

LACTIC ACIDOSIS COMPLICATING METFORMIN AND NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITOR COMBINATION THERAPY: A SMOLDERING THREAT IN THE POST-HAART ERA

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Dear Editor,

The prevalence of type 2 diabetes (DM-2) in HIV-infected patients and the concomitant use of metformin (MTF) and non-nucleoside reverse transcriptase inhibitors (NRTI) is rising. Through inhibition of NADH dehydrogenase and DNA pol- γ , both drugs hinder oxidative phosphorylation that may lead to lactic acidosis (LA)¹. Among NRTIs, abacavir and tenofovir have the lowest mitochondrial toxicity, with only a few LA cases reported²⁻⁴. We describe here a case of MTF-associated LA (MALA) secondary to the interaction with NRTI.

A 28-year-old man with DM-2 and HIV infection presented in the emergency room with headache, blurred vision, fever, and abdominal pain. He was on MTF (2,550 mg/day), NPH insulin (40 IU/day), abacavir (600 mg/day), tenofovir (300 mg/day), and lopinavir/ritonavir (800/200 mg/day). His vitals were normal and laboratory showed pH 7.38 (nl, 7.35-7.45),

HCO₃⁻ 22 mmol/l (nl, 22.2-28.3), and lactate levels of 5.3 mmol/l (nl, 0.5-1.6). Central nervous system infections were ruled out, and he was discharged after resolution of the hyperlactatemia. However, when MTF was reinitiated, he relapsed. Arterial blood gases showed pH 7.33, HCO₃⁻ 14 mmol/l, lactate levels of 9.5 mmol/l (0.5-1.6), and anion gap 18 mmol/l. Fundoscopy showed subretinal hemorrhages (Fig. 1) and uveitis was ruled out as a cause of this abnormality. MALA was suspected and MTF was withdrawn with a favorable outcome, including the subretinal hemorrhages.

Since MALA risk factors were absent and LA relapsed on rechallenge with MTF, this case suggests interaction of this drug with NRTIs. As fundoscopy had not been previously performed in this patient and uveitis was ruled out, subretinal hemorrhages may represent a new physical finding of MALA. In conclusion, LA must be continuously monitored in every patient receiving both MTF and NRTIs.

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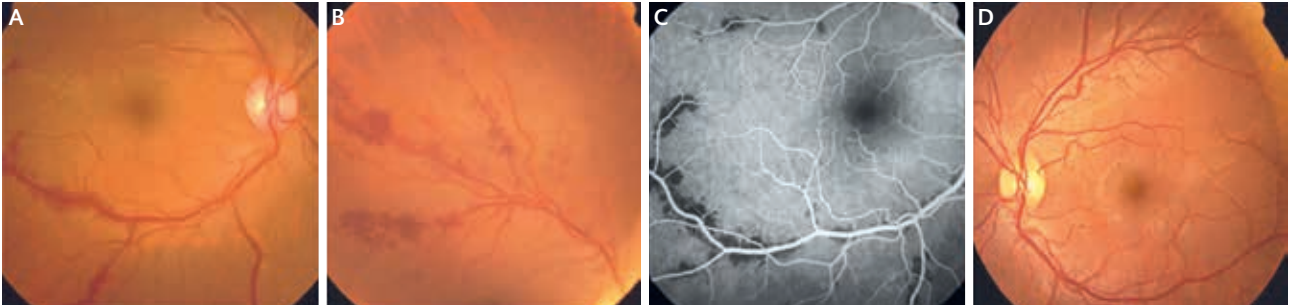
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Figure 1. Fundoscopy (A, B and D) and fluorangiography (C) showing digitiform subretinal hemorrhages and hypofluorescent areas parallel to vascular pathways (A, B and C). D: Follow-up fundoscopy showing hemorrhage resolution.



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