Serum angiotensin converting enzyme activity and serum copper levels in covert silicosis

Abstract
The present case report describes asymptomatic worker working in quartz crushing unit and having crepitations on auscultation in the middle zone of right lung, diagnosed as grade 1/1 silicotic according to ILO Classification of Pneumoconiosis. The patient had elevated levels of SACE and serum Copper. This is the first time that SACE and serum copper levels were measured in a covert case of silicosis particularly in India.

Key words: Serum copper, Serum angiotensin converting enzyme, Silicosis

INTRODUCTION
Silicosis is the most frequently occurring pneumoconiosis caused due to exposure to free silica dust. Stone quartz grinders who are involved in crushing quartz stone into powder form, which is then used as a precursor for glass manufacturing industry, are exposed to excess risk of silicosis as the stone contains approximately 100% free silica and the process liberates huge amount of silica dust in the working environment.

Till recently, the diagnosis of silicosis was mainly based of clinical examination of the subjects with special emphasis on respiratory system, measurement of pulmonary function specially lung volumes and grading of profusion according to the International Labour Organization classification of Pneumoconiosis. But after Lieberman in 1975 first reported the elevation of Serum Angiotensin Converting Enzyme (SACE) in sarcoidosis, several investigators have confirmed that the SACE activity is increased in a large proportion of patients having granulomatous diseases like sarcoidosis and silicosis.

Angiotensin 1-converting enzyme (ACE, peptidyldeipeptide hydrolase, EC 3.4.15.1) is a membrane-bound glycoprotein, which converts Angiotensins 1 to 2 and participates in bradykinin degradation. The ACE is bound to the luminal membranes of endothelial cells, and its action takes place mainly in the pulmonary circulation. The serum activity of ACE in pulmonary diseases is of interest owing to its principal localization in the large capillary bed of the lungs.

Also as it is reported in the literature that Cu has a fibrogenic property and as the primary pathologic changes in silicosis include fibrosis and the proliferation of collagen tissue in the lungs there could be possible association with raised levels of serum Cu. Although the mechanism of increase in serum Cu is still not understood, it has been suggested that an increase in ceruloplasmin levels in silicotics, which contains eight Cu atoms may be responsible for such an increase. Moreover, other studies have also reported elevated levels of serum Cu in silicotics.

However both these parameters are reported in the overt cases of silicosis with severe grades of profusion. However, we have reported the elevated levels of these parameters in a covert case of silicosis with only 1/1 profusion grade in Chest Radiograph when classified according to ILO Classification of Pneumoconiosis.

CASE REPORT
A large number of contractual workers work in the stone quartz crushing units of Godhara, Gujarat, India. The workers belong to low-socio-economic strata and work under poor working environment. The dust generated during the process of stone crushing is huge and it contains approximately.
100% free silica. Moreover the workers do not use any personal protective devices such as facemask to prevent the inhalation of dust. In our past studies also it was reported that because of such huge amount of dust and high concentration of free silica, the workers have developed silicosis even with 1–3 years of exposure. This is the first time that an attempt was made to measure SACE and serum copper levels among covert case of silicosis as literature suggest that these parameters are frequently raised in the severe grades of silicosis. With this background we are presenting the case history of a covert case of silicosis.

A 22-year-old male, nonsmoker having a height of 162 cm and weight of 42 kg, is working in the stone quartz crushing units since last 2 years. The subject belonged to the lower socio-economic strata according to the socio-economic classification scale used in the country. This was subject’s first job. During the study the subject was asymptomatic having no symptoms of silicosis, viz cough, chest pain or shortness of breath. Even the symptoms suggestive of tuberculosis such as haemoptysis, evening rise of temperature or loss of weight were not reported. The history also revealed that he was not on any medication. The blood pressure was measured with mercury sphygmonanometer. The auscultation revealed few crepitations on the right middle lobe region. The chest radiograph postero-anterior view, carried out using 300 mA equipment [Figure 1]. The pulmonary functions were measured using Spiravit SP-10 (Maker Schiller AG, Switzerland). After calibrating the spirometer according to the procedure given in the catalog, three readings of each ventilatory function were taken. The readings showing the highest value were recorded. Blood sample was collected from the subject and centrifuged for the separation of serum, which was kept frozen until analysed for SACE and serum copper levels. The SACE activity was measured according to the spectrophotometer method and the synthetic tri-peptide substrate used was N-[3-(2-furyl) acryloy]-L-phenylalanylglycylglycine (FAPGG). The method is based on the principle of hydrolysis of FAPGG to furylacryloylphenylalanine and glycylglycine.\(^{[14]}\) Hydrolysis of FAPGG results in a decrease in absorbance at 340 nm. The ACE activity in the sample is determined by comparing the sample reaction rate to that obtained with the ACE calibrator. The serum copper levels were measured using Atomic Absorption Spectrophotometer. The findings of clinical examination are summarized in [Table 1].

DISCUSSION

In the present study, on the basis of occupational history of working in stone quartz unit, asymptomatic nature, normal pulmonary function tests and presence of abnormal finding on chest radiograph, the subject was diagnosed as a covert case of silicosis with numerous p/p, 1/1 opacities in both lungs [Figure 1]. This covert case of silicosis reported elevated levels of SACE and Serum copper. The levels were higher than the other subjects exposed to silica dust but having no disease (Mean SACE levels: 66.85 ± 14.38 IU/L and Mean Serum Copper levels: 86.64 ± 51.44 mg/dl) and also the controls (Mean SACE levels: 64.28 ± 6.94 IU/L and Mean Serum Copper levels: 100.94 ± 37.7 mg/dl). The elevated SACE levels can be attributed to the fibrotic involvement of lung tissue including capillaries as the endothelial cells in the capillary bed have a high ACE content.\(^{[7,8,15,16]}\) Partly it might have released from the macrophages due to degradation of macrophages by toxic silica dust. The increase in serum copper level can be attributed to an increase in ceruloplasmin levels, which contains eight Cu atoms and thus may be responsible for such an increase.\(^{[10]}\) The rise in SACE activity due to hypertension can be ruled out as the blood pressure measurement revealed normo-tension. Similarly the elevated levels of serum copper due to smoking as reported in few studies\(^{[17–19]}\) can also be ruled out, as the subject was a nonsmoker.

Thus, as mentioned in the literature that these two parameters viz. SACE and serum copper levels are elevated in fibrotic

Table 1: The important clinical findings of the subject

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
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<tbody>
<tr>
<td>Haemoglobin</td>
<td>11 gm% (normal:13–15 gm%)</td>
</tr>
<tr>
<td>ESR</td>
<td>29 mm at the end of first hour by Westergren’s method (normal:0–10 mm)</td>
</tr>
<tr>
<td>Peripheral smear examination</td>
<td>Microcytic hypochromic anaemia</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>110/70 mm Hg</td>
</tr>
<tr>
<td>Chest X-ray PA View</td>
<td>Bilateral 1/1 p/p silicotic opacities</td>
</tr>
<tr>
<td>FEV(_1)</td>
<td>2.5 l/s</td>
</tr>
<tr>
<td>FVC</td>
<td>2.93 l</td>
</tr>
<tr>
<td>PEFR</td>
<td>7.33 l/s</td>
</tr>
<tr>
<td>SACE</td>
<td>82 IU/l (normal:8–52 IU/l)</td>
</tr>
<tr>
<td>Serum Copper</td>
<td>104 mg/dl (normal:70–150 mg/dl)</td>
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diseases in lung, these can be tried for potential biomarker of silicosis not only in the classical cases of silicosis but also in the covert cases of silicosis so that the preventive measures can be taken.

REFERENCES