He later gave a six year history of heavy solvent abuse (four litres of Evostick per week, which he inhaled from a plastic bag). He denied intravenous drug abuse and the consumption of any drugs or alcohol on the day of admission. Urine screen for toluene breakdown products was strongly positive (urine hippuric acid concentration = 2.5 g/l; normal range 0.1-0.2 g/l). A complete drug screen was otherwise negative. The results of routine blood tests and chest x ray examination were normal.

Comment

Considerable emphasis has been placed on cardiac arrhythmias as the major cause of sudden death in solvent abuse. We believe that reversible respiratory arrest, despite a normal electrocardiogram, has not been reported. Nevertheless, respiratory depression in solvent abusers might be expected, since studies in animals have shown that toxic concentrations for the central nervous system and cardiac sensitisation are similar. Depression of central nervous system function by solvents probably occurs in a similar manner to the depressant effects of most general anaesthetic agents. Central nervous system toxicity in rats evolved from tremor to narcosis, followed by shallow respiration and death from respiratory depression. Death was inevitable above a critical toxic concentration.⁴ For this reason patients who lose consciousness during or after solvent abuse should be closely monitored.

We believe that this case report supports the theory that respiratory depression alone may be an important cause of sudden death in solvent abusers. There may be no distinctive features at necropsy suggestive of the mode of death, and this probably accounts for the rarity of respiratory depression as a postmortem diagnosis in solvent abusers.

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Pregnancy after chemotherapy induced ovarian failure

Several groups have studied reproductive function after MVPP (mustine, vinblastine, procarbazine, and prednisolone) or MOPP (mustine, vincristine, procarbazine, and prednisolone) chemotherapy for Hodgkin's disease, and the incidence of amenorrhoea has ranged from 15% to 62%.¹⁻⁴ The cessation of menses is related to age and is accompanied by an increase of serum gonadotrophin concentrations and a decreased serum oestradiol value consistent with primary ovarian failure. Apart from age, there have been no clear differences noted between those women who become amenorrhoeic and those who do not. Schilsky *et al*, in their long term follow up of ovarian function in women treated with quadruple chemotherapy for Hodgkin's disease, concluded that if premature ovarian failure developed, then it was invariably permanent. We describe a patient in whom amenorrhoea was not permanent and in whom pregnancy occurred only because she disregarded the advice of her doctors concerning sex steroid replacement therapy.

Case history

In June 1978 a 23 year old woman presented with cervical lymphadenopathy and an enlarged liver and spleen. Histologically a biopsy sample of lymph node showed nodular sclerosing Hodgkin's disease. Between July 1978

and May 1979 she received eight courses of quadruple chemotherapy with MVPP. Subsequently she remained well and required no further treatment for Hodgkin's disease.

Up until early 1981 she had taken the oral contraceptive pill but this was stopped as she was interested in the possibility of fertility. By January 1982 she had seen only one period in the past nine months. Serum follicle stimulating hormone and luteinising hormone concentrations (>32 IU/l) and serum oestradiol concentration (104 pmol/l; 28 pg/ml) were consistent with primary ovarian failure. She was advised that the cause of her amenorrhoea was chemotherapy induced ovarian failure and that she required sex steroid replacement therapy. Treatment with ethinyloestradiol-levonorgestrel (Microgynon 30) was begun but she remained concerned about her chances of fertility. Thus in order to provide further information about her fertility prospects a laparoscopy and ovarian biopsy were performed in March 1983. The biopsy samples showed complete absence of ovarian follicles and she was advised to continue with Microgynon 30. She did not take her sex steroid replacement therapy. Between July and December 1983 she had five normal periods, and in January 1984 the progesterone concentration on day 21 was consistent with ovulation. In February pregnancy was confirmed, and at the end of September she delivered a healthy baby boy weighing 3400 g.

Comment

This young woman showed clinical and biochemical features of primary ovarian failure as a result of quadruple chemotherapy for Hodgkin's disease. The amenorrhoea was thought to be permanent in the light of the ovarian biopsy findings and the "known" course of chemotherapy induced ovarian failure.³

In young women with ovarian failure sex steroid replacement therapy is advised to prevent dyspareunia, loss of libido, and the risk of osteoporosis. During treatment it is impossible to determine if the ovarian failure is reversible and, of course, infertility is permanent.

Our patient's history indicates that cytotoxic induced ovarian failure may be reversible, and this poses a therapeutic dilemma in patients similarly treated who wish to conceive. It may be argued that we were unwise to assume an absence of residual primordial follicles from an ovarian biopsy sample obtained at laparoscopy.⁵ Thus to ensure that enough ovarian material has been obtained for adequate histological evaluation, laparotomy and ovarian wedge resection may be required in some of these young women; these procedures, however, are not without their own complications.⁵ Under similar circumstances, if an otherwise asymptomatic young woman who is desirous of a pregnancy prefers not to undergo a laparotomy and ovarian wedge resection she may choose not to take sex steroid replacement therapy despite the increased risk of osteoporosis.

The reproductive history of this patient illustrates that it is unwise to assume that amenorrhoea and infertility are inevitably permanent after chemotherapy induced ovarian damage.

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Correction

Blood group as a prognostic indicator in breast cancer

In the results section, third paragraph, third line, and in table III of the article by P J Holdsworth *et al*, published on 2 March (p 671) "M stage" should read "N stage."