Letters to the editor

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Physical examination revealed numerous subcutaneous tumors on the upper limbs and, to a lesser extent, on the trunk and lower limbs. These were clearly circumscribed, firm, and, in some instances, painful to the touch (Figure 1).

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Angiolipomas and Antiretroviral Therapy

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fibrin thrombi (Figure 2). Angiolipoma was diagnosed.

Blood tests revealed hyperlipidemia and elevated transaminase levels, and imaging studies (computed tomography scan of the chest and abdomen and abdominal ultrasound) revealed hepatic steatosis, with no other alterations in visceral fat deposits. Immunological findings were acceptable (550 CD4+ cells/µL), and the viral load was undetectable. The patient has remained stable since then, hence, no changes in antiretroviral treatment were considered necessary.

Use of protease inhibitors has been associated with abnormalities in the distribution of fatty tissue, producing morphological changes (central adiposity, peripheral lipoatrophy, mammary hypertrophy) and abnormal blood test results (hyperlipidemia, hyperinsulinemia). The proposed mechanism of action involves inhibition of cytochrome P450 3A in peripheral adipocytes, interfering with the metabolism of retinoic acid and producing abnormalities in apoptosis and adipocyte differentiation.

Angiolipomas are benign adipose neoplasias that are differentiated from lipomas clinically by their greater sensitivity, histologically by their greater vascular component, and cytogenetically by the absence of karyotype abnormalities.

Few similar cases have been reported since the first descriptions, although the condition is probably underdiagnosed. At least 4 patients are known to have developed multiple angiolipomas while being treated with protease inhibitors before the present case. All of the cases reported to date were in middle-aged men, except for the patient described by Daudén et al. Lesions mainly appeared on the upper limbs—just as in idiopathic angiolipomas—but they have also been observed on the lower limbs and trunk. In 2 of the cases described, previous lesions were present, but these increased in number and size when antiretroviral treatment began. The drug implicated in 4 of the cases, including our own, was indinavir; while in the other patient it was saquinavir.

The mechanism responsible for producing these benign tumors is considered similar to that implicated in lipodystrophy syndrome, which has a similar latency period of between 3 months and 1 year. However, 2 of the cases reported did not present abnormalities in the distribution of fatty tissue, suggesting that other factors may be implicated in the pathogenesis. In most studies, a greater prevalence of lipodystrophy associated with protease inhibitors was seen in women, whereas angiolipomas—both associated with protease inhibitors and idiopathic—are more frequent in men. Also, in 1984, 7 homosexual men were described with multiple angiolipomas but who had no known HIV infection and were not undergoing antiretroviral treatment. These observations suggest that infectious agents and genetic factors (sex, individual predisposition, familial traits) could be implicated in the development of these tumors. Up until now, the known cases have been found in the early stages of HIV disease and were patients responding favorably to antiretroviral therapy, suggesting that serious immunosuppression is not a predisposing factor.

In previously reported patients, and in the case described here, antiretroviral drugs other than protease inhibitors were used, including nucleoside reverse transcriptase inhibitors. However, these drugs have not been linked to the development of adipose tissue tumors, despite their capacity to produce lipodystrophy.

Although the development of angiolipomas has been known to be halted by substituting one protease inhibitor for another, changes to the antiretroviral treatment of these patients are not generally considered justified. Furthermore, it is worth noting that in the present case the angiolipomas continued to appear after indinavir was substituted by another protease inhibitor, nelfinavir.
References