

Persistent Multiple Pulmonary Nodules in a Nonimmunocompromised Woman after Varicella-Related Myelitis Treated with Acyclovir

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Persistent multiple pulmonary nodules were observed on the chest X ray of a nonimmunocompromised woman 6 months after she was treated with acyclovir for a varicella-related myelitis without respiratory symptoms. Early antiviral therapy given for varicella infections might decrease the intensity of clinical symptoms without actually preventing the occurrence of varicella-zoster virus-related lesions such as the persistent pulmonary nodules reported here.

CASE REPORT

In January 2002, a varicella skin eruption followed by neurological signs of myelitis, i.e., thoracic and abdominal dysesthesia and reduced sensitivity, developed in a 46-year-old woman. This patient, who had spent her entire life in France, had no history of chicken pox during her childhood. The varicella skin eruption was typical, and her son developed chicken pox at the same time. Biological parameters in the blood were undisturbed except for inflammation markers (increased erythrocyte sedimentation rate and C-reactive protein). Cerebrospinal fluid was collected, and a mild lymphocytosis (16 lymphocytes out of 17 leukocytes per μ l), a slightly increased protein level (0.66 g/liter), and a normal glucose level were observed; moreover, varicella-zoster virus (VZV) DNA was revealed by a commercial PCR assay (Herpes Consensus assay; Argene Biosoft, Varilhes, France). Results for anti-VZV immunoglobulin G and immunoglobulin M were positive (commercial enzyme-linked immunosorbent assay; DiaSorin, Antony, France) in the serum collected 3 weeks after the varicella skin eruption. The patient was given intravenous acyclovir for 10 days (10 mg/kg of body weight every 8 h intravenously), and the myelitis symptoms progressively disappeared during the treatment. A chest X ray was performed because of intercostal pains, and it showed multiple pulmonary nodules (Fig. 1). The thoracic pain, which was not clearly related to the observed pulmonary lesions, finally disappeared with conventional pain therapy.

In July 2002, because of persistent asthenia and pulmonary nodules on the chest X ray, biopsies were performed in order to explore a potential metastatic cancer. Histopathology showed necroinflammatory and granulomatous lesions, suggesting tuberculosis or other granulomatous pulmonary diseases, including persistent VZV-related damage. This diagnosis was suggested because of the varicella observed earlier in January. Bacteriological investigation for tuberculosis was negative, although VZV DNA was detected by PCR (homemade

PCR using published oligonucleotidic primers) (14). This result was confirmed by a repeated PCR test. Although normal lung tissue was not available for a PCR assay, positive VZV DNA results for the pulmonary nodules and the histological data taken 6 months after primary VZV infection allowed us to eliminate the cancer hypothesis and to retain a VZV etiology. Finally, the clinical evolution was satisfactory in spite of an anorexic tendency and some thoracic pains in this terribly anxious patient.

The VZV infection is known to have the potential to progress to visceral involvement in both immunocompromised and immunocompetent patients despite acyclovir therapy. A greater risk for pneumonia is observed in adults who did not have the varicella infection when they were children (8). Over the past 20 years, VZV infection has had a tendency to affect many more adults than before. As reported for varicella pneumonitis in England and Wales, for example, adult cases involving VZV are commonly more serious than those in children (5, 9). VZV pneumonia is usually contemporary with varicella skin lesions but can also appear up to 10 days after the appearance of vesicles and is most often accompanied by the respiratory symptoms of coughing and dyspnea (2). Even though clinical symptoms usually clear up within 2 or 3 days, this pathology is a true concern in adults and can even be fatal despite the advent of parenteral acyclovir (1, 6, 7, 8, 12, 13).

Early antiviral therapy may indeed help in controlling various severe VZV-related symptoms. For example, it was suggested that early intravenous acyclovir given for varicella pneumonia in adults could prevent respiratory failure and death. A 10-year retrospective review that included patients admitted to a teaching hospital in the United Kingdom reported severe cases of varicella pneumonitis treated with intravenous acyclovir. Coughing was present in 100% of the cases, and dyspnea was present in 92% of the cases (4, 8). In this study, X rays showed diffuse nodular shadowing; in the end the clinical outcome of the infection was good.

We encountered a nonimmunocompromised patient with

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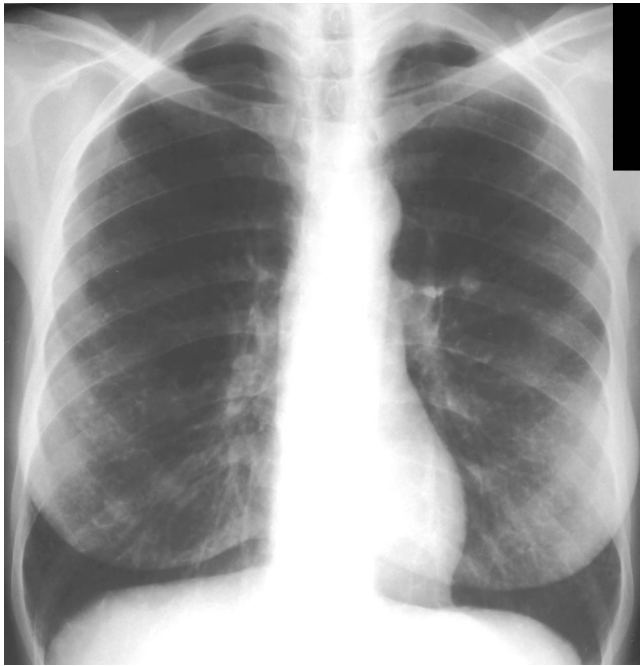


FIG. 1. Chest X ray (February 2002) showing multiple pulmonary nodules.

persistent pulmonary nodules. These lesions were preceded by a varicella-related myelitis without respiratory symptoms. Under acyclovir treatment, which resolved neurological symptoms, the clinical state of the patient improved. Multiple pulmonary nodules were detected on a chest X ray performed at the end of the acyclovir treatment given for the varicella-related myelitis. Six months after the first VZV infection, persistent multiple pulmonary nodules were observed on a second chest X ray and were accompanied by asthenia. Lung biopsies were decided upon in order to look for a potential cancer or microbial granulomatous lung disease; histological examination and positive VZV-DNA PCR strongly suggested a varicella etiology. Thus, we were able to detect VZV by PCR, first in the cerebrospinal fluid and 6 months later in a lung biopsy, confirming the cause of the persistent pulmonary nodules and differentiating them from a metastatic carcinoma.

Meyer et al. reported persistent pulmonary nodular lesions in an immunocompetent woman after her recovery from varicella pneumonia which, in this case, had been accompanied by respiratory symptoms (cough and shortness of breath) (10). This type of pulmonary lesion was also observed in an annual chest X ray of a woman with chronic lymphocytic leukemia; histological findings and positive PCR for VZV DNA proved an asymptomatic pulmonary involvement in VZV infection (11). To our knowledge, this is the first description of persistent pulmonary nodules after a varicella infection without re-

spiratory symptoms in an immunocompetent patient treated with acyclovir for VZV-related neurological symptoms.

We can assume that in our patient, the early acyclovir treatment given for VZV-related myelitis prevented any real respiratory symptoms in spite of the development of histological lesions. Thus, antiviral therapy might modify the course of VZV infections, decreasing the intensity of clinical symptoms without actually preventing the occurrence of VZV-related lesions. In this context, VZV detection using PCR may be useful (3). When we explore tumor-like lesions on chest X rays, potential early anti-VZV therapies in VZV infections, which are affecting more and more adults, should be taken into account. Thus, investigation for possible related granulomatous lesions, excluding a metastatic cancer, should be considered.

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