**Case Study**

**Liver Angiosarcoma Caused by 22-Year Exposure to Vinyl Chloride Monomer**

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Many experimental studies demonstrated that VCM can produce malignant transformation1). For example, after one-year exposure of rats to VCM in a 3% concentration by volume in air, cutaneous cancers, pulmonary adenocarcinomas and chondrosarcomas of the extremities developed2). In another experiment on rats exposed to VCM (26 to 76,800 mg m⁻³) again for 12 months hepatic angiosarcomas were observed3).

Liver angiosarcoma is a rare tumour developing more often in men exposed to various chemical compounds4–10). Cases of this tumour were seen to develop following exposure to VCM, arsenic, radium and thorotrast, an X-ray contrast agent11).

**Case Report**

The patient, a man aged 47, married (case record No. 4033/94) with a history of exposure to VCM in the years 1972–1994, was admitted to our hospital because of rapidly progressing weight loss, weakness, breathlessness, aching and a feeling of distension in the right epigastrium, with fever up to 38°C. The beginning of these symptoms was 2 months earlier. Before that, he had had no disease except an appendectomy. He smoked about 15 cigarettes daily, and drank alcohol occasionally. The family history was 2 months earlier. Before that, he had had no disease except an appendectomy. He smoked about 15 cigarettes daily, and drank alcohol occasionally. The family history was not relevant. From 1972 to March, 1994 he had been working always in the same work location in three-shift work. Autoclaves were cleaned 2–3 times during every working shift, and each cleaning took about 25 min. During the work he was wearing protective clothes, mask, gloves and goggles.

The VCM concentration in air samples taken always at the same places in the autoclave was determined during cleaning 2–3 times during every working shift, and geometrical means were calculated from these values. In the first years of his work (1972–1979) the peak VCM concentrations were 1,300 mg m⁻³, and the mean time-weighted eight-hour concentration in these years was 85.3 mg m⁻³. In the years 1979–1994 the mean time-weighted concentration in eight hours ranged from 2.5 to 4.8 mg m⁻³. It can be assumed that in the first seven years his exposure to VCM was very high: HPC and MAIPC in Poland are 5 mg m⁻³ and 30 mg m⁻³ respectively13). The patient worked 2,995 days under conditions of VCM exposure and in that time he absorbed about 0.8105 kg of VCM, that is about 0.11254 kg of VCM/kg of body weight (assuming that the volume of air inhaled by the man during 8 working hours was 10 m³2), and 40% of VCM present in the air was absorbed3). Table 1 shows the concentrations of VCM in the air in various years.

On admission, the physical examination of the patient found evidence of cachexia, yellow skin and sclerae and hepatomegaly with the liver projecting 4 cm under the right costal arch, with an even, rounded, rather hard margin. No signs characteristic of scleroderma, acroosteolysis, Raynaud’s syndrome, splenomegaly or superficial or profound sensation disturbances were present. Dilatation of periumbilical veins (caput Medusae) was absent.

Table 2 shows the results of haematological and biochemical tests. Abdominal ultrasonography was done on the 6th day in hospital and it revealed high grade hepatomegaly, with hepatic parenchyma not homogenous, with round hyperechogenic foci of the “bulleye” type. The spleen was slightly enlarged. No evidence of portal hypertension was noted. Fiberscopic examination on the 9th day in hospital of the upper digestive tract showed erosive gastritis, confirmed by histological examination. No oesophageal varices were found. Computerized tomography of the abdomen and chest on the 15th day in hospital showed significant hepatomegaly, with extensive, irregular, hypodense areas in segments V and VI of the right hepatic lobe. The outlines of the lesions were uneven and jagged, with isolated microlacifications. The kidneys, spleen and pancreas were normal. Fluid was present in the right pleural cavity, and the volume of lung segments IX and X was reduced. The segmental bronchi were patent (Fig. 1).

The patient died after 26 days in hospital. The clinical diagnosis was hepatic angiosarcoma with pulmonary metastases: cachexia. The autopsy disclosed angiosarcoma of the liver with metastases to the right lung.

**Findings among Fellow Workers**

In the years 1972–1994 in the vinyl chloride polymerization division, where the patient was working, 371 workers were employed (304 males and 67 females,
aged 19 to 57 years, mean age 35.5) among them 89 male workers were operators of the emptying equipment. History taking in 32% of the workers revealed paraesthesiae of the hands, in 26% hypersensitivity to cold, in 12% superficial hypaesthesia and in 3.5% full Raynaud’s syndrome was present. Four workers had raised increased ASA T, ALA T, γ-GTP concentrations and a low prothrombin index. No other abnormalities were found in biochemical investigations. Only one case of liver tumour, reported here, was noted. No other neoplasms were observed.

Table 1. Geometrical means of VCM concentration in air measured inside the autoclave in years 1972–1994

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<tbody>
<tr>
<td>Short-term peak concentration [mg m⁻³]</td>
<td>1,600</td>
<td>1,100</td>
<td>1,300</td>
<td>600</td>
<td>200</td>
<td>72</td>
<td>40</td>
<td>30</td>
<td>28</td>
<td>29</td>
<td>26</td>
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<tr>
<td>Time-weighted average concentration [mg m⁻³]</td>
<td>132.3</td>
<td>86.2</td>
<td>76.2</td>
<td>82.5</td>
<td>47.5</td>
<td>20.2</td>
<td>7.5</td>
<td>4.8</td>
<td>2.9</td>
<td>3.5</td>
<td>2.4</td>
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Table 2. The results of haematological and biochemical investigations of patient with liver angiosarcoma on the 1st and 26th days of therapy

<table>
<thead>
<tr>
<th>ESR</th>
<th>HGB</th>
<th>HCT</th>
<th>RBC</th>
<th>WBC</th>
<th>PLT</th>
<th>Total protein</th>
<th>Prothrombin index</th>
<th>ASAT</th>
<th>ALAT</th>
<th>BIL</th>
<th>ALP</th>
<th>γ-GTP</th>
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<tbody>
<tr>
<td>[mm/h]</td>
<td>[g/100 ml]</td>
<td>[%]</td>
<td>[× 10⁶ cells/m³]</td>
<td>[× 10⁶ cells/m³]</td>
<td>[× 10⁶ particles/m³]</td>
<td>[g/l]</td>
<td>[arb U]</td>
<td>[IU/l]</td>
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<tr>
<td>1st day of therapy</td>
<td>26</td>
<td>17.7</td>
<td>32</td>
<td>3.3</td>
<td>4.6</td>
<td>260</td>
<td>84</td>
<td>0.30</td>
<td>15</td>
<td>23</td>
<td>8.77</td>
<td>66.2</td>
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<tr>
<td>26th day of therapy</td>
<td>30</td>
<td>16.1</td>
<td>29</td>
<td>3.0</td>
<td>5.6</td>
<td>280</td>
<td>76</td>
<td>0.36</td>
<td>16</td>
<td>27</td>
<td>8.20</td>
<td>69.0</td>
</tr>
</tbody>
</table>

ESR, erythrocyte sedimentation rate; HGB, haemoglobin; HCT, haematocrit; RBC, red blood cells; WBC, white blood cells; PLT, platelets; ASAT, aspartate aminotransferase; ALAT, alanine aminotransferase; BIL, bilirubin; ALP, alkaline phosphatase; γ-GTP, gamma-glutamyl transpeptidase.

Discussion

A consequence of the carcinogenic action of VCM is an increasingly frequent incidence of hepatic angiosarcoma, and tumours of the brain, skin, lungs, kidneys and thyroid, as well as lymphomas and leukaemias in the exposed populations3, 5, 10, 14, 16). Although the connection between VCM exposure and the prevalence of certain neoplasms is still a matter of controversy, angiosarcoma has been regarded as a specific consequence of this exposure4, 5, 8, 10, 17). The risk of angiosarcoma development in the liver as a result of exposure to VCM is severalfold higher than in non-exposed populations3, 5, 8, 9, 14). The time from the beginning of exposure to tumour development is from 9 to 35 (Mean=24) years7). High VCM concentrations can shorten the induction of hepatic angiosarcoma to 2 years10). The phase of asymptomatic tumour development is therefore long. Hepatic angiosarcoma shows a tendency to the formation of metastases, usually to the lungs and to the lymph nodes of splenic and hepatic hilif, the metastases being are found in about 60% of the patients7). According to official data, no case of angiosarcoma caused by VCM exposure has been recorded as yet in Poland7).

The first symptoms remembered by the patient appeared in March, 1994, which means that the tumour developed asymptotically for 21 years. The clinical symptoms lasted only 4 months. The course of the disease was highly dramatic, with metastases developing in the lungs and pleura, and with cachexia.
References


