Case Report

Varicella Zoster Complicated By Disseminated Intravascular Coagulation: Clinico-Pathological Correlation Of A Rare Clinical Manifestation Of A Benign Disease

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Abstract

Varicella Zoster Virus (VZV) infections are considered to be mild and ubiquitous infections predominantly affecting the pediatric population. However, in adults and immunocompromised patients, this apparently benign self-limiting course can have protean complications with a rapidly downhill course. We present a rare case report of a young individual with a probably compromised immune system who had a fulminant VZV infection complicated with disseminated intravascular coagulation (DIC) resulting in death.

Keywords:

Chickenpox; Disseminated intravascular coagulation; Varicella Zoster Virus Infection

Introduction

Chickenpox is a common contagious systemic viral infection of childhood caused by VZV, a double stranded DNA virus of the herpes virus family. As per the national statistics, India reported a total of 75,288 cases of VZV infection in the year 2017 with 99 fatalities1. The primary infection usually occurs in young children and is almost always symptomatic with a characteristic cutaneous vesicular rash. Recovery is complete in majority of the cases; however, the disease may be severe and fatal in neonates aged less than two weeks, in adults and in immunocompromised. The morbidity and mortality rates are 10 to 20 times higher in adults than in healthy children.2 Around 50% of varicella associated deaths occur among patients aged greater than or equal to 20

years. Widespread systemic disease, though rare, can manifest as varicella pneumonia, DIC and abnormal renal and/or hepatic functions. Other complications include thrombocytopenia manifesting as purpura, hematuria or a hemorrhagic rash.3 We report a case of primary varicella in probably an immunocompromised adult who developed fulminant infection resulting in DIC with a rapidly fatal outcome.

Case Report

Clinical History

A 25-years-old male, reported to a secondary care hospital with complains of fluid-filled rashes over face and trunk of one day duration along with retrosternal chest pain and dysphagia. The patient gave history of anuria in the last 24 hours. Clinical evaluation revealed a characteristic vesiculo-papular rash over face, shoulders, arms and abdomen. Other relevant clinical findings included oro-pharyngeal candidiasis (Fig 1A), upper abdominal guarding, mild hepatomegaly and sluggish bowel sounds. With a working diagnosis of chickenpox with oro-pharyngeal candidiasis, the patient was started on injection ceftriaxone, tablet itraconazole and chlorhexidine mouthwash. Within six hours of admission, there was an increase in the severity and spread of the cutaneous eruptions in the form of appearance of fresh lesions on the trunk and grouped vesicular lesions over the gluteal region as well as the right thigh (Fig 1B). The patient had a history of high-risk behavior in the form of unprotected intercourse a few months ago following which he developed multiple reddish spots in and around his external genitalia, for which he had claimed to be under treatment from a "local practitioner" at his native place. He wasn't evaluated for any form of immunodeficiency in detail due to the fulminant course of his illness, however his initial workup for viral markers in the form of human immunodeficiency virus (HIV), hepatitis B and hepatitis C were negative.

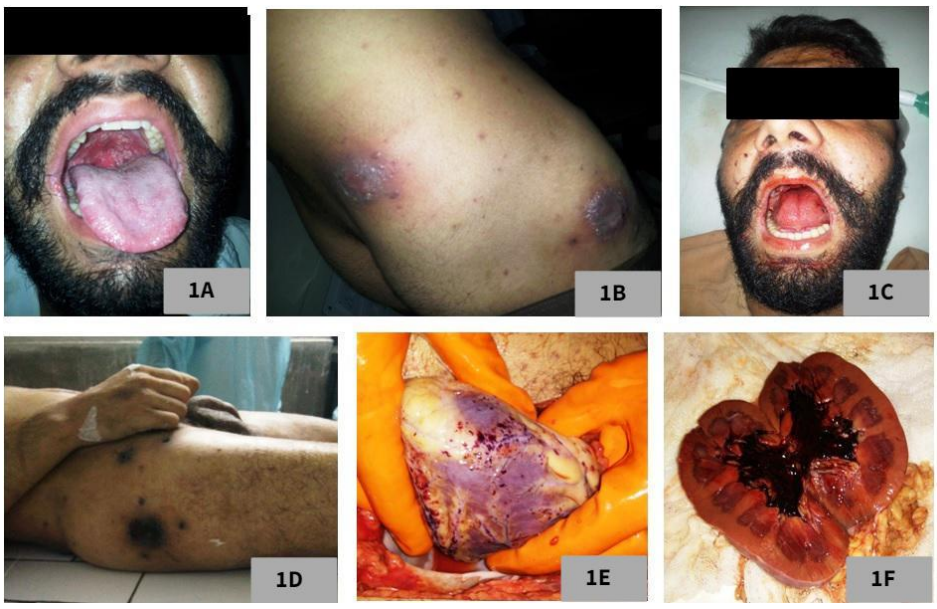

Figure 1: 1A – Oropharyngeal candidiasis, 1B – Grouped vesicular lesions on right thigh and gluteal region, 1C – Bleeding from the mucosal lesion in oral cavity, 1D – Congregated and haemorrhagic vesiculo-papular lesions in the right lower limb, 1E – Scattered hemorrhagic spots on the epicardial surface, 1F – Large areas of cortico-medullary hemorrhages

Upper gastrointestinal endoscopy (UGIE) performed on the day after his admission revealed widespread Candida infection with multiple small ulcers all along the mucosal area along with areas of active bleeding suggestive of acute esophagitis secondary to esophageal candidiasis with superadded bacterial infection. Owing to esophageal involvement, the individual was started on injection acyclovir and was managed with barrier nursing techniques. During the course of hospital stay, he started bleeding from the skin and the mucosal lesions (Fig 1C). Subsequently, he developed hematemesis (vomitus around 400 milliliters of blood).

Laboratory investigations revealed a persistently high total leukocyte count (TLC) with mild transaminitis and preserved renal function. Evidence of DIC was present in the form of thrombocytopenia, prolonged prothrombin time (PT), raised D-dimer and fibrin degradation products (FDPs) and reduced fibrinogen. Fresh frozen plasma (FFP) and whole blood were transfused to correct the deranged coagulation profile. Despite vigorous treatment, the patient's condition progressively deteriorated as he developed hematuria, continued to ooze blood from the skin lesions along with multiple episodes of hematemesis. On the third day of admission, the patient succumbed to his illness.

Pathological Findings

Postmortem examination was carried out after taking an informed consent from the next of kin. Salient gross findings included congregated and haemorrhagic vesiculo-papular lesions all over the face, neck, chest, abdomen, back, arms and both lower limbs (Fig 1D). Cardiopulmonary evaluation revealed hemorrhagic pleural effusion (200 milliliters), oozing of fresh blood from lung parenchyma, hemorrhagic pericardial effusion (100 milliliters) with scattered hemorrhagic spots on the epicardial surface as well as pericardial cavity (Fig 1E). Cut surface of both kidneys revealed large areas of cortico-medullary hemorrhages (Fig 1F). Esophageal candidiasis was present corroborating the UGIE ante-mortem findings. Fresh as well as altered blood was noted in the lumen of stomach and intestine. On microscopic examination, lungs revealed mononuclear inflammatory infiltrate in the parenchyma, alveolar hemorrhage along with congestion of pulmonary vasculature (Fig 2A), liver showed marked Kupffer cell hyperplasia along with mild biliary stasis (Fig 2B) whereas the kidneys showed presence of cortico-medullary hemorrhage (Fig 2C). Histopathological evaluation of the vesicular eruption revealed intra-epidermal clefting with hemorrhage in the cavity. No viral inclusions were noted in the epidermal cells.

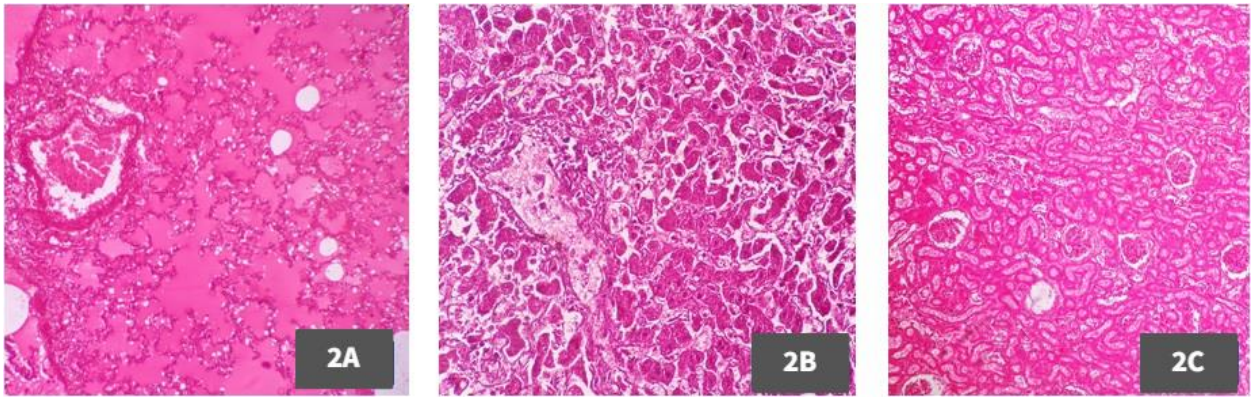

Figure 2 2A – Alveolar hemorrhage along with congestion of pulmonary vasculature (H&E; 100x), Figure 2B – Kupffer cell hyperplasia along with mild biliary stasis (H&E; 100x), Figure 2C – Cortico-medullary hemorrhage (H&E; 100x)

Discussion

VZV is a human alpha-herpes virus (HHV3) which causes varicella (chickenpox) and herpes zoster (shingles). Primary infection with VZV leads to varicella while reactivation of the latent virus in dorsal root ganglia causes herpes zoster. Transmission occurs via the respiratory route followed by localized replication in the nasopharynx with subsequent seeding of the reticulo-endothelial system eventually leading to viremia. The incubation period of chickenpox ranges from 10 to 21 days with an average span of 14 - 17 days. Patients are infectious approximately 48 hours prior to the onset of rash and remain so till all the lesions have crusted4. The disease is usually a benign, self-limiting one. However, in susceptible groups, various complications have been documented resulting in severe disease with prolonged hospitalization which occasionally turn out to be fatal. These groups include adults, immunocompromised persons, pregnant women and neonates. Immunocompromised patients are particularly at a higher risk for visceral complications, which can be fatal in the absence of antiviral therapy. The most common complications include secondary bacterial infection of skin lesions, pneumonia and central nervous system manifestations in the form of meningoencephalitis and cerebellar ataxia. Other rarer complications include hepatitis, nephritis and hematological complications like thrombocytopenia5. DIC is a grave complication which can be seen in some immunocompromised patients6.

The case in discussion had history of high-risk conduct along with clinical signs of immunodeficiency in the form of oro-pharyngo-esophageal candidiasis; however, the precise cause of his altered immunity was obscure. Administration of steroids by local practitioners ("quacks") is a common malpractice which could be a possibility for his depressed immunity7, eventually giving rise to the fulminant course of his illness. This possibility cannot be ruled out which might have ultimately caused the visceral complications in the form of DIC, massive hematemesis and visceral bleed steering to hemorrhagic shock, multi-organ dysfunction and in the end, death. Very few cases of VZV infection leading to DIC have been reported in literature, which have been highlighted in Table 1.

This case report highlights the rapidly fatal course of a fairly common and apparently benign disease such as chickenpox. In spite of aggressive management with injectable antivirals, antibiotics, FFP and other supportive measures, the young patient succumbed to DIC. It also lays emphasis on the need for VZV active vaccination in susceptible population as is recommended by various authorities in the form of two-dose schedule for all persons aged more than 13 years at an interval of six weeks8. Although the vaccine is highly efficient in disease prevention, breakthrough infections are known to befall, which however are much trivial in severity than those in unvaccinated individuals8. This case also emphasizes and underlines the importance of barrier nursing and prompt chemoprophylaxis of all the close contacts and probable contacts with acyclovir, as echoed by nil cases of chicken pox amongst the healthcare workers who were involved in managing the case actively.

Conclusion

To conclude, we report a case of tortuous VZV infection with a rare severe complication i.e., DIC in a suspected immunocompromised patient resulting in rapidly deteriorating course despite aggressive management in the form of injectable antivirals and coagulation component support. The other worthy and notable aspect of the case is the significance of barrier nursing and chemoprophylaxis in preventing any cross-infection and the importance of VZV vaccination in susceptible adults in minimizing the transmission of this highly contagious disease.

S no	Year	Author	Country	No of cases	Case	Outcome
1.[9]	1994	Anderson et al	USA	01	Varicella Hepatitis: A Fatal Case in a Previously Healthy, Immunocompetent 26 y/o male.	Succumbed
2.[10]	1998	U Hollenstein, F ThaIhammer, H. Burgmann	Austria	01	Disseminated Intravascular Coagulation (DIC) and Rhabdomyolysis in Fulminant Varicella Infection in a 30 y/o female with Multiple sclerosis	Recovered
3[11].	2001	Tucciarone et al	Italy	01	Disseminated intravascular coagulation in chickenpox. Report of a case in a 05 y/o male child	Recovered
4.[12]	2004	Lee S et al	Japan	01	Fulminant varicella infection complicated with acute respiratory distress syndrome, and disseminated intravascular coagulation in an immunocompetent 23 y/o male	Recovered
5.[13]	2008	Sudheer P S Ahamed, Abdullah Balkhair, Rajan Krishnan	Oman	01	Fulminant Varicella Zoster Infection with Multiorgan Involvement In a 22 y/o female	Recovered
6.[14]	2013	Hideharu Hagiya, Maya Kimura, Toru Miyamoto and Fumio Otsuka	Japan	01	Systemic VZV infection with DIC in a 69 y/o male	Recovered
7.[15]	2017	Salunke et al	India	01	Cyclophosphamide and varicella zoster virus induced disseminated intravascular coagulopathy with fatal outcome in a 28 y/o male with Pemphigus vulgaris	Succumbed
8.[16]	2018	Sahay et al	India	01	35 y/o male with bleeding and DIC. VZV diagnosed on autopsy	Succumbed
9.[17]	2019	Furuto et al	Japan	01	Successful management of visceral disseminated varicella zoster virus infection during treatment of membranous nephropathy in a 36 y/o female	Recovered
10.[18]	2020	Zhang et al	China	01	Fatal hemorrhagic varicella in a patient with abdominal pain in a 19 y/o female	Succumbed
11.[19]	2020	Bastard et al	France	01	16 y/o male with Nephrotic syndrome	Succumbed
12.[20]	2020	Vassia et al	Italy	01	Unusual presentation of fatal disseminated varicella zoster virus infection in a 49 y/o female with lupus nephritis	Succumbed
13.[21]	2021	Wang D, Wang J, Tao X	China	01	Fatal visceral disseminated varicella-zoster virus infection in a 33 y/o male renal transplant recipient	Succumbed
14.[22]	2021	Takahashi et al	Japan		Pneumonia and central nervous system infection caused by reactivation of varicella-zoster virus in a living-donor kidney transplantation 30 y/o male patient	Succumbed
15.[23]	2022	Kuwano et al	Japan		An Autopsy Case of Disseminated Varicella Zoster Virus Infection during the Treatment of Nephrotic Syndrome in a 68 y/o female	Succumbed
16.[24]	2023	Jing Jiang et al	China		Varicella-associated disseminated intravascular coagulation secondary to Henoch-Schönlein purpura with renal and gastrointestinal system involvement in an 08 y/o female child	Recovered

17.	2023	This case	India	01	25 y/o male with VZV infection and upper GI candidiasis complicated with DIC	Succumbed

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