Clear Cell Sarcoma 101:
Things Patients and Clinicians Should Know

Clear cell sarcoma (CCS) is a rare tumor of soft tissue with a poor prognosis which affects mostly teens and young adults. The rarity of CCS impacts diagnosis and mis-diagnosis as most oncologists and even sarcoma specialists have never seen a patient presenting with CCS. CCS has two variations, the more common is found mainly in the extremities, often in feet or hands (although can be found almost anywhere) and the rarer version is CCS of the GI tract. When the first tumor is detected

Are there common symptoms?

CCS often shows up as a bump that was noticed over a long period of time which becomes painful, sometimes after a trauma to the area. Often, it is only after surgical intervention is attempted that the seriousness and complexity of the disease begins to become apparent.

How is CCS Diagnosed?

To definitively diagnose CCS, FISH testing, RT-PCR or sequencing is required to identify the presence of the fusion gene EWSR1-ATF1 (or less commonly EWSR1-CREB1). Immunohistochemical screening of tumors shows consistently positive S-100 protein, and variable or focal expression of CD57, bcl-2, HMB45, Melan A, microphthalmia transcription factor (MITF), synaptophysin, cytokeratin, CD34, c-erbB-2, c-kit, and c-met. The tumors are generally negative for alpha-smooth muscle actin, desmin, and cytokeratin. CCS is named for the presence of pale-staining or clear cells that grow in a nested or fascicular growth pattern in the tumor that in the more common variant (non-GI version) display phenotypic features similar to malignant melanoma (Melan-A, MITF, HMB-45), which can complicate diagnosis if EWSR1-ATF1, -CREB1 presence is not known.

What causes CCS?

The cause or causes of CCS are not clear. There is speculation that an early radiation exposure or agent orange exposure may be part of the etiology. A subsequent inflammatory cascade, perhaps due to a trauma, may create the environment for CCS to grow aggressively.

What are the treatments for CCS?

Currently the best option for treatment is surgical removal with clear margins. Even with a successful surgery, CCS will generally come back. Correct diagnosis made in a timely manner is very important for the best outcome for the patient. Treating CCS with chemotherapies designed for Ewing's Sarcoma or other sarcomas is not optimal for CCS. In fact, these treatments often lead to worse outcomes than surgery alone. Treatment options should be carefully discussed with the oncologist. Two clinical trials specific to CCS have been launched in 2020 (see clinicaltrials.gov).

Roadblocks patients may encounter

The correct diagnosis often takes two or more months, during which time doctors may be eager to start treatment. However, without an accurate diagnosis, mistakes may be made in choosing a treatment path. Currently there is no standard of care protocol for CCS and no way to track the disease (no ICD-10 code which insurance companies use for categorizing diseases and treatment options). In addition to that, patients are often not involved in choosing treatment options with their oncologist, and not given details why one treatment is chosen over another. Considering the rarity of CCS, patients and their caregivers have to be their own advocates, educating themselves about current knowledge of CCS and treatments options.

Are there resources for those diagnosed with CCS?

CCS is very rare and for this reason not much attention has been given to the disease or those diagnosed with it. Sara's Cure was started as a patient advocacy group for CCS and to push for and fund research to find treatments and ultimately a cure.

Sarascure.org