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CLINICAL REPORT

Internal jugular vein thrombosis associated with venous hypoplasia and protein S deficiency revealed by ultrasonography

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Abstract A 41-year-old woman, who had no thrombotic risk factors and past history except congenital scoliosis, underwent central venous catheterization (CVC) before correction of the scoliosis. When internal jugular vein (IJV) catheterization using the anatomical landmark technique failed, CVC under ultrasound guidance was tried. As a consequence, thrombosis and hypoplasia of the right IJV were incidentally detected by ultrasonography. Central venous catheters were then successfully placed in other veins under ultrasound guidance. Also, after examinations to rule out the possibility of pulmonary embolism and to clarify the causes of the IJV thrombosis, the patient was found to have protein S deficiency. CVC under ultrasound guidance should be recommended to prevent the failure of cannulation and complications such as thromboembolism in patients who could possibly have anomalies of vessels as a result of anatomical deformities caused by severe scoliosis, even if patients do not have thrombotic risk factors such as a history of central catheter insertion or intravenous drug abuse, cancer, advanced age, cerebral infarction, and left ventricular dysfunction. Also, if venous thrombosis is found in patients without predisposing risk factors, one should ascertain the cause of the hypercoagulable state, for example protein S deficiency, and perform appropriate treatment and prevention of venous thromboembolism.

Keywords Protein S deficiency · Ultrasonography · Venous thrombosis · Venous hypoplasia

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Introduction

Central venous catheterization (CVC) is commonly used in the operative setting for central venous pressure monitoring, drug administration, and rapid resuscitation of fluids. Usually, the right internal jugular vein is the preferred access site.

We incidentally found thrombosis of the right internal jugular vein (IJV), which was hypoplastic, via ultrasonography (USG) which took place after failure of right IJV catheterization by the anatomical landmark technique (ALT), in a 41-year-old woman who was scheduled for correction of scoliosis.

Risk factors for intravenous thrombus are a history of central venous catheter insertion or intravenous drug abuse, advanced age, cerebral infarction, bedridden state, and left ventricular dysfunction. There are several reports of IJV thrombosis detected by ultrasonography during CVC in patients with thrombotic risk factors [1, 2]. However, the patient in this case did not have any preexisting risk factors. Also, isolated IJV thrombosis seems to develop primarily as a result of long-term placement of central venous catheters [3, 4]. However, in this case, multiple attempts at guide wire insertion became a provoking factor of the thrombosis despite its ultra short duration. We also report her hypercoagulable state associated with protein S deficiency found during examinations to rule out the possibility of pulmonary embolism (PE), and clarify the causes of the IJV thrombosis.

Case report

A 41-year-old, 50 kg, 148 cm woman, diagnosed with congenital scoliosis, was admitted because of back pain

and scheduled for correction of scoliosis (T3–L5). She had no past history of CVC, neck surgery, hormone therapy, or venous thromboembolism (VTE). She had no limitation of ordinary physical activity, and her head was tilted slightly to the right because of scoliosis. Electrocardiogram (ECG), pulmonary function test, transthoracic echocardiography, and routine blood examinations were normal.

On the operation day, the patient was premedicated with midazolam 2 mg IM and glycopyrrolate 0.2 mg IM. Monitors for electrocardiogram (ECG), noninvasive blood pressure, pulse oximetry (SpO_2), capnogram, spectral entropy, and a nerve stimulator for train-of-four (TOF) stimulation were applied using an S/5TMmulti channel anesthesia monitor (Datex-Ohmeda, USA). Her initial blood pressure (BP) was 135/85 mmHg, heart rate (HR) 90 beats/min, and oxygen saturation 100% in room air. Anesthesia was induced with propofol, 100 mg IV, and rocuronium, 35 mg IV, to facilitate endotracheal intubation. Mechanical ventilation was started with a fraction of inspired oxygen (FiO_2) of 0.5 using O_2 and air, tidal volume of 450 ml, and respiratory rate of 12 breaths/min. Anesthesia was maintained with a target-controlled infusion of propofol with a target concentration of 3–5 μg/ml and remifentanil with a target concentration of 1.5–3.5 ng/ml, titrated according to the spectral entropy and hemodynamic responses. The end-tidal CO_2 concentration ($ETCO_2$), spectral entropy, and TOF ratio were kept at 35–40 mmHg, 40–60, and 0.1–0.5, respectively. We started invasive BP monitoring by radial artery cannulation and measured the esophageal temperature with a body-temperature monitor. Motor evoked potentials were also monitored to prevent neurologic injury during the operation. Afterwards, ALT was used for right IJV catheterization. After placing an 18 gauge thin wall needle into the right IJV, we tried 3 times to insert a guide wire into the vein while changing the direction the J-tip was inserted through the needle, but, because of resistance, the wire could not be advanced further than 1 cm from the tip of the needle. Venipuncture of the right IJV was attempted, and once more the attempts to insert a guide wire were made 3 times, but the wire could not be inserted more than the aforementioned depth. After withdrawal of the wire, a substantial amount of blood clot was found on the tip. We decided to use USG to reduce the number of needle passes and complications. The ultrasonogram showed the right IJV was partially obstructed by a thrombus situated just under the clavicle (Fig. 1). So, we inserted a catheter in the right external jugular vein after confirming via USG that no obstructive lesion was in the right subclavian and innominate veins. In consideration of the risk of massive bleeding because of the nature of the operation, the second CVC was performed in the left IJV using USG.

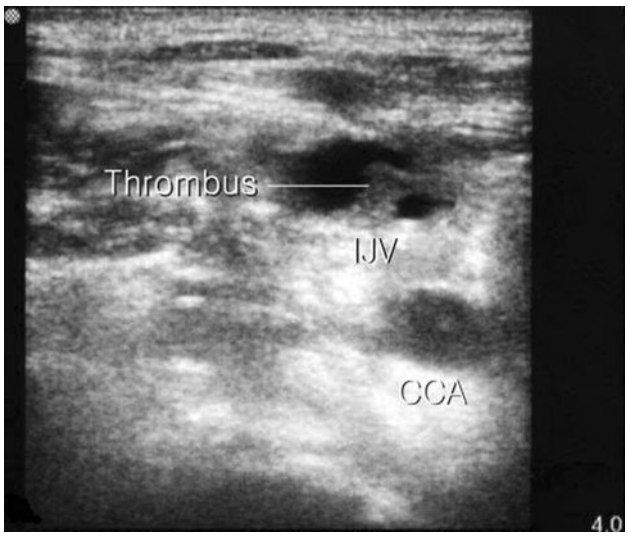

Fig. 1 Neck ultrasound image in the Trendelenburg position after anesthesia induction (short-axis view at the level of the clavicle). Inhomogeneously echogenic intraluminal thrombus (thickness 0.5 × 0.7 cm, *white line*) in the right internal jugular vein (*IJV*) (diameter 0.7 × 1.0 cm) can be observed. The right IJV is partially obstructed by a thrombus. *CCA* common carotid artery

During the operation, the patient's vital signs were stable with BP at 110–150/60–90 mmHg, HR 80–110 beats/min, SpO_2 98–100%, body temperature 35.5–36.5°C except during the 20 min period when the systole BP dropped to 70–80 mmHg as the rods were being assembled and the spine was being straightened. Total duration of surgery was 305 min. Initial hemoglobin and central venous pressure were 14 g/dL and 7 mmHg, respectively. They remained relatively steady during the operation and were 11.6 g/dL and 5 mmHg at the end of the operation. Total estimated blood loss was approximately 4500 mL and the total amounts of blood transfusion given were 13 units of packed RBC and 13 units of fresh frozen plasma. There were no evident signs of PE, for example sudden fall of $ETCO_2$, SpO_2 or BP during the operation.

The patient complained of chest pain, 20 min after arriving at the recovery room. The ECG showed extensive T-wave inversion in leads II, III, and V3 to V6. Arterial blood gas analysis showed unremarkable results. However, vital signs were stable and the chest pain disappeared after approximately 1 h. Cardiac enzyme, troponin T was within normal range. D-dimer, antithrombin III, fibrinogen, PT/aPTT, and protein C/S activity were examined to rule out the possibility of PE and to clarify the causes of the IJV thrombosis. The results showed D-dimer increased to 5420 ng/ml (normal range 0–500 ng/ml) and protein S activity decreased to 34% (normal range 58.7–119.2%), but other factors were within normal range. No thrombus could be detected in her heart by transthoracic echocardiography and her heart chambers showed normal regional wall motions. But her systolic pulmonary artery pressure

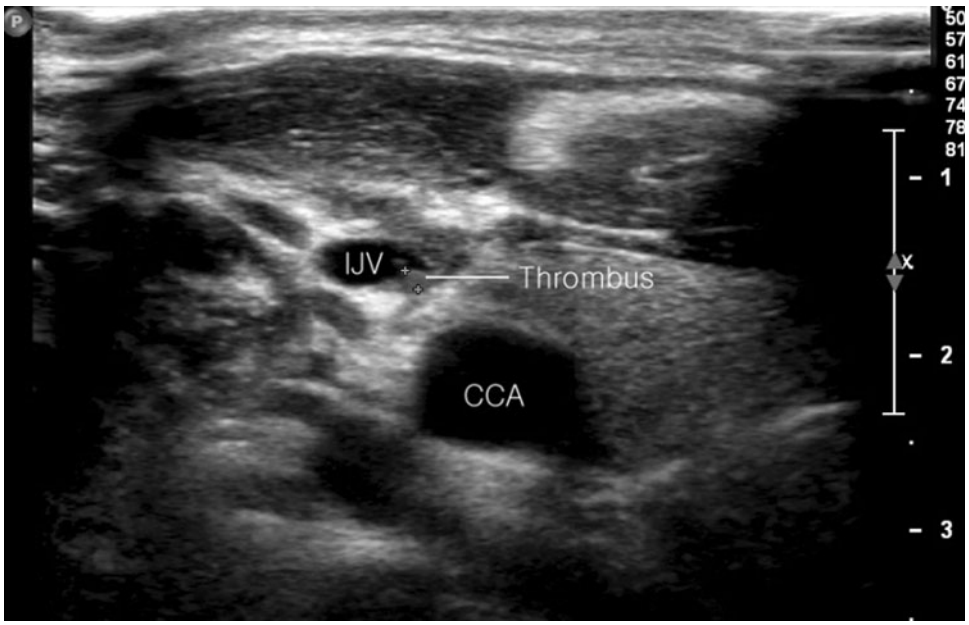

Fig. 2 Neck ultrasound image in the supine position (postoperative day 1). The hypoplastic right internal jugular vein (*IJV*) (diameter 0.3 × 0.7 cm) with eccentric peripheral thrombi (thickness 0.1 × 0.1 cm) can be noted. The diameter of the IJV is smaller than in Fig. 1. *CCA* common carotid artery

(32 mmHg) was elevated compared with its preoperative value (12 mmHg).

A follow-up neck USG showed hypoplasia of the right IJV with eccentric peripheral thrombi at the same level as the cut of Fig. 1 (Fig. 2). The size of the thrombi was substantially reduced compared with that before the operation. A neck CT showed severely narrowed right IJV, and a definite asymmetry between the inferior portions of the right and left IJV, but no distinguishable thrombus could be seen (Fig. 3). We consulted a pulmonologist on the possibility of PE in relation to a decrease in thrombus size on images, onset of chest pain, and increased D-dimer value. PE CT, which was recommended by the pulmonologist, showed no emboli in both central pulmonary arteries.

She was discharged on postoperative day 19 with no adverse medical events. Because she had undergone major surgery which increased risk of bleeding, we decided to closely observe the patient with follow-up intervals of 1 month without any anticoagulation therapy. Also, we decided to perform neck USG and PE CT at 6 months if she did not complain of symptoms such as dyspnea, and to offer her the same initial and long-term anticoagulation therapy as that received by patient with symptomatic VTE if any thrombus or embolus was found in that time. During the first 3 months of follow-up, she complained of no specific symptoms and total and free protein S antigen were normal, but protein S activity was still reduced to 53% and D-dimer was increased to 2540 ng/ml.

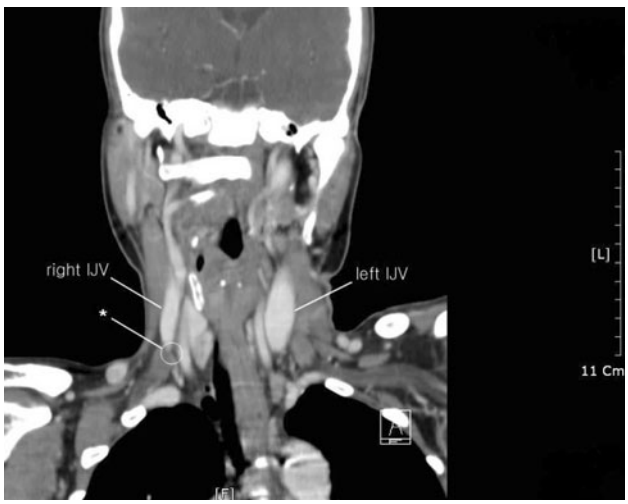

Fig. 3 Neck CT image (postoperative day 2). The right internal jugular vein (*IJV*) is severely narrowed in the field marked with an *asterisk* (*) and definite asymmetry between the inferior portions of the right and left IJV can be noted, but no thrombus is distinguishable in the hypoplastic right IJV

Discussion

Traditionally, IJV catheterizations have been performed using the ALT. However, a catheterization failure rate of 12% and a complication rate of 10% have been reported in adults with use of this technique [5]. Lichtenstein et al. [6] noted that in 62.5% of patients asymmetry between the right and left IJV could be found. The right IJV was dominant in only 68% of these cases and 23% of the 160 IJVs had a cross-sectional area of 0.4 cm^2 or less. Thus, Ayoub et al. [7] suggested that use of USG for CVC should be adopted by new clinicians and experienced practitioners as their first-line treatment, especially in cases of obesity, edema, coagulation disorders, and difficult anatomical landmarks. In this case, if sufficient attention had been paid to the possibility of secondary changes of vessels caused by

spinal deformities, we would not have used the ALT. In fact, her USG results showed the diameter of left IJV to be even greater than that of right IJV, as a result of its hypoplasia.

IJV thrombosis is commonly related to a history of central venous catheter insertion and intravenous drug abuse. Other risk factors include surgical instrumentation, Lemierre syndrome, head and neck tumors, malignancy, and assisted conception therapy [3]. No preexisting risk factors for IJV thrombosis could be found in this case, but repeated attempts to insert the guide wire might be a provoking factor for the thrombosis formation.

Deep vein thrombosis is caused by a combination of hypercoagulability, stasis of venous blood, and injury to vein wall intima, that is, Virchow's triad [8]. The IJV thrombosis in this case is thought to have been caused by the combination of venous stasis generated in the narrow hypoplastic portion of the IJV, the hypercoagulability associated with protein S deficiency, and the repeated attempts to insert the guide wire, which became a provoking factor.

Protein S (PS) is a vitamin K-dependent protein that acts as a cofactor to protein C, which inhibits coagulation by inactivation of activated coagulation factors V and VIII. Deficiencies of natural anticoagulants, including PS, are associated with a tenfold increase in the risk of VTE [9]. Symptomatic subjects with PS deficiency present with VTE, PE, or both. Approximately half of the thromboembolic events are preceded by surgery, trauma, immobilization, pregnancy, or systemic hormonal contraception, but the other half is unprovoked [10]. The IJV thrombosis in this case could have been provoked by repeated attempts to insert the guide wire—6 times in total.

The significance of, and clinical outcome of patients with, asymptomatic VTE are still uncertain. Recent guidelines of the American College of Chest Physicians suggest careful assessment of the potential risks and benefits of long-term anticoagulation for each patient [11]. Because the patient had undergone major surgery, increasing the risk of bleeding was thought to be undesirable and because the thrombi were very small, we decided to observe her closely without the use of anticoagulant with follow-up intervals of 1 month and to perform neck USG and PE CT after 6 months.

In this case, judging by a decreased thrombus size on images, it is supposed that the thrombi occurred as a result of repeated attempts to insert the guide wire, and, because the thrombi which formed acutely were relatively flaccid, they were gradually liberated during the operation which had a hyperdynamic circulation caused by massive bleeding and transfusion. Although these events would increase the risk of PE, there were no definite signs or symptoms of PE, and no embolic lesion on PE CT. Despite liberation of the thrombi, it is supposed that the embolism was limited to a minimal lesion, and accordingly, the developed PE had been subclinical. The chest pain in the recovery room also supports this diagnosis. Considering the ECG change, reduced thrombus size, increased D-dimer value, and increased systolic pulmonary artery pressure on the postoperative echocardiography, the cause for chest pain was more likely to be subclinical pulmonary embolism rather than myocardial ischemia or simple chest wall pain. Consequently, the PE caused by the IJV thrombosis was fortunately limited to a subclinical lesion. However, considering the risk of catastrophic embolic events that could be caused by the IJV thrombosis, we should have cancelled this surgery and begun workup to search for pulmonary thromboembolism and the background for the patient's hypercoagulability.

In conclusion, CVC under ultrasound guidance should be recommended to prevent the failure of cannulation and complications such as thromboembolism in patients who possibly have anomalies of vessels because of anatomical deformities caused by diseases such as scoliosis, even if patients do not have known thrombotic risk factors such as a history of VTE, cancer, advanced age, or hypercoagulability [12]. If venous thrombosis is found in these patients, one should ascertain the cause of the hypercoagulable state, for example PS deficiency and the occurrence of VTE, and properly treat patients on a case-by-case basis with consideration of the potential risks and benefits. Also, once unexpected thrombosis is found in a major vessel, cancellation of elective surgery should be considered, especially before major operations.

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