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CASE REPORT

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Generalized tetanus complicated with Takotsubo-cardiomyopathy in a septuagenarian following a laceration injury with soil contamination – a case report

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Abstract

Background Tetanus is a clinical rarity due to the successful globally adopted childhood vaccination programme. The rising elderly population in the United Kingdom creates a subset of individuals whom are prone to develop Tetanus as they preceded this vaccination drive.

Case summary A 76 year old Caucasian lady presented with a soil contaminated laceration injury on her knee following a fall. Though she received urgent assessment and wound care, the relevance of the injury in the backdrop of her age was not appreciated and her tetanus post exposure prophylaxis was overlooked. She readmitted seeking further management 1 week later with an infected wound with Trismus and clinical features favoring Generalized tetanus. During her stay she developed Takotsubo-cardiomyopathy with congestive cardiac failure and required prolonged care in the intensive unit with mechanical ventilation and rehabilitation before being discharged home.

Conclusion First contact physicians should have a greater appreciation of the types of injuries and at-risk individuals who are more prone to develop tetanus upon exposure to ensure early and appropriate identification. There should be greater situational awareness with regard to the elderly in view of their heightened risk of development of tetanus specially those born before the vaccination drive. Knowledge regarding post exposure prophylaxis measures for tetanus should be regularly updated using local guidance to ensure awareness, so as to despite its rarity Tetanus remains an adequately appreciated disease.

Keywords Tetanus, Elderly, Vaccination, Post exposure prophylaxis, Cardiac complications, Takotsubo-cardiomyopathy

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Introduction

Tetanus is a potentially fatal disease caused by *Clostridium Tetani*, an anaerobic organism which is mainly found in the soil and is globally ubiquitous. Soil contaminated wounds are the primary source of entry for this organism, which produces Tetanospasmin, an endotoxin that results in muscle spasms [1]. Childhood vaccination schedule inclusive of Tetanus Toxoid (TT) has resulted in marked reduction of cases globally. However, it still remains a prevalent problem in developing nations [2, 3]. According to Public Health England (PHE), only 7 cases of Tetanus were reported in the year 2020 in the United Kingdom(UK), of which 5 of the patients were born before 1961, the year when routine childhood vaccinations inclusive of TT were introduced to the UK [4, 5]. The primary reason to develop Tetanus following exposure is attributed to non-vaccination or incomplete vaccination, predisposing the individual to develop Tetanus [6]. The UK has an ageing population, with nearly 5.4 million people above the age of 75 years [7], this creates a unique subset of elderly populace who are at-risk to develop Tetanus upon initial exposure and more so when inadequate post-exposure prophylaxis measures are practiced. We present a case of a septuagenarian who developed Tetanus with cardiac complications after an initial soil contaminated laceration injury following a fall.

Case presentation

An independent and self-caring 76 year old female presented to the emergency department on the same day following an accidental fall in the garden. Her past medical history included well controlled chronic obstructive airway disease, sciatica, gastroesophageal reflux and hyperlipidaemia. Her regular medications were oral Simvastatin 10 mg nocte, Omeprazole 20 mg once daily, Carbocisteine 750 mg twice daily, Symbicort 200/6 mcg/dose twice daily, Tiotropium 1mcg OD and Salbutamol inhaler PRN. Upon initial review, she only had a superficial laceration to the left lower leg. Her remaining systemic clinical examination was normal and there were no signs of significant trauma. Her wound was cleaned and dressed with steri-strips and she was discharged. She was initiated on antibiotics and pain relief, with oral Flucloxacillin 500 mg QDS for 7 days duration along with oral Paracetmol 1gm QDS/PRN with advice and guidance due to a likely infection. However, due to gastrointestinal side effects of Flucloxacillin she was only compliant for 3 doses and her antibiotics were changed to oral Clarithromycin 500 mg BD. However, on day 8 her clinical situation worsened as there was active discharge from the wound. The laceration appeared infected which prompted urgent readmission to the Emergency Department. Upon preliminary review, the laceration site appeared inflamed and infected with surrounding skin appearing necrotic [Fig. 1]. She additionally complained of reduced intake of food and was only managing sips of fluids. Further questioning revealed this was due to her inability to open her jaw fully and this was new in onset and had progressively worsened in the preceding 24 h. Suspecting Tetanus further inquiry revealed she had not received her childhood Tetanus vaccination as it was not yet a routine health practice during her time. On examination she appeared to be uncomfortable at rest. She had limited capacity to open her mouth actively or passively and the clinical picture was suggestive of Trismus. Her vitals were normal with a pulse rate of 86 beats per min with a blood pressure of 126 mmHg systole and 74mmHg diastole. She was afebrile and her on air saturation was 97% with a respiratory rate of 16 per minute which appeared normal in effort. Her cardiovascular, respiratory, abdominal and remaining neurological examination were normal. Her whole blood analysis revealed a neutrophilic predominance [8.6×10^9/L (4–11)] with a white cell count at the upper normal limit. The rest of the investigations including liver functions, renal functions, coagulation profile and C-reactive protein were normal (Table 1). Her baseline 12-lead electrocardiograph (ECG) demonstrated normal sinus rhythm. The initial venous blood gas was normal. She was initially given intravenous (IV) diazepam 5 mg along with IV magnesium infusion of 5gm over 2 h to reduce her muscle spasms. She was also given intramuscular Tetanus immunoglobulin 500 units and IM tetanus toxoid vaccine(Revaxis 0.5 ml) at a separate site. Additionally, she was started on IV Benzylpenicillin 1.2 gm QDS and IV metronidazole 500 mg TDS as antibiotic cover along with normal saline infusion for hydration after taking blood and wound swab for cultures. She was reviewed by a multidisciplinary team of intensivists, orthopaedic surgeons, ENT surgeons and General physicians and the initial working plan was for ward-based care with close observation of vitals. As her clinical condition failed to improve, she underwent nasogastric tube(NG) insertion under Flexible Nasal Endoscopy (FNE) guidance to avoid aspiration and facilitate feeding, with the FNE showing no immediate airway concerns. She maintained on air saturation at 96% and the recommendation was for fibreoptic nasal intubation if and when the need arose. On the same day she underwent urgent surgical debridement of the infected wound under local anaesthesia and the tissue was also sent for culture. She remained stable with limited progression of her neurological symptoms.She was planned for initial ward-based care as she remained stable. On day 10 she required 1 L oxygen via nasal cannula to maintain saturations, however other vital parameters were stable with a respiratory rate of 18/min, pulse rate of 67/min and blood pressure of 152mmHg systole and 76mmHg diastole. On day 11 she acutely deteriorated with new onset

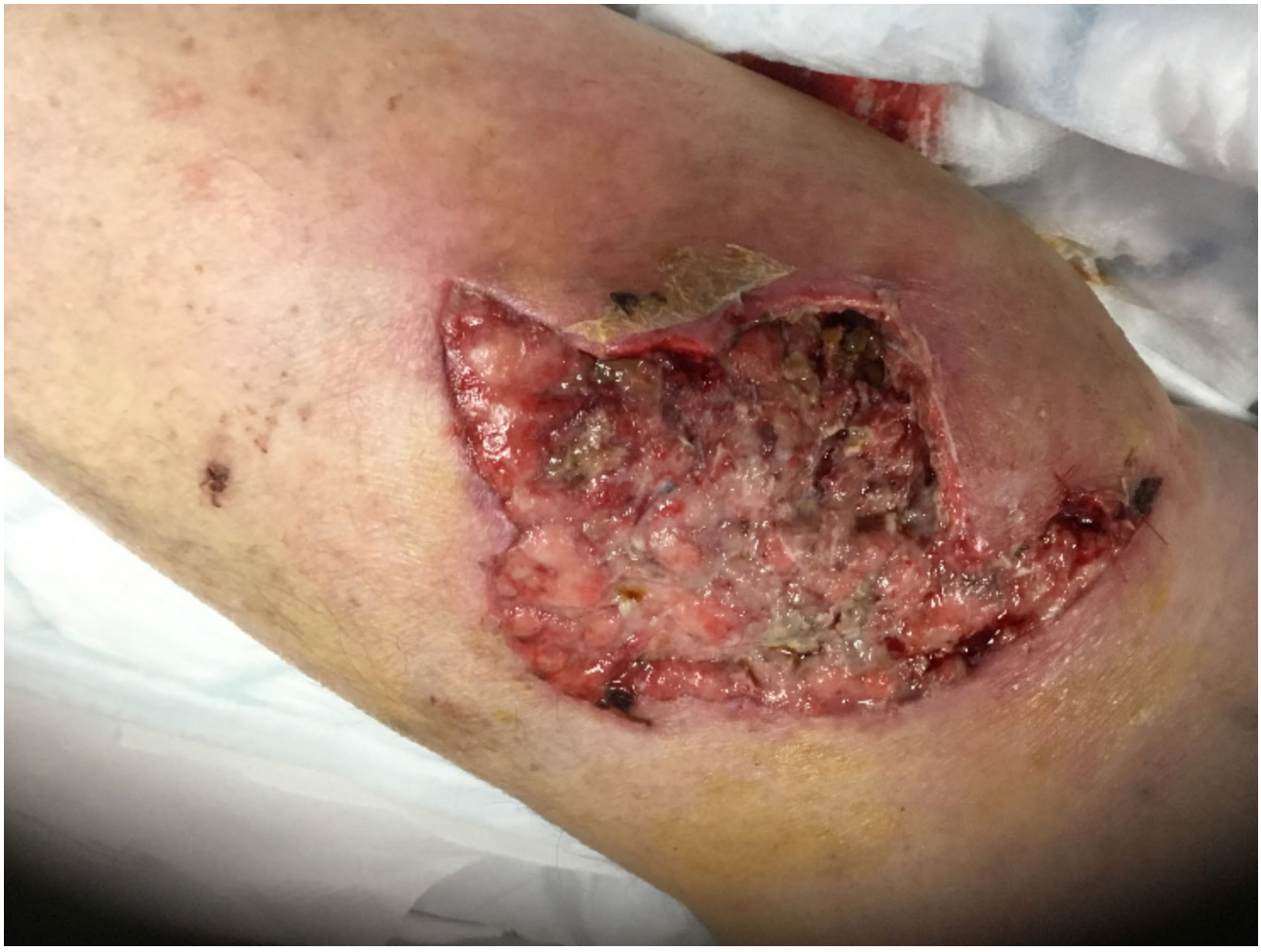

Fig. 1 Infected laceration injury following the fall

respiratory distress with active oral secretions. She was found to be tachycardic with a heart rate of 126 beats per minute and an elevated respiratory rate of 35 per minute and with a low blood pressure 87 mm Hg systole and 56 mmHg diastole. She required 40% oxygen through venturi mask to maintain saturation at 97% and auscultation of the lungs revealed bilateral wheeze and crackles. On reassessment She had grade 3 Trismus with normal neck movement. Repeat urgent FNE confirmed NG position and also showed adequate glottic space and vocal cord movement with no upper airway obstruction, but mucus secretions were noted. But given the clinical deterioration a consensus was reached between the intensivists and medical team that she was at high risk of further worsening, and hence she pre-emptively underwent emergency fibreoptic guided nasal intubation in theatre and was managed in the ITU with sedation. Due to cardiogenic shock she was urgently initiated on IV Noradrenaline 1 mcg/kg/min to maintain her blood pressure targeting a MAP of 65 mmHg. Considering the role of autonomic dysfunction, she was also started on a variable rate IV magnesium sulfate infusion of 0.5- 5gm/hr targeting a serum Mg 2+of >2 mmol/l. Her investigations were repeated and an elevated Troponin I at 537 ng/L [<5 ng/L] was noted with a subsequent repeat Troponin I showing further rise with elevated Pro BNP levels. The inflammatory markers were also raised [Table 2]. arterial blood gas demonstrated Type 1 respiratory failure [Table 2]. A repeat ECG showed Q waves from V1-V6. A transthoracic 2D echocardiogram demonstrated a normal sized left ventricle but with a reduced ejection fraction of 37% (Simpsons Biplane) with multiple regional wall motion abnormalities including akinesis in mid-apical segments. Her chest X-ray demonstrated bilateral small effusions. The initial suspicion was Takotsubo cardiomyopathy with congestive cardiac failure in the background of Tetanus. To treat her pulmonary oedema she was given IV furosemide 60 mg BD, while she was also started on dual antiplatelets, Aspirin 75 mg nocte and Clopidogrel 75 mg nocte as a precautionary measure in view of covering a potential acute coronary event.

Table 1 Baseline laboratory parameters- day 08

Investigations and reference ranges	Values
Full blood count	
White blood cells [x109 /L (4–11)]	10.2
Neutrophil [x109 /L (7.5–11)]	8.6
Lymphocytes [x109 /L (1.5-4.0)]	0.9
Haemoglobin [g/L (115–165)]	126
PCV [L/L (0.4–054)]	0.361
Platelet counts [x109/L (150,000-450,000)]	366
Renal functions	
Serum Sodium [mmol/L (135–145)]	136
Serum Potassium [mmol/L (3,5-5.1)]	3.5
Serum Creatinine [µmol/L (44–97)]	58
Blood Urea [mmol/L (2.5 to 7.1)]	4.9
EGFR ml/min/1.73m^2	87
Electrolytes	
Serum chloride [mmol/L (95–108)]	106
Inorganic phosphate [mmol/L (0.8–1.5)]	0.97
Total calcium [mmol/L (2.12–2.62)]	2.35
Adjusted calcium [mmol/L (2.20–2.60)]	2.46
Magnesium [mmol/L (0.7-1.00)]	0.88
Inflammatory markers	
C-Reactive protein [< 5 mg/dl]	19
Coagulation screen	
APTT [23.0–31.0 s]	27
PT [9.5–13.5 s]	12
PT ratio [0.8–1.25]	1.03
Liver functions	
Bilirubin [0-21umol/l)	11
Alanine transaminase [< 41 iu/L)	25
Albumin [35–50 g/L)	38
Alkaline phosphate [30–130 U/L)	61
Total protein [60–80 g/L)	68

Table 2 Laboratory parameters

Investigations and reference ranges	Values			
	Day 11	Day 12	Day 13	Day 14
Cardiac markers				
Troponin I (HS) [< 5 ng/L]	537	644	381	340
NT Pro BNP [< 300 pg/ml]	1971			
Inflammatory markers				
C-Reactive protein [< 5 mg/dl]	26	52	257	92
Renal functions				
Serum Sodium [mmol/L (135–145)]	136	139	149	141
Serum Potassium [mmol/L (3,5-5.1)]	3.5	4.4	3.6	4.1
Serum Creatinine [µmol/L (44–97)]	58	72	62	59
Blood Urea [mmol/L (2.5 to 7.1)]	4.9	5.5	4.4	7
EGFR ml/min/1.73m^2	87	71	85	87
Electrolytes				
Serum chloride [mmol/L (95–108)]	106	108	108	104
Inorganic phosphate [mmol/L (0.8–1.5)]	0.97	1.07	1.03	1.47
Total calcium [mmol/L (2.12–2.62)]	2.35	2.13	1.94	1.83
Adjusted calcium [mmol/L (2.20–2.60)]	2.46	2.29	2.19	2.09
Magnesium [mmol/L (0.7-1.00)]	0.88	1.19	2.92	2.15

On day 13, her tissue culture report returned confirming *Clostridium Tetani*. As Tetanus is a notifiable disease, Public Health England was informed through proper channels. She gradually stabilized during her intensive care stay and inotropes were successfully tapered down slowly and was stopped on day 17 with the diuretics being tapered down as well. Her antibiotics were completed at day 22 and were stopped. As she remained ventilator dependant and in view of potential prolonged intubation, she underwent staged tracheostomy. Though she subsequently remained well with normal haematological and haemodynamic parameters, she stayed in the intensive care for a total of 64 days primarily for ventilation purpose and required another further 20 days for slow respiratory weaning.

After being successfully weaned off respiratory support she subsequently underwent tracheostomy reversal along with physiotherapy, rehabilitation and was successfully discharged back home.

Discussion

The implementation of childhood vaccination programmes worldwide has caused a significant reduction in the incidence of Tetanus cases. However, it still remains a cause for concern among the groups at extremes of age. In the developed nations it is primarily a disease afflicting the elderly [8, 9]. Immunity against Tetanus can only be gained through immunization, with inactivated Tetanus toxoid (TT) containing vaccines. These vaccines maybe single antigen vaccines (monovalent) or more commonly part of a Tetanus Toxoid containing vaccines (TTCV) e.g., diptheria, tetanus and acellular pertussis (DTP), pentavalent (5 in 1) or hexavalent (6 in 1) vaccines [10]. In the United Kingdom, as per NHS guidance the hexavalent vaccine [Infanrix hexa®] is administered at 8, 12 and 16-weeks following birth and confers protection against Tetanus. An interval of 4 weeks between each dose is needed to induce adequate immune response and after the 3rd dose the effectiveness is very high. In UK subsequent TT containing vaccine booster doses are given at pre-school (3 years 4 months) and at adolescence (14 years) to ensure sufficient immunity to last through early adulthood which helps prevent Tetanus. [11, 12] As the vaccination programme had only commenced after 1961, those born before this year are naturally more vulnerable to develop Tetanus as a complication and in the United Kingdom with an ageing population the highest incidence of Tetanus was noted in those above the age of 65 years [5].

Identifying wounds at risk for Tetanus is crucial as it will help dictate immediate management which could be lifesaving. When clinically relevant, wounds should be classified as Tetanus-prone wounds when they include (a) puncture type wounds e.g., due to gardening, (b)

when they contain foreign bodies and debris or (c) associated with compound fractures (d) burns with systemic sepsis or (e) are wounds that are due to certain animal bites and scratches. The risk category is further increased to high-risk tetanus-prone wounds when there is greater contamination, extensive devitalised tissue and wounds that required surgical debridement but were delayed greater than 6 h. The initial principals of management include wound care and if needed early debridement, use of antibiotics with adequate spectrum of anaerobic cover and based on risk assessment timely post exposure prophylaxis(PEP). [12, 13] When the wound is Tetanus prone, the need of PEP also depends on the vaccination history e.g., having received a priming course and booster doses, or if there is uncertain immunisation history and if the patient was born before 1961. If the latter two criteria are met the current guidance strongly recommends the use of PEP with Immunoglobulins to hasten the escalation of antibody levels in those lacking adequate antibody levels or with inadequate rapid memory response due to incomplete or no prior vaccination. The recommendation is to administer intra-muscular tetanus immunoglobulin (IM-TIG) 250 IU immediately or 500 IU if more than 24 h have passed. This will result in adequate anti-toxin levels 2–3 days post administration which can last up to 4 weeks. If IM-TIG is unavailable a recommended alternative option is human normal immunoglobulin (HNIG), the dose of which dependant on body weight. Additionally, IM Tetanus toxoid should also be co-administered at a separate site as Tetanus does not induce immunity [Supplementary table] [12–16]. The value of immunoglobulins even when there is delay to seek medical care is justified due to the variable incubation period. The mechanism of action of immunoglobulins is by neutralizing the circulating unbound toxin, tetanospasmin. However, once tetanospasmin binds to neural tissue the damage is irreversible, stressing the need for early accurate identification of Tetanus prone wounds and the timely use of IM-ITG or an equivalent [15] as this has shown to improve survival [17].

Clostridrium Tetani has a variable incubation period ranging from 1-day up to 60 days, with shorter period of incubation being associated with severe symptoms. The patterns of presentation of Tetanus is variable but generalised Tetanus is the commonest in adults while cephalic and localised forms are seen less often. The classical "Lock Jaw" tends to be seen frequently and usually tends to be the first sign of an evolving spectrum of manifestations [18]. Based on severity of neuromuscular manifestations and cardiorespiratory compromise Tetanus can be graded from Stage I-IV according to Ablett's classification [19]. The focus of management at this point shifts towards supportive care with ample use of benzodiazepines for spasm, monitoring and managing autonomic dysfunction, maintaining ventilation and efficient nursing with good bed care [12]. Tetanus can cause a spectrum of cardiac manifestations due to autonomic dysfunction ranging from labile blood pressure to arrythmias and can result in sudden cardiac arrest and death. It has become an important cause of mortality in severe forms of Tetanus more so than respiratory failure due to the improvements in mechanical ventilation and ICU care [20, 21].

Takotsubo cardiomyopathy is a form of reversible heart-failure that occurs as an infrequent complication to a stressor, and this phenomenon is mostly observed in postmenopausal elderly females. The stressor can either be a physical or an emotional trigger [22]. The postulated mechanisms include hypothalamic pituitary adrenal axis activation with an ensuing catecholamine surge that causes cardiac insult. This insult occurs due to either direct myocardial toxicity or is indirectly brought about by myocyte hypoxia caused by a mismatch between oxygen supply and demand. This ensuing myocardial damage usually causes regional wall abnormalities in multiple territories beyond a single coronary vascular bed and results in heart failure, as was observed in our patient [Supplementary data] [23, 24] Bacterial, viral and parasitic Infections can trigger cardiomyopathy due to complex mechanisms, similarly they can also precipitate acute cases of Takotsubo cardiomyopathy which are documented [25]. Sympathetic overactivity resulting in adrenergic crisis is a phenomenon seen in Tetanus, and Takotsubo cardiomyopathy has been rarely documented in patients complicated with severe Tetanus [26, 27].

Tetanus can be fatal and has a variable rate of mortality ranging from 10% up to 90% in different countries [12, 28]. Adequate intensive care facility along with good supportive care and rehabilitation plays a pivotal role in reducing fatality rates which may explain the comparatively lower mortality rates in developed nations [29]. Regardless due to the nature of the illness, the period of hospitalisation usually tends to be prolonged with a similar time needed for rehabilitation and return to baseline functionality [9]. Furthermore, when it comes to elderly patients this situation gives rise to concern as to the uncertainty of final outcome and possible increased mortality, as prolonged ICU stay in elderly has been shown to have a higher mortality [30, 31], as elderly patients tend to be at a poor baseline health status to begin with, and concomitant comorbidities which may determine the patient outcome [31]. Because of this, there is also an added financial burden on the healthcare system, as the overall cost per patient can be very high when managing Tetanus [9]. This highlights the importance of prevention rather than actively managing the complication of a fully evolved Tetanus. In such situations referring proper guidance is vital, either hospital trust guidelines or National guidelines. To reinforce this NHS UK provides

clear, updated and comprehensive guidance with a dedicated chapter on Tetanus in the Immunization against infectious disease (green book), the national guidelines for vaccines and infectious diseases [12].

Our patient was a classic example of an at-risk individual by virtue of her age and the absence of childhood vaccination. She sustained a typical Tetanus prone wound and did not receive appropriate PEP. There was rapid evolution of symptoms implying a short incubation period as she developed a severe generalised tetanus with cardiac complications. She was the text book example of a patient whose clinical manifestation of Tetanus could have been avoided had there been timely recognition of her predisposing risk factors e.g., her age and exposure and that she met the criteria met for utilisation of PEP.

Conclusion

This case highlights the need for greater clinical awareness of identification of situations predisposing to Tetanus and where following protocols of preventive therapy is imperative, rather than recognising the overt clinical manifestation of Tetanus that follows as a complication. Tetanus is becoming a rarity and this subsequently resulted in reduced situational awareness amongst first contact physicians who though having the knowledge to recognise the hallmark manifestations of classic Tetanus, may fail to appreciate the finer nuances of guidance on at-risk situations and not take the necessary measures including administration of PEP essential to counter the disease. It may be worth implementing policies that recommend to act proactively to prevent tetanus on first contact, such as recognising recurrent fallers who often happen to be elderly, for tetanus vaccinations prophylactically when seen in the emergency department, who often happen to be elderly.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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SB: Data collection, data analysis, manuscript composition and critical appraisalRNM: Data collection, data analysis and manuscript composition and revisionMI: Data collection, data analysis and revision UM: Data collection, data analysis and revision.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval
Not applicable.

Consent for publication
Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Consent to participate
Written informed consent was obtained from the patient/participant for writing this case report.

Competing interests
The authors declare no competing interests.

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