Cancer Association of South Africa (CANSA)

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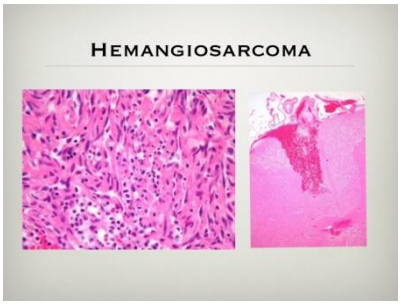
Fact Sheet on Haemangiosarcoma

Introduction

Cancerous (malignant) tumours of the connective tissues are called "sarcomas". Sarcoma arises in the connective tissue of the body. Normal connective tissue include, fat, blood vessels, nerves, bones, muscles, deep skin tissues, and cartilage.



[Picture Credit: Hemangiosarcoma]

Sarcomas are divided into two main groups, bone sarcomas and soft tissue sarcomas. They are further sub-classified based on the type of presumed cell of origin found in the tumour. They all share certain microscopic characteristics and have similar symptoms.

Sarcomas can develop in children and adults. For children under 20 approximately 15 percent of cancer diagnosis are sarcomas. The majority of childhood sarcomas are one of three types. Although they are often called *Paediatric Sarcoma* because of their prevalence in children, they can occur in adults as well. As these cancers are relatively common among childhood cancers, there are relatively standard treatments.

Adolescents and young adults (AYA) with paediatric sarcoma face more than the usual challenge from cancer. In cancer treatment, *adolescents and young adults* are people between age 15 and 39. One of the challenges is that it is studied less than sarcoma in children and older adults. But the major challenge for youth with sarcoma is how to get the best treatment.

Haemangiosarcoma

Haemangiosarcoma is a very aggressive, rapidly growing form of cancer that affects the blood vessels. It is also known as angiosarcoma. It can form anywhere in the body, but more than half of the cases originate in the spleen; this condition is also known as "splenic angiosarcoma." This form of cancer can develop in patients of any age, but mainly affects those over 50 years of age.

Haemangiosarcoma of the spleen is a rare tumour. However, it is the most common malignant, primary, non-lymphoid tumour of the spleen. It usually presents itself as a well-defined haemorrhagic nodule, or it involves the spleen diffusely. Clinical symptoms usually are diffuse

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abdominal pain and left upper quadrant mass. Associated clinical findings are anaemia, thrombocytopenia, and coagulopathy. Haemolytic anaemia is caused by damage to erythrocytes from irregularly lined vascular channels in the tumour. The prognosis is poor. Metastases are usually to the liver, lung, and lymph nodes. Survival is usually less than 1 year.

Spiker, S.M., Mangla, A. & Ramsey, M.L. 2021.
"Angiosarcoma (AS) comprises 1% of all soft-tissue sarcoma (STS), which are themselves a rare malignancy. They arise from lymphatic or vascular endothelial cells and are 'high-grade' by definition, which demonstrates their aggressive behavior. Although AS can occur in any part of the body, it most commonly presents as a cutaneous disease in elderly white men or on the chest wall after receiving radiation therapy (RT) for breast cancer. The treatment is very challenging, and the prognosis is poor, especially if AS is diagnosed in the metastatic stage. The best approach to patients with AS is offered in a multidisciplinary tumor board setting. Like any other STS, surgical resection with a negative margin affords the best outcomes in terms of overall survival. Combining radiation therapy (RT) with weekly paclitaxel has been demonstrated to bear durable responses for cutaneous angiosarcoma. Doxorubicin and paclitaxel are recommended regimens for advanced or metastatic disease. Due to the increased vascularity of AS, targeted therapy against vascular endothelial growth factor (VEGF) has gained traction, however, yet remains to be proven in a prospective study."

Incidence of Haemangiosarcoma in South Africa
The National Cancer Registry (2017) does not provide information regarding the incidence of Haemangiosarcoma in South Africa.

Diagnosis of Haemangiosarcoma
Utilising anti-p53 antibody (Ab) levels has been found to be higher in patients with haemangiosarcoma.

Kiyohara, M., Aoi, J., Kajihara, I., Otuka, S., Kadomatsu, T., Fukushima, S. &, Ihn, H. 2020.
"There is no biomarker for detecting the status of angiosarcoma patients. Studies have reported that serum anti-p53 antibody (Ab) levels are often high in patients with various types of malignant tumors, suggesting the potential use of this Ab as a biomarker for various tumors, including angiosarcoma. The aim of this study was to assess the usefulness of serum anti-p53 Ab as a potent angiosarcoma biomarker. Nineteen angiosarcoma patients were included. All patients had histologically been diagnosed with cutaneous angiosarcoma. We compared p53 protein expression and serum p53 Ab levels between angiosarcoma in the scalp patients (n = 19) and normal controls (n = 30). We evaluated Ab levels before and after therapy. Increased p53 expression was detected in angiosarcoma skin tissues compared with that observed in normal skin tissues. We evaluated serum from angiosarcoma patients and controls for the presence of the anti-p53 Ab. Serum anti-p53 Ab levels were significantly higher in angiosarcoma patients than in controls. Serum anti-p53 Ab levels of patients who showed disease progression after therapy increased in correlation with the medical condition. The Ab levels of three patients, who showed partial response after therapy, decreased in correlation with the medical condition. The Ab levels of the other three patients were low at all time points. Anti-p53 Ab levels were significantly higher in angiosarcoma patients than in the controls. We demonstrated that serum anti-p53 Ab levels would reflect the clinical course of angiosarcoma

patients, suggesting that serum anti-p53 Ab can be a potent diagnostic and prognostic biomarker of angiosarcoma."

Causes, Symptoms and Treatment of Haemangiosarcoma

Long-term exposure to certain environmental hazards and chemicals, including arsenic, vinyl chloride, and thorium dioxide, has been linked to a number of cases of haemangiosarcoma. Patients who have been exposed to these types of chemicals - often used in certain types of industry - are at particular risk for developing this form of cancer.

Symptoms are often mistaken for those of other conditions, which can make rapid diagnosis and treatment very difficult. Distinctive symptoms typically include abdominal pain or splenomegaly (an enlargement of the spleen).

Patients with this condition also run a high risk of splenic rupture, which can result in severe blood loss and often death. This condition develops in the spleen and will often spread to the lungs and/or liver.The highly aggressive nature of this form of cancer, and lack of symptoms until it has progressed fairly significantly, makes it very difficult to treat. A physician will usually conduct a thorough physical exam, followed by scans that might include a CT or CAT, MRI, or X-rays.

These scans can help to determine the size and precise location of the mass; an MRI can provide a more detailed image of the tumour that can help to determine the progression of the condition. The size, location, and stage of the tumour will then determine the best course of treatment.

A combination of chemotherapy and a splenectomy, surgery to remove the tumour on the spleen, have been the most successful. A splenectomy itself can give the patient a survival time of 1-3 months; the addition of chemotherapy can extend the survival rate to 5-7 months.

Heinhuis, K.M., IJzerman, N.S., van der Graaf, W.T.A., Kerst, J.M., Schrage, Y., Beijnen, J.H., Steeghs, N., van Houdt, W.J. 2020.

"Angiosarcoma is an extremely rare and aggressive malignancy. Standard of care of localized tumors includes surgery ± radiation. Despite this multimodal treatment, >50% of the angiosarcoma patients develop local or distant recurrent disease. The role of neoadjuvant systemic therapy is still controversial and we therefore performed a systematic review of the literature to define the role of neoadjuvant systemic therapy based on available evidence. We focused on the effects of neoadjuvant systemic therapy on: 1. The success of surgical resection and 2. the long-term survival. All articles published before October 2019 on Ovid Medline, Ovid Embase, Cochrane library and Scopus were evaluated. Eighteen case reports and six retrospective cohort studies were included. There were no randomized controlled trials. This literature showed a beneficial role of neoadjuvant chemotherapy on downsizing of the tumor resulting in an improvement of the resection margins, especially in patients with cardiac or cutaneous angiosarcoma. However, no definitive conclusions on survival can be drawn based on the available literature lacking any prospective randomized studies in this setting. We advise that neoadjuvant chemotherapy should be considered, since this could lead to less mutilating resections and a higher rate of free resection margins. An international angiosarcoma registry could help to develop guidelines for this rare disease."

Chan, J.Y., Lim, J.Q., Yeong, J., Ravi, V., Guan, P., Boot, A., Tay, T.K.Y., Selvarajan, S., Md Nasir, N.D., Loh, J.H., Ong, C.K., Huang, D., Tan, J., Li, Z., Ng, C.C., Tan, T.T., Masuzawa, M., Sung, K.W., Farid, M., Quek, R.H.H., Tan, N.C., Teo, M.C.C., Rozen, S.G., Tan, P., Futreal, A., The, B.T. & Soo, K.C. 2020.

"Angiosarcomas are rare, clinically aggressive tumors with limited treatment options and a dismal prognosis. We analyzed angiosarcomas from 68 patients, integrating information from multiomic sequencing, NanoString immuno-oncology profiling, and multiplex immunohistochemistry and immunofluorescence for tumor-infiltrating immune cells. Through whole-genome sequencing (n = 18), 50% of the cutaneous head and neck angiosarcomas exhibited higher tumor mutation burden (TMB) and UV mutational signatures; others were mutationally quiet and non-UV driven. NanoString profiling revealed 3 distinct patient clusters represented by lack (clusters 1 and 2) or enrichment (cluster 3) of immune-related signaling and immune cells. Neutrophils (CD15+), macrophages (CD68+), cytotoxic T cells (CD8+), Tregs (FOXP3+), and PD-L1+ cells were enriched in cluster 3 relative to clusters 2 and 1. Likewise, tumor inflammation signature (TIS) scores were highest in cluster 3 (7.54 vs. 6.71 vs. 5.75, respectively; $P < 0.0001$). Head and neck angiosarcomas were predominant in clusters 1 and 3, providing the rationale for checkpoint immunotherapy, especially in the latter subgroup with both high TMB and TIS scores. Cluster 2 was enriched for secondary angiosarcomas and exhibited higher expression of DNMT1, BRD3/4, MYC, HRAS, and PDGFRB, in keeping with the upregulation of epigenetic and oncogenic signaling pathways amenable to targeted therapies. Molecular and immunological dissection of angiosarcomas may provide insights into opportunities for precision medicine."

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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