Thrombocytopenia due to rifampicin

Sir,

Rifampicin is one of the most widely used and effective antituberculosis drug. Adverse effects are uncommon, except for occasional hepatotoxicity, skin-rash, gastrointestinal upsets, and flu-like syndrome. Rarely allergic and other autoimmune manifestations including thrombocytopenia are seen especially with high-dose intermittent treatment. Here we report a case of thrombocytopenia caused by daily administration of rifampicin after interruption of the drug for two months in view of its rare occurrence.

A 36-year-old man presented with cough, expectoration, chest pain, and fever of three months duration. He had taken two courses of antibiotics along with supportive treatment but without any clinical response. Past medical history was negative. He was a smoker and laborer.

General examination of the patient was normal. Examination of the respiratory system revealed bronchial breathing and crepitations over right upper lung field. Other systems were normal. Skiagram chest PA view showed cavitary lesion in the right upper zone.
Laboratory investigations revealed normal hemogram with an ESR of 110 mm in 1st hour. Sputum was positive for acid fast bacilli on smear examination.

Based on the above findings, antituberculosis treatment was started with isoniazid 300 mg, rifampicin 450 mg, pyrazinamide 1.5 gm, ethambutol 800 mg, and streptomycin 0.75 gm daily. There was marked clinical improvement and all symptoms were relieved within three weeks. Because of recovery from symptoms, he stopped the treatment on his own.

About two months after interruption of the therapy, his symptoms relapsed. Treatment was restarted with isoniazid, rifampicin, streptomycin, pyrazinamide, and ethambutol in the same dosages. Seven days later he presented with fever, gum bleeding, and purpuric rash over the trunk and the extremities.

On examination his vital parameters were normal. His investigations revealed normal hemoglobin, total and differential leukocyte counts but platelet count was only 13,500/mm³. It was decided to omit all antituberculosis drugs and oral prednisolone was started in dose of 1 mg/kg body weight/day. Platelet transfusion was also given. On further investigations, microscopic haematuria was detected and bone marrow aspirate showed normocellular picture with increased megakaryocytes. His bleeding time was 2.3 min and clotting time 3.8 min. Liver function tests, renal function tests, and antinuclear antibodies tests were normal. Dengue viral markers were also negative. Over the next three days, his gum bleeding stopped and purpura disappeared. Platelet count steadily rose to 1,80,000/mm³ in five days.

One week later, it was decided to reintroduce the antituberculosis drugs, one at a time, under supervision and after informed consent. However, within five hours after the administration of rifampicin with lower doses (300 mg), he developed purpura over legs. His platelet count dropped to 28,000/mm³, thus providing level 1 evidence of rifampicin induced thrombocytopenia. Rifampicin was stopped immediately.

The patient was then continued on isoniazid, streptomycin, pyrazinamide, and ethambutol. He continued to show clinical improvement and his platelet count returned to normal. The steroids were gradually tapered and finally stopped after three weeks. Streptomycin and pyrazinamide were stopped after two months. He is at present well and asymptomatic after having completed his course of treatment for 12 months. He has been warned against taking rifampicin for the rest of his life.

Serious reactions to antituberculosis drugs are uncommon. Rifampicin-induced thrombocytopenia is an uncommon but potentially life threatening complication of antituberculosis treatment. Rifampicin-induced thrombocytopenia was first reported by Bachman and co-workers in 1970. Most of the described cases were observed with high dose intermittent therapy with rifampicin (1200 mg twice weekly). Only a few cases of thrombocytopenia have occurred during daily treatment or after administration of rifampicin following on interruption of therapy. Tuberculosis Research Centre, Chennai, reported only a single case of rifampicin-induced thrombocytopenia among over 8000 patients treated for tuberculosis over 30 years. In our case, patient developed thrombocytopenia after interruption of antitubercular treatment for two months on daily regimen.

It has been observed that rifampicin-induced thrombocytopenia is caused by presence of anti-rifampicin antibodies. These antibodies fix a complement on the platelets in the presence of rifampicin resulting in platelet destruction. A sizable number of patients taking antituberculosis drugs interrupt treatment prematurely due to various reasons and although most are subsequently restarted on the same drugs, thrombocytopenia is very uncommon. It has been found that antibodies against rifampicin can be demonstrated in a significant number of patients after stopping the drugs. Yet rifampicin-induced thrombocytopenia is still relatively rare. Low incidence of thrombocytopenia inducing effect of rifampicin during daily dosage has been attributed to the possible presence of development of neutralizing antibodies formed during continuous treatment or may be that the antigen-antibody complex is continuously removed without causing an allergic reaction. Thus, daily dosing of rifampicin may result in immunologic tolerance, whereas intermittent dosing favors sensitization. Interruption of treatment may be a risk factor for such complication in daily regimen of rifampicin for few patients as seen in our case.

In patients with clinically drug-induced thrombocytopenia, an etiological agent can be identified in only 10% cases. In the remaining cases, the etiological diagnosis can be pointed out by a prompt rise in the platelet count upon withdrawal of offending drug. This case recorded a score of 9 on Naranjo ADR Probability scale incriminating the drug as a definite cause for the reaction.

It has been recommended that rifampicin-induced thrombocytopenia is an absolute contraindication to further therapy with rifampicin. However, Bhasin and co-workers has suggested that rechallenges should be done before finally withdrawing rifampicin. In our opinion, when it is necessary to re-start rifampicin, one should always check the platelet counts frequently and this should be treated under supervision with coverage of steroids.

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Letters to Editor

Sir,
We read with interest manuscript titled “Subcutaneous emphysema due to bronchial foreign body demonstrated by multidetector-row computed tomography (MDCT)”, by Wani et al, published in Lung India. 2011:Oct;28(4):291-3.

We wish to point out that MDCT virtual bronchoscopy (VB) is useful in evaluating bronchial stenosis and obstruction caused not only by endoluminal pathology but also by external compression and in addition it has the advantage of looking beyond stenosis. We agree with the authors that its main application lies in providing the exact location of suspected foreign body, prior to bronchoscopy. However, we would like to add that it still fails to disclose exact nature of obstructing pathology which is finally detected by rigid/ flexible bronchoscopy.

It is pertinent to add here that Sodhi et al, in their study of 43 children evaluated the potential use of MDCT and VB in the evaluation of tracheobronchial patency in children with suspected bronchial obstruction and compared its findings with fibreoptic / rigid bronchoscopy or surgery. They found obstructive pathology in 26 children, which included endoluminal foreign body, mucus plugs in 13 children, endobronchial tumor in three children and extrinsic compression (lymph node, aberrant Vessels, mediastinal cysts / tumors) of the tracheobronchial tree in 10 children. Multidetector computed tomography and virtual bronchoscopy: Role in bronchial obstruction in children In 17 children, no obstructive lesion was identified. Excellent positive correlation was obtained, between MDCT-VB and bronchoscopy/surgery. They concluded that MDCT-VB is useful in evaluating bronchial stenosis and obstruction caused by both endoluminal pathology and extrinsic causes.

VB is a non-invasive technique that provides a 3D view of internal surface of the trachea and major bronchi by using MDCT images. VB enables simultaneous visualization of inner and outer structures of the tracheo bronchial tree thus clearly depicting the cause of obstruction.

In another study by Adaletli, et al, there were 82% true positives in VB when compared with bronchoscopy.

Another aspect which we wish to emphasize is that this virtual technique does not require any additional radiation exposure in children, but provides additional information to the MDCT images, that is indicated anyway for suspected narrowing or compression of the tracheo bronchial tree. As opposed to fibreoptic bronchoscopy, the virtual technique is noninvasive and does not require general anaesthesia and can be performed with simple sedation. The other advantages of VB include visualization of airway distal to obstruction, segmental and sub segmental bronchi can be evaluated easily with thin section MDCT images, simultaneous evaluation of mediastinal and lung pathologies responsible for symptoms of the child, and evaluation of vascular anomalies in children.

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