In utero exposures due to smoking during pregnancy may increase the risk of both diabetes and obesity through programming, resulting in lifelong metabolic dysregulation, possibly due to fetal malnutrition or toxicity. The odds ratios for obesity without type 2 diabetes are more modest than those for diabetes and the scope for confounding may be greater. Smoking during pregnancy may represent another important determinant of metabolic dysregulation and type 2 diabetes in offspring. Smoking during pregnancy should always be strongly discouraged.

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Drug points

Ticlopidine associated with acute arthritis

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Ticlopidine is an antiplatelet thienopyridine drug that works by non-competitive antagonism of the ADP receptor. It is used widely to prevent thrombosis after coronary stent placement and has been shown to be at least as effective as aspirin in preventing events in patients with cerebrovascular disease.[1 2] Its most common side effects include diarrhoea, nausea, vomiting, and skin rash.[3] It also has serious—but rare—side effects such as neutropenia, thrombotic thrombocytopenic purpura, and bone marrow aplasia.[3] We report a case of acute arthritis associated with ticlopidine.

A 65 year old woman was admitted to hospital because of chest pain. She was known to be taking insulin for diabetes and had developed non-Q wave myocardial infarction. She was also hyperlipidaemic. Cardiac catheterisation showed two vessel coronary artery disease, for which she had successful angioplasty with stent placement. She was discharged home after taking ticlopidine 250 mg twice daily for five days in addition to her previous drugs (aspirin, pravastatin, and insulin).

She started to develop a diffuse rash one week after discharge and had pain and swelling in the joints of her hands, wrists, and knees. No fever, chills, or malaise was reported. She had no history of allergies or drug adverse reactions. On physical examination she was afebrile and had erythematous urticarial lesions over the trunk and extremities. Examination of her joints showed erythema, hotness, swelling, and tenderness in all the proximal interphalangeal and metacarpophalangeal joints, the wrists, and knees. Her blood tests at that time showed a packed cell volume of 0.34, a white blood cell count of 9700 cells/mm^3, and a platelet count of 211 000 cells/mm^3. Her erythrocyte sedimentation rate was 97 mm/h and her serum uric acid concentration was 250 µmol/l. Her test results were negative for hepatitis B surface antigen, hepatitis C antibodies, IgM and IgG parvovirus antibodies, antinuclear antibodies, and rheumatoid factor. Chest radiography was normal and analysis of her urine showed no haematuria or proteinuria.

The presumptive diagnosis was a symmetrical polyarthritis associated with ticlopidine intake. Treatment with ticlopidine was discontinued, and one week later her rash resolved completely but her arthritis persisted. After treatment with a non-steroidal anti-inflammatory drug (diclofenac 75 mg intramuscularly twice daily) for 10 days, her arthritis gradually resolved. Two weeks later her joints were completely normal and her erythrocyte sedimentation rate decreased to 32 mm/h. On her last evaluation, six months after the onset of arthritis, she had had no recurrence of her joint pain, and her erythrocyte sedimentation rate had dropped to 18 mm/h.

The clinical features and laboratory findings of arthritis in this case suggest a drug induced hypersensitivity (leucocytoclastic) vasculitis. Before March 2001, one case of polyarthritis and three cases of arthralgia associated with ticlopidine had been reported to the Committee on Safety of Medicines in the United Kingdom. Two case reports of arthritis associated with clopidogrel have also been published.[4] Clopidogrel is a thienopyridine drug with a similar chemical structure to ticlopidine and is commonly used in patients undergoing coronary stent implantation. Sanofi-Synthelabo, the manufacturer of ticlopidine, has not reported any case of polyarthritis associated with taking the drug. We suggest that thienopyridine derivatives be considered as a potential cause of acute arthritis.

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