commonly seen in young patients (32%-77% of patients were younger than 20 years of age in a large series [4]) and is more commonly described in individuals of Asian ethnicity. Aneurysm formation occurs in 15%-30% of patients with TA, particularly children [4]. The cause of TA is unknown, although an autoimmune process has been postulated. There were early reports of Mycobacterium tuberculosis infection in association with TA in areas where tuberculosis is highly endemic, but a direct causal relationship has not been demonstrated [5]. No cases of concurrent TA and HIV infection were found in a review of the world literature despite these diseases having similar geographic distributions and age incidences in Asia. No direct causal relationship could be demonstrated between HIV infection, suspected tuberculous infection, and large vessel arteritis in this case, and the patient’s ethnicity and geographic location may make this a chance occurrence. However, the possible autoimmune nature of TA and the observed frequency of autoimmune phenomena in HIV infection should make this combination more likely, especially in children.

We propose that large vessel arteritides such as TA should be considered in HIV-infected individuals, including children, who present with persistent fever when an initial workup has been nondiagnostic.

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![Figure 1. Initial mean mean corpuscular volumes (MCVs) before initiation of stavudine treatment for HIV-infected patients](image1.png)

Stavudine-Induced Macrocytosis During Therapy for Human Immunodeficiency Virus Infection

Nucleoside analogue reverse transcriptase inhibitors are important components of most treatment regimens for HIV infection. Three of these agents (zidovudine, zalcitabine, and didanosine) have been known to cause leukopenia, anemia, and/or thrombocytopenia. Zidovudine has been associated most frequently with dose-related bone marrow toxicity manifested as macrocytic anemia. Stavudine and lamivudine have not been reported to cause hematologic toxicity at currently recommended doses [1, 2].

We noted that as patients’ treatments were switched from zidovudine- to stavudine-containing regimens, there was minimal or no decrease in macrocytosis, while there was a rapid return to baseline mean corpuscular volumes (MCVs) in patients receiving non-stavudine-containing regimens. Zidovudine-naive patients who began stavudine treatment were noted to have increases in MCVs similar to those in patients taking zidovudine therapy. Some of the MCVs were remarkable enough (>110 fL) to prompt investigation of vitamin B12 and folate levels (which were normal in all seven patients tested). Although phase I studies revealed that anemia and macrocytosis occurred in patients receiving dosages higher than those currently used, stavudine at currently recommended dosages has not been reported in the literature (or the package insert) to cause hematologic abnormalities [3].

We retrospectively reviewed the charts of 122 patients whose treatment regimens included stavudine. Thirty-one patients (10, 10.3 to 29.3 fL; P < .05) were stavudine therapy for <3 months; 10, poorly documented or changing treatment regimens; 7, documented noncompliance; and 4, lost to follow-up) were excluded from the study. Of the 91 remaining patients, none had a known history of alcohol abuse or malabsorption syndromes.

The results of the chart review are shown in figure 1. Macrocytosis was observed in 89% of patients as defined by an MCV of >95.0 fL and in 73% as defined by an MCV of >100.0 fL. The mean MCV at initiation of stavudine treatment was 96.3 fL (range, 78.9–118.8 fL). The mean MCV at least 3 months after initiation of stavudine treatment was 104.6 fL (range, 79.0–122.1 fL). The mean increase in MCV was 9.3 fL (range, −10.3 to 29.3 fL; P < .05).

Fifty-three percent of patients were zidovudine naive before initiation of stavudine treatment. These patients had a mean MCV of 89.5 fL (range, 78.9–99.5 fL) at initiation of therapy and a mean increase in MCV of 13.9 fL (range, 0.1–29.4 fL; P < .05) at least 3 months after initiation of stavudine treatment.
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Forty-seven percent of patients had previously received zidovudine treatment before stavudine therapy was initiated. These patients had a mean MCV of 103.9 fl (range, 81.3–118.8 fl) at initiation of therapy and a statistically insignificant mean increase in MCV of 2.2 fl (range, 10.3–20.2 fl; P = .11) at least 3 months after stavudine was substituted.

Stavudine was used in conjunction with lamivudine therapy for 79 (87%) of the patients. Of 12 patients taking stavudine without lamivudine therapy, 10 (83%) had an MCV of >95.0 fl and five (42%) had an MCV of >100.0 fl. Lamivudine monotherapy (as used in phase 2/3 trials) is uncommonly associated with macrocytosis (only at doses at least twice as high as those currently administered).

Macrocytosis induced by zidovudine is often associated with anemia. Anemia has not typically been associated with stavudine therapy. In our patients, there was actually a small, but statistically significant, increase in hemoglobin levels with stavudine therapy. This increase was accentuated in patients whose treatment was switched from zidovudine who had an initial hemoglobin concentration of <12 g/dL. The mean baseline hemoglobin level for all 91 patients was 13.4 g/dL (range, 8.4–17.2 g/dL), and the mean hemoglobin level after at least 3 months of stavudine treatment was 14.2 g/dL (range, 10.1–17.1 g/dL; P < .05). For those patients for whom stavudine was substituted for zidovudine treatment, the mean baseline hemoglobin level was 12.9 g/dL (range, 5.5–17.2 g/dL), and the mean hemoglobin concentration after at least 3 months of therapy was 14.1 g/dL (range, 11.7–17.1 g/dL; P < .05).

As treatment of HIV infection has evolved, ever more complex regimens with five or more drugs in combination are being used. There have been limited clinical trials of many of the drugs before widespread use, and toxicities are discovered only after significant use outside of these trials. Unexplained macrocytosis in an HIV-infected patient receiving combination therapy may lead to an extensive workup for bone marrow or gastrointestinal disease. Alternately, macrocytosis may be attributed to a new agent as a yet undescribed toxic effect. Fortunately, macrocytosis associated with stavudine, at the currently recommended doses, is not associated with anemia.

We conclude that the finding of isolated macrocytosis, without anemia, in a patient being treated with stavudine may be due primarily to stavudine itself and may not warrant further evaluation.

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References

Refractory Craniofacial Actinomycetoma Due to *Streptomyces somaliensis* That Required Salvage Therapy with Amikacin and Imipenem

Mycetoma is a chronic skin infection that can be caused by aerobic actinomycetes (actinomycetoma) and fungi (eumycetoma). Most mycetomas involve the legs and feet, and only few cases of craniofacial mycetoma have been reported. Mycetoma results from inoculation of the microorganism through a minor injury caused by a thorn or infection of an existing lesion. We report a case of mycetoma of the face and skull due to *Streptomyces somaliensis* resistant to co-trimoxazole clinically and in vitro.

A 27-year-old Mauritanian female had a 10-year history of craniofacial mycetoma. Initially, specific therapy with isoniazid, rifampin, and pyrazinamide was started for presumptive cutaneous tuberculosis. The skin lesions had evolved into firm nodules and abscesses. In 1995, biopsy was carried out, and histological examination (performed by Dr. M. Huere, Institut Pasteur, Paris) confirmed that the granulomatous lesions were due to *S. somalien-