Dr. Mitsuyasu has been doing clinical research in patients with AIDS-related Kaposi’s sarcoma (KS) since the beginning of the AIDS epidemic, and his review reflects this breadth of experience. It provides a well-rounded and up-to-date assessment of the pathophysiology, evaluation, and treatment of AIDS-related KS that should be a useful guide for practicing physicians.

While research in this area proceeded relatively slowly during the first decade of the AIDS epidemic, the last several years have seen substantial advances. As Dr. Mitsuyasu notes, analysis of the role of cytokines and angiogenic factors in the development of KS, general advances in the field of angiogenesis, and the discovery of a new herpesvirus called Kaposi’s sarcoma-associated herpesvirus (KSHV) or human herpesvirus-8 (HHV-8), have led to a marked increase in our understanding of the pathogenesis of KS. In addition, several effective new drugs for KS have entered clinical practice in the past few years, and new approaches based on an understanding of the pathogenesis of this tumor are being developed.

Pathophysiology of Kaposi’s Sarcoma

With regard to the pathophysiology of KS, it is worth highlighting and expanding on certain points made in Dr. Mitsuyasu’s article. First of all, it appears that KSHV/HHV-8 is an essential factor in the development of KS, but not all patients infected with KSHV/HHV-8 develop KS. The best available evidence indicates that virtually all KS patients are infected with KSHV/HHV-8. In addition, populations with a high incidence of KS also have a high incidence of KSHV/HHV-8 infection, and infection with KSHV/HHV-8 precedes the development of KS.[1,2]

However, as noted in the Mitsuyasu article, patients coinfected with KSHV/HHV-8 and HIV have a much higher incidence of KS than those without HIV infection. Thus, HIV plays an important role in the development of KS. Several mechanisms may contribute to this effect, including HIV-induced immunodeficiency, activation of KSHV/HHV-8 by HIV or HIV-encoded Tat protein, and HIV-induced cytokine production.[3,4]

It is not surprising that the incidence of KS has decreased in cohorts of patients receiving highly active antiretroviral therapy (HAART), and there are reports of KS tumors shrinking in patients who have been started on HAART. However, our experience is that KS lesions in many patients, particularly those with more advanced disease, do not respond to HAART. Also, it is not unusual to see KS progress in patients when they develop resistance to anti-HIV therapy. We echo the sentiment made in Dr. Mitsuyasu’s article that the incidence of AIDS-associated KS may well increase over the next several years as resistance to anti-HIV drugs increases, and we should not be lulled into a false sense of security.

Kaposi’s sarcoma is even more common in other parts of the world such as sub-Saharan Africa. In a cancer registry in Uganda, for example, KS represented more than 50% of all tumors in adult males.[5] It is worth noting that KSHV/HHV-8 is not only an etiologic agent for KS, but also for multicentric Castleman’s disease and primary effusion lymphoma.[6] Physicians caring for KS patients should be alert for these diseases as well. In particular, KS patients who develop pleural or peritoneal effusions should be examined for primary effusion lymphoma.

Treatment of Kaposi’s Sarcoma

The review gives a well-rounded summary of the principal therapies used to treat KS. In this area too, there has been substantial progress in the past 5 years, and the two principal chemotherapeutic agents used to treat advanced disease—liposomal anthracyclines and the taxanes—were developed.
for use in KS during this period.
One of the principal decisions facing the practitioner treating KS is whether to use local or systemic therapy. As Mitsuyasu notes, patients with pulmonary or other visceral disease or with extensive pulmonary disease generally require systemic therapy. Also, cytotoxic chemotherapy is warranted in patients with extensive cutaneous disease. However, it is difficult to give precise criteria in the latter group of patients, and experience with treating KS is useful in making an optimal decision about therapy.

Certain local therapies including cryotherapy and topical alitretinoin (Panretin) can result in hypopigmentation around the lesions, and some patients who receive local treatment of multiple lesions may, in fact, respond better to systemic therapy. One point worth stressing is that systemic steroids can cause rapid exacerbation of KS, and we have seen rapid growth of KS in a patient being treated for simultaneous AIDS lymphoma with a prednisone-containing combination regimen. For this reason, we utilize a reduced dose of dexamethasone when premedicating KS patients with paclitaxel (Taxol).[7]

**New Directions**
Finally, a number of exciting approaches are now being explored for possible use in KS. It is worth highlighting the effort to develop novel antiangiogenic agents. Kaposi’s sarcoma lesions are highly vascular, in part because KSHV/HHV-8 contains several viral mimics of cytokines and proangiogenic factors, including viral interleukin-6 and viral macrophage inflammatory proteins (vMIP1 and vMIP2).[8] Kaposi’s sarcoma is, therefore, an interesting tumor in which to test antiangiogenic approaches.

In addition to the compounds mentioned in the Mitsuyasu article, there is preliminary evidence that interleukin-12 has activity in KS.[9] Studies of other antiangiogenic compounds, including Col-3 and EMD 121974, are either underway or being planned. There is an explosion of research in this area, and it is quite likely that this will translate into better therapies in the near future.

**Conclusions**
While the incidence of KS has decreased somewhat, it continues to be the most common tumor in AIDS patients, and there remain many patients coinfected with HIV and KSHV/HHV-8 who are at high risk for developing KS. As described in the Mitsuyasu article, a number of effective local therapies are available and several cytotoxic chemotherapeutic agents have recently been developed. However, none of these are curative, and in most cases, therapy has to be administered for long periods.

Research is underway to develop new agents for advanced KS that are based on an understanding of its pathogenesis and that may be less toxic than the chemotherapeutic drugs presently available.

**References:**


Source URL:
http://www.cancernetwork.com/review-article/aids-related-kaposi%E2%80%99s-sarcoma-current-treatment-options-future-trends-0

Links:
[1] http://www.cancernetwork.com/review-article
[4] http://www.cancernetwork.com/authors/robert-yarchoan-md