. And what that means is that if you look under the microscope at the tissue and you see little vessels. Those little vessels often have tumor in them. You can see the tumor cells inside the vessels. Either these could be either vascular or lymphatic vessels. And that's how the tumor travels. So these do have a higher rate of lymphovascular invasion or LVI. And therefore, they present with lymph node metastases, a diagnosis more commonly than urothelial carcinoma. And also, they present with distant metastases more commonly than regular urothelial carcinoma. So in terms of the treatment of non-muscle-invasive micropapillary tumors, the response to BCG is not very good. So, that needs to be taken into consideration. If this is a micropapillary non-muscle-invasive tumor, BCG will not work as well. They have a high rate of progression and also, a high rate of developing metastatic disease from non-muscle-invasive disease.



So, because of that, the treatment would be cystectomy instead of treating them with BCG. So, another rare variant is sarcomatoid carcinoma. These can be carcinoma and sarcoma, either and or. Really, really rare. They account for about .6% of bladder cancers. And there's different histologies. In order of frequency, there's osteosarcoma, there's chondrosarcoma, there's rhabdomyosarcoma, there's liposarcoma, angiosarcoma, and mix.

And the risk factors for developing sarcomatoid carcinoma is radiation therapy, intravesical cyclophosphamide. The mean age is 66 years of age. These are high stage and grade tumors, frequently have lymph node and distant metastases. They're very aggressive. They're more aggressive than standard urothelial carcinoma, even when adjusted for stage. And there really isn't a good way of treating them. They don't respond well to chemotherapy. Radiation is often incorporated into the treatment. Surgery can often be incorporated into treatment. But in patients that have these tumors, it's important to have a multimodal approach. And what that means is that the medical oncologist, the urologist, and radiation oncologist should discuss the case to see what the best treatment option is for a particular case.





Plasmacytoid urothelial carcinoma is very rare. And it is associated with peritoneal involvement, that's the abdominal cavity, and local circumferential growth. So they can encase, for example, the rectum. These tumors do respond to chemotherapy, but they come back. So like in muscle-invasive tumors, you give them chemo, they downstage, but then within a year, the cancer comes back metastatic. These are aggressive tumors.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