Fatal haemorrhagic varicella in a patient with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis

Sirs,

A 23-year-old male patient was admitted due to a diffuse vesiculo-haemorrhagic rash. The patient was diagnosed with ANCA-associated vasculitis two months earlier, with increasing dyspnea, bilateral pulmonary infiltrates, sinusitis, positive cANCA and capillaritis with interstitial inflammation in a lung biopsy. He was treated with prednisone 60 mg daily and monthly pulses of cyclophosphamide.

He reported that 10 days prior to admission, his 3-year-old nephew who had active chickenpox, had visited him. A week later a rash appeared. On admission, the patient appeared ill. He had a diffuse vesiculo-haemorrhagic rash primarily on the face, scalp and trunk consistent with chickenpox. Examination elicited hepatosplenomegaly. Laboratory tests revealed leukopenia, anaemia and thrombocytopenia. Liver transaminases were elevated. Prothrombin time and partial thromboplastin time were prolonged, fibrinogen was low and d-dimer level was high, indicative of disseminated intravascular coagulation (Table I). Intravenous acyclovir and cefamezin were administered. The patient was transferred to the intensive care unit, where he was also treated with VariZig, but died within hours due to multi-organ failure and refractory shock. Polymerase chain reaction performed on fluid from an unroofed vesicle confirmed the diagnosis of varicella. Blood cultures were positive for methicillin-sensitive *Staphylococcus aureus*.

As high as 10% of adults are seronegative for varicella antibodies and loss of varicella immunity over time had been described (1). Disseminated haemorrhagic varicella had been previously reported in immunocompromised hosts (2, 3).

Current Advisory Committee on Immunization Practices (ACIP) guidelines encourage routine vaccination for all adults without evidence of immunity to varicella with 2 doses of varicella vaccine or a second dose if they have received only 1 dose (4). With regard to immunosuppressed hosts, vaccination is generally contraindicated since it is a live-attenuated vaccine preparation.

Table I. Selected laboratory data. NA: not available.

Variable	Reference range	Admission	6 hours post admission	18 hours post admission
White cell count (per mm^3)	4,500-11,000	1,600	17,600	13,500
Haematocrit (%)	41-53	35.2	27.2	21
Platelets (per mm^3)	150,000-350,000	15,000	47,000	66,000
Urea nitrogen (mg/dl)	8-25	5	15	18
Creatinine (mg/dl)	0.6-1.5	1.2	1.72	2.66
Aspartate aminotransferase (U/litre)	9-32	2240	4956	NA
Alanine aminotransferase (U/litre)	7-30	1269	2740	NA
Lactate dehydrogenase (U/litre)	110-400	19,370	32,780	NA
International normalised ratio (INR)	1	2.2	2.9	4.7
Prothrombin time (sec)	12-16	28.2	36.1	54.4
Partial thromboplastin time (sec)	24-34	41.7	71.7	99.1
Fibrinogen (mg/dl)	150-400	187	104	84
D-dimer (ng/ml)	<500	28,360	NA	NA

Nevertheless, varicella-related fatalities in immunosuppressed hosts can be prevented while practicing simple, yet pivotal measures. Patient education is critical. Patients should avoid contact with sick children, especially those with fever or rash. Vaccination of close contacts ("cocooning") should be considered (4). In case of exposure, medical care should be sought immediately as immunoprophylaxis (*i.e.* VariZig) may be effective in reducing disease severity and should be administered as soon as possible after exposure.

Less often, immunosuppressive treatment may be delayed. In such circumstances, active vaccination should be considered in patients who are tested negative for varicella antibodies. However, the exact timing of administering immunosuppressive therapy and its effects on vaccine efficiency are not clear.

Of note, in a study by Zhang *et al*. no evidence was found to support an association between methotrexate and varicella zoster virus infection in rheumatoid arthritis patients (5, 6), but this conclusion cannot be drawn as yet, for patients that are treated with corticosteroids or cyclophosphamide (2, 3, 7).

Considering the growing utility of immunomodulating agents, those measures should be recognised.

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