Clear Cell Sarcoma: A Literature Review
and Case Studies

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Abstract

Clear cell sarcoma (CCS) is a very rare soft tissue slow growing tumor with very poor prognosis that will start in lymph nodes and metastasize. CCS occurs most commonly in extremities of young adults, and rarely occurs in bone and the gastrointestinal tract. There are only 300 cases of CCS reported in the world and accounts for less than 1% of all soft tissue sarcomas. Once the tissue is correctly identified under a microscope then a treatment plan is put into place for the patient. Treatments vary from patient to patient, but can include anything from amputation, surgical excision, and chemotherapy.
**Introduction**

“Clear cell sarcoma (CCS) is a high-grade soft tissue sarcoma seen in adolescents and young adults, with melanosytic differentiation typically involving tendons and aponeuroses” (Rodriguez-Martin, Ortiz-Cruz, Del Rio, Vivanco, & Lopez-Amor, 2011, p.156). CCS is a very slow growing tumor that will establish in lymph nodes and metastasize to other lymph nodes, lungs, soft tissue, mainly in distal extremities, and rarely occurs in the bone. CCS appears as a large mass in the region of the affected area, swelling, redness, and tenderness will be present. CCS is named because of the presence of abundant amount of intracytoplasmic vesicles. Diagnosis for CCS is very difficult because it is so uncommon and every case is different. Therefore, treatment for CCS varies depending on the tumor itself.

**Literature Review**

When seeking to analyze CCS and its characteristics, many have examined it. The origin for CCS is most common in soft tissue extremities; foot and ankle being most frequent, and a slight female predominance. Not many cases have been reported because this type of sarcoma “accounts for less than 1% of malignant tumors in adults” (Ipach et al. 2012, p. 412). Cases for CCS have reported to be found in other tissues such as bone, kidney, colon, and gastrointestinal tract. Treatment for CCS is very challenging because each case is so different and no specific tumor markings are present.

**Clear Cell Sarcoma Symptoms**

In the beginning, CCS may not have any symptoms or direct pain of the site. Depending on the depth of the tumor will determine how noticeable the mass is. Usually the tumor is located in tissues and grows into a solid mass. The tumor might interfere with function of tendons and
organs as it grows and invades neighboring tissues. Over time, symptoms of more advanced cancer might develop, including fatigue, weight loss, and loss of appetite.

**Clear Cell Sarcoma Diagnosis**

After the tumor is located, a biopsy is performed to make a diagnosis. A biopsy will remove a piece of the tumor and will be examined under the microscope. Two different types of biopsies are useful; an open biopsy where a surgical incision is made to remove a sample or more preferable a core needle biopsy where a large needle is used to take a bigger sample. The core needle biopsy is preferred because it takes enough tissue to not only show the presence of cancer, but it can better help categorize it as CCS. After the biopsy is taken it will be examined under a microscope.

**Clear Cell Sarcoma Histology**

Sarcomas are very uniform in their appearances; CCS is identified by its histological patterns. After the tumor sample is taken, it is observed under a microscope by a pathologist. CCS has a close similarity to malignant melanoma which makes it difficult to correctly diagnose. According to Hersekli et al., (2005)

The gross appearance of clear cell sarcomas is usually that of a lobular and well-bordered or encapsulated lesion. The tumor cells are polygonal or spindle-shaped and have eosinophilic or clear cytoplasm. The nuclei have one or two large nucleoli. Some tumor cells may contain melanin pigment (p. 167). (See Figure 1)

CCS shows distinct features from other sarcomas because of the positive stain feedback from protein S-100 and antibody HMB-45.

**Clear Cell Sarcoma Medical Imaging**
Medical imaging plays an important role in CCS. Medical imaging helps track the patient’s tumor growth, metastases, and any other changes. CCS tumors are usually imaged by a Magnetic Resonance Imaging (MRI). MRIs are preferred because of the low dose for patients. MRIs are useful because they show the contrasting tissues compared to the tumor creating a grayscale image. CCS tumors can be further categorized by using an MRI contrast agent. Radiographs, Sonography, and Computed Tomography (CT) scans are also functional to check with metastases which are very common with CCS. Positron Emission Tomography (PET) scans also can be used to detect metastases in the body.

**Classification of Clear Cell Sarcoma**

The phase of CCS is determined by a combination of the histology of the tissue, how aggressive the cells appear, size of the tumor, location of the tumor, if metastases is present. All of these characteristics are put together to form a treatment plan by the oncologist.

**Clear Cell Sarcoma of the Kidney, Bone, and Gastrointestinal Tract**

**Kidney**

According to Franco, Dao, Lewis and Biddinger (2011) clear cell sarcoma of the kidney (CCSK) is a very rare and aggressive tumor found in pediatric patients, aged 6 months to 12 years. Franco et al., (2005) states “CCSK is a malignant mesenchymal neoplasm that includes undifferentiated cells, cords and nests separated by fibrovascular septa, and abundant extracellular matrix” (p.9). CCSK tumors start as a cyst like formation and arise from the medullary region of the kidney. Since CCSK is an aggressive cancer it will eventually metastasize. Sites for metastasizing include anywhere from the abdomen to unusual places such as the nasopharynx. The most efficient imaging modality to help evaluate CCSK is ultrasound.
CLEAR CELL SARCOMA

CT and MRI have little advantages with CCSK. CT is helpful when it comes to evaluating the actual size of the mass, but it also adds to the patient dose. MRI is chosen over CT if needed because of the lower dosage of CT. CCSK has no specific tumor markings which makes it difficult to diagnose. For the reason that CCSK is a fast growing tumor it makes up “4% of childhood renal tumors” (Franco et al., 2011, p.9). Pediatric patients with an abdominal mass, but have regular bowel movements, should be reevaluated for renal tumors.

**Bone**

“CCS, also known as malignant melanoma of soft tissue, is a very rare soft tissue neoplasm which comprises 1% of all musculoskeletal sarcomas” (Liu, Zahng, Dong, 2011, p.1). CCS primarily located in the bone is extremely rare; CCS usually starts in tendons and ligaments of attachment and then invade the bone. “Only six cases of primary clear cell sarcoma of the bone have been reported in English literature” (Yokoyama et al., 1996, Brekke et al., 1998, Ggczer et al., 1999, as cited in Liu, 2011, p.1). CCS of the bone can be seen on radiographs, but is best evaluated with CT or MRI.

**Gastrointestinal Tract**

Gastrointestinal (GI) CCS is a little different than CCS of the kidney, bone, and soft tissue. GI CCS doesn’t start with a growing mass or tenderness around the site. Signs and symptoms of GI CCS include “fever, weight loss, anorexia, abdominal pain, bloody stools, and anemia” (Lagmay, Ranalli, Arcila, & Baker, 2009, p. 215). “These tumors have many overlapping immunohistochemical and ultrastructural features with malignant melanoma (MM)” which make it very difficult to diagnose correctly (Lagmay et al., 2009, p.214). As of 2009, only 5 pediatric cases have been reported. Although most cases for GI CCS are adults, pediatric GI CCS works more aggressively.
Prognosis and Treatment Options

“The prognosis for patients with CCS is poor, and they have a high propensity for regional lymph node and distant metastases” (Rodriguez-Martin et al., 2011, p.158-159). Most patients with CCS receive total surgical resection of the mass as well as a small removal of the normal tissue surrounding the tumor to make sure that as much as the tumor is removed. Amputation, chemotherapy, and postoperative radiation therapy also could be included in the treatment plan.

Radiation therapy is often used after the removal of the tumor to reduce the chance of local reappearance. Sometimes radiation therapy is used before removal of the tumor to help shrink the size of the mass. Chemotherapy is used because it quickly kills the cancer cell and stops it from growing. This works nicely because CCS is a slow growing tumor and chemotherapy works so rapidly. The most promising treatment for CCS are targeted therapies; these are targeted specifically to fight features of CCS cancer cells.

CCS is more complicated when located in the kidneys. CCSK is resistant to conventional chemotherapy used to treat similar tumors. “Treatment [of CCSK] consists of nephrectomy and chemotherapy with current long-term survival rate of 60-70%” (Lowe et al., 2000, as cited in Franco, 2011, p.9).

Patients with CCS of the bone can be treated with amputation or limb salvage operation followed by chemotherapy. CCS of the bone is so rare, Liu et al. (2011) found that no specific chemotherapy medicine had been known to treat CCS, so an osteosarcoma treatment has been used on previous cases. “Survival rates and metastatic incidence of primary clear cell sarcoma of the bone are unknown because of the limited number of cases reported” (Liu et al., 2011, p.3).
Prognosis for CCS patients are fully based on the location, the stage of CCS, and the size. This information is useful when considering the appropriate treatment and follow-up procedures for the patients involved. Prognosis for CCS also varies because each disease is difficult to catch in the beginning and continues to spread after the initial diagnosis. The largest determining factor in patient prognosis is size of the tumor before surgery. As said by Jacobs, Chang, Guzman, and Salti (2004) tumors greater than 5 cm have a poorer prognosis and a higher frequency of local regrowth. Lucas et al., 1992 as cited in Jacobs et. al, 2004, states “the 5-, 10-, and 20-year survival has been reported as approximately 67 percent, 35 percent, and 10 percent” (p.302). Metastasis of CCS can occur during the first stage or dormant years after diagnosis. Unfortunately, when the sentinel node biopsy is positive, metastasis will appear within two years.

Case Studies

Clear Cell Sarcoma of the Kidney

In this case, Roy H., Mondal, Dey & Roy S. (2011) present a case involving clear cell sarcoma of the kidney (CCSK). A 2-year-old boy was having abdominal swelling but no history of weight loss or vomiting. When examined the abdomen was extended with a firm non-tender mass on the right lumbar region. The patient first received a chest x-ray, followed by an ultrasound and CT scan showing a mass arising from the right kidney. (See Figure 2) The patient underwent surgery to remove the right kidney. Radiation therapy and chemotherapy were given for treatment for 10 weeks following surgery.

Clear Cell Sarcoma in the Tendons

In this case, Rodriguez-Martin et al., (2011) present a case involving the first metatarsophalangeal joint. It is evaluated; a 42-year-old woman had a soft tissue mass around the first metatarsophalangeal joint present and was diagnosed with bursitis of the great toe. She was
treated with shoe insoles, therapy, and anti-inflammatory drugs, but the pain was not improving. A radiograph and MRI were ordered followed by a biopsy; results came back positive with CCS. (See Figure 3) A full body computed tomography was then ordered along with a detailed MRI to see if the CCS metastasized. The patient agreed to undergo amputation for her treatment. (See Figure 4) A splint was then placed for protection and help with immobilization. After 6 weeks the patient was able to bear full weight without crutches.

**Clear Cell Sarcoma of the Bone**

In this case study Liu et al., (2011) present a case involving CCS of the humerus. It is evaluated with medical imaging. A 20-year-old female was admitted with palpable, tender, and swollen firm mass occurring in the proximal right humerus. A radiographic image presented a defect in the proximal humerus, magnetic resonance imaging illustrated an irregular shaped mass, and a computed tomography guided biopsy was performed. (See Figure 5) The patient then received a CT guided biopsy. After the tumor was diagnosed the patient underwent a total tumor excision-alcohololization-replantation (EAR). The EAR comprised of sawing the humerus in half where the proximal tumor end underwent a biopsy. The humerus medullary canal was then scraped to free the bone of the cancer cells, followed by soaking the bone in 95% ethanol to destroy any remaining cells. The patient received a limited contact dynamic compressive plate in her arm to stabilize the bone. (See Figure 6) After the operation, the patient underwent chemotherapy for two years.

**Clear Cell Sarcoma of the Stomach**

Lagmay et al., (2009) presents a case study involving a 10-year-old female. This patient had a history of fatigue, bloody stool, fevers, vomiting, and weight loss. Numerous tests she received on stool occult blood, testing for colon cancer, came back negative. An abdominal CT
scan revealed a tumor extending from the posterior wall of the stomach and enlarged lymph nodes. (See Figure 7) A partial gastrectomy and resection of the liver and lymph nodes was performed. At the time of this report, this patient completed a total of seven cycles of the same chemotherapy and radiation therapy and remains in remission.

**Clear Cell Sarcoma of Soft Tissue**

This case study presents CCS of soft tissue in the right leg of a 45-year-old male. Approximately 10 years ago he had his family doctor look at a lump on the back of his right leg. His doctor thought it was a lipoma and when he went to remove it in his office, found blood vessels running through it and said it wasn't what he thought it was. About 5 years ago this patient visited a vascular institute for a free vascular screening since his doctor had said the mass was full of vessels, at this time the mass was a little smaller than a ping pong ball. He was then told that the lump was a varicose vein. In March of 2012, while at a yearly checkup with a new family doctor, his doctor looked at it, and assuming that it was a varicose vein, told the patient to let him know when he was ready to take care of it, and he would send a referral for him to see a general surgeon. From March to July the mass almost tripled in size; this patient was experiencing swelling and pain in his foot and leg below the mass. (See Figure 8) On Aug 21st, 2012 the general surgeon sent him to see a radiologist for an ultrasound of the mass. The radiologist looked at it, and determined that it did not involve the muscle of his leg and ordered an MRI and a chest X-ray. (See Figure 9) Two days later, on August 23rd, 2012 the patient was informed that the mass was a tumor. The general surgeon referred this patient to a cancer institute. Before a biopsy was completed a chest x-ray was ordered with results showing small masses in his lungs. The patient received surgery on September 26th, 2012 to remove the remainder of the tumor and its margins. The surgeons took skin from his thigh and grafted it to
the site of the tumor removal. (See Figure 10) The remainder of the tumor was tested to verify CCS. Post operation he received a PET scan the results showed the masses in his lungs are also cancer, and have grown. He will be meeting with a chemotherapy doctor at the cancer institute in the near future to set up a chemotherapy treatment plan.

**Discussion**

Franz M. Enzinger first discovered clear cell sarcoma in 1965. CCS is mainly found in children and young adults, but in rare instances it can affect anyone above the age of 40. Some reports have found that CCS is more dominant in females and in the Caucasian race. The most common sites of this sarcoma are the extremities, favoring the foot and ankle region. Effective management of clear cell sarcoma is correctly identifying the histological features. Once it is identified as CCS the patient’s treatment plan is put into place. Duration of symptoms the patient shows is not very helpful just because CCS is a varying slow growing tumor; the main indicator for diagnosis is the size of the tumor. Medical imaging plays an important role in the diagnosis for CCS.
Figures

**Figure 1.** Microscope graph shows the histology of CCS and the positive stain from S-100.


![Microscope Graph](image1)

**Figure 2.** CT of kidney with right renal mass present.


![CT Scan](image2)

**Figure 3.** Radiograph shows a soft tissue mass by the first metatarsophalangeal joint.

Figure 4. Postoperative radiograph taken of amputated foot.

Figure 5. Radiograph of proximal humerus of a 20-year-old female shows a destructive lesion of the right proximal humerus. The MRI shows the irregular shaped mass growing around the proximal humerus.
Note. The following images were taken from “Primary clear cell sarcoma of humerus: Case report,” by X. Liu, H. Zhang, & Y. Dong 2011. World Journal of Surgical Oncology, 9(163), p. 2-3. Copyright 2011 by World Journal of Surgical Oncology

**Figure 6.** The patient received a limited contact dynamic compressive plate in her arm to stabilize the bone after the medially canal was scraped free of CCS cells.
**Figure 7.** An abdominal CT scan revealing a tumor extending from the posterior wall of the stomach and enlarged lymph nodes.


![Abdominal CT scan](image)

**Figure 8.** Lateral view of right leg presenting a mass on dorsal side of leg below knee.

Note. The following images were used by permission from the patient in a personal interview, November 2012.

![Lateral view of right leg](image)
Figure 9. MR image shows mass located on medial side of right leg not attached to the muscle.

Figure 10. Image of right leg after surgery including the area of the skin graft and three months after surgery.
References


