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Original Article

Prevalence and Characteristic Features of Deep Venous Thrombosis in Patients with Severe Motor and Intellectual Disabilities

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Sudden death associated with patients with severe motor and intellectual disabilities (SMID) have been thought to be caused in part by venous thromboembolism (VTE), but actual situation of VTE in SMID is not clear. We examined the prevalence and location of deep venous thrombosis (DVT), and the relation of the development of crural veins in 16 patients with SMID, using ultrasonography. The maximum diameter of soleal vein was 1.6±0.5 mm. In most cases, DVT was found in the femoral veins. We could not detect thrombus in the soleal veins. In the present study, the detection ratio of DVT was high in patients with SMID who had restricted mobility capability and were bedridden, and we found the veins centrally from popliteal veins in DVT in SMID, not soleal veins, as the initial sites of the DVT. In the literature, the mean diameter of soleal veins, in healthy adults is 6.7±1.8 mm, that in contrast in SMID being smaller. Underdevelopment of intramuscular veins is possibly related to the mechanism of DVT in SMID. In the current guidelines for the management of VTE, there is limited in scope of ambulatory adults and no application cases who exhibit to SMID restricted mobility of the lower extremities and are bedridden associated with cerebral palsy and developmental motor disabilities, and such patients have associated high risk of the complications of DVT. According to our present study, it is necessary to provide appropriate guidelines for DVT in SMID considering characteristic features. (This is a translation of Jpn J Phlebol 2017; 28: 29–34.)

Keywords: severe motor and intellectual disabilities (SMID), deep venous thrombosis, soleus vein, duplex ultrasonography

Introduction

In addition to complications of the respiratory system, such as aspiration pneumonia, it is very important that we deal with complications of the circulatory and vascular systems to ensure the smooth provision of medical care for patients with severe motor and intellectual disabilities (SMID).

Most patients with SMID have motor paralysis of the extremities and restricted mobility due to abnormalities in muscle tone associated with cerebral palsy and developmental motor disabilities, among others[1,2]; they are also associated with a high rate of complications of the vascular system, especially venous thromboembolism (VTE).[2–4] Contrarily, respiratory tract infections, including pneumonia, reportedly represent the most common cause of mortality in SMID, for which the rate of sudden death is over 4.2%.[5] VTE is partly noticeable for underlying diseases.[3,4] However, in provision of VTE, there is a present guideline of VTE[6] for adult person acquiring ability to gait, not corresponding SMID with non-ability to walk. In patients with SMID confined to the bed and with decreased mobility of the lower extremities, there is prolonged bed rest and a higher risk of VTE complications.[2–4] We previously examined deep venous thrombosis (DVT) in patients with SMID and observed asymptomatic DVT at a high rate; however, we did not detect thrombosis in the soleal veins, finding it mostly in the femoral veins. We reported no differences in circumstances of the thigh.[3,4] Here, we have reported the relationship between the di-

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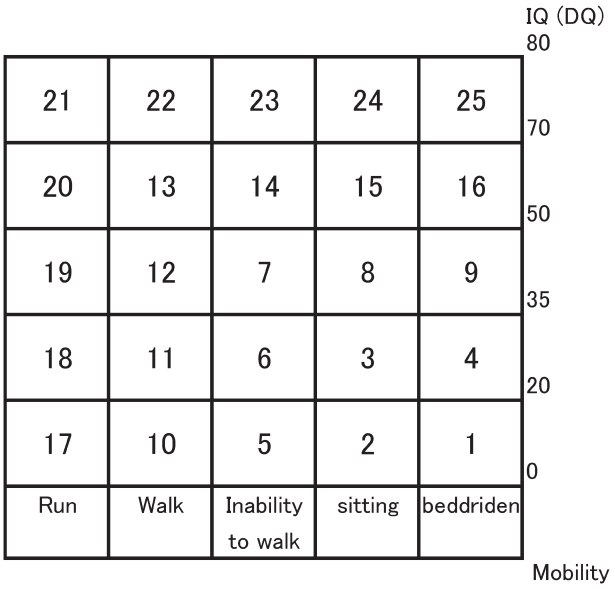

Fig. 1 Ohshima's Classification for severe motor and intellectual disabilities.
Ohshima's Classification shows the degree of intellectual and physical disabilities consisting IQ (DQ) and mobility. IQ: intelligence quotient, DQ: developmental quotient.

Table 1 Case profile

	n=16
Gender	
Male	7
Female	9
Age in years, mean (range)	43.1 (11–67)
Ohshima's Classification	
Grade 1	16
Tube feeding	14
Nasogastric tube feeding	1
Gastrostomy feeding	13
Tracheostomy	6
Deformity of the spine	15
Dislocation of the hip	12
Right side	4
Left side	2
Bilateral	6
Thickness of soleus muscle (mm)	7.3±1.5
Maximum diameter of soleal vein (mm)	1.6±0.5
Maximum diameter of femoral vein (mm)	5.4±1.3
Motor ability in developmental history	
Walking	3
Standing with support	5
Crawling	3
Sitting	1
Bedridden	4

Data presented as n, mean±SD.

ameter of soleal veins and thickness of soleus muscles and the incidence of DVT in patients with SMID.

Materials and Methods

Patients

Sixteen patients with SMID (male, 7 cases; female, 9 cases; mean age, 43.1 years) classified as class 1 of Ohshima's Classification criteria for SMID (**Fig. 1**)[7] having physical and intellectual disabilities, including inability to maintain a sitting position and being bedridden, were eligible for this study. We included those under intensive medical treatment with long-term hospitalization for SMID in the wards of the National Hospital Organization Yanai Medical Center (**Table 1**). Also, in the definition of SMID, they have overlapping features of SMIDs including children and adult and SMID has been defined for the Child Welfare Act, not medical diagnosis.[1] Further, the criteria for SMID are currently generally determined based on Ohshima's Classification.[7] There are approximately 3,800 persons in Japan with SMID.

All these patients had severely decreased mobility of the lower extremities and required medical care, such as tube feeding, tracheostomy, laryngotracheal separation, mechanical ventilation, and nutritional management; there were 14 cases of tube feeding (13 of gastrostomy, 1 of nasogastric tube), 7 cases of tracheostomy (5 of mechanically ventilated patients and 2 had undergone laryngotracheal separations), 1 case of noninvasive positive pressure ventilation, and 14 cases (87.5%) of epilepsy in the 16 cases included in this study.

Methods

We evaluated DVT in the deep veins of the lower extremities serially ongoing venous sonography using a GE Healthcare LOGIQ-S6 or LOGIQ-e (GE Healthcare Japan) and an 8- to 12-MHz variable linear probe in the 16 patients.

A laboratory skilled ultrasound technician investigated DVT, thickness of soleus muscles, and diameter of soleal veins at the central flexor portion of the lower thigh for deep veins of the lower extremities.

The standard procedure is basically performed in the supine position for the iliac and femoral regions and in the sitting position for the popliteal and crural regions with fully congested blood flow of the lower veins. However, using ultrasonography, we endeavored to examine in the supine position at the iliac and femoral regions and in the supine position with drooping foot at the bedside in the lower leg regions at dilated intramural veins possibly because most patients with SMID could not maintain a sitting position.

For the diagnosis of DVT by venous ultrasonography, we confirmed a directly non-collapsed vein with the creation of vessels using B-mode ultrasound transverse imaging and compression of the probe, and on the basis of blocking of the blood flow by color Doppler ultrasonography with or without respiratory variation on a pulse Doppler method arbitrarily.

Furthermore, in terms of ethical aspects, we performed our research, with anonymous clinical data under close supervision, after obtaining approval from the medical ethics committee of our hospital (approval number: Y-23-2).

Statistical analysis

Descriptive results were expressed as mean±standard deviation. Data were statistically analyzed using the Student's t-test for unpaired or Chi-squared test samples. $p<0.05$ was considered statistically significant.

Results

In the soleus muscles and soleal veins of the lower extremities, there were 7.3 mm±1.5 mm in thickness of soleus muscles and 1.6 mm±0.5 mm in maximum diameter of soleal veins compared with 19.7 mm±4.0 mm[8] in that of soleus muscles and 6.7±1.8 mm[9] in that of soleal veins for literature data in healthy adult (**Table 1**, **Fig. 2**). Further, there were 5.4 mm±1.3 mm at average of maximum diameter of femoral veins (**Table 1**). Seven of the 16 cases (43.8%) of DVT in the lower extremities were asymptomatic (mean age, 45 years; 3 men and 4 women) (**Table 2**). We did not detect thrombosis in the soleal veins, finding it mostly in the femoral and common femoral veins. There were significantly no differences in the maximum diameter of soleal veins between the 7 cases in DVT group and the 9 cases in non-DVT group, and they were significantly smaller in thickness of soleus muscles and maximum diameter of femoral veins for the DVT group than that of non-DVT group ($p<0.05$) (**Table 3**). Also, regarding the developmental history of motor abilities, the non-DVT group acquired walking levels in developmental stages, whereas the DVT group did not acquire walking skills; further, from bedridden to sitting levels and standing with support, most of them were prolonged bedridden states (**Table 3**).

Regarding the spinal deformity contractures of the hip, all cases had deformities and contractures of hip and knee joints, 13 of 16 cases having moderate to severe deformities of the spine (scoliosis) in the thoracolumbar region and 12 of 16 cases having dislocation of the hip (6 cases in bilateral sides, 4 cases in the right side, and 2 cases in the left side) (**Table 1**). However, there were no differences between the DVT and the non-DVT group in terms of orthopedic findings. There were no differences among all cases in the circumferences of lower extremities.

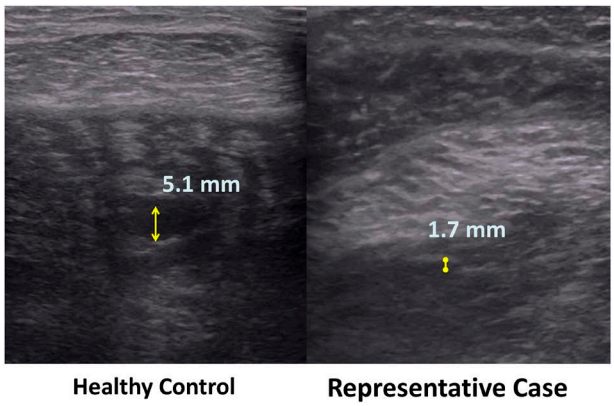

Fig. 2 Short axis scan of the left soleal vein of representative case by ultrasonography. The vessel (the diameter of the vessel, 1.7 mm) is smaller compared to that of healthy control (the diameter of the vessel, 5.1 mm).

Table 2 Location and size of deep vein thrombosis

Case	Age	Sex	Location of thrombus	Size of thrombus (mm)
1	23	F	rt-CFV	7.9×15.0
2	57	M	lt-CFV	3.5×12.0
3	67	M	lt-CFV-DFV, rt-PTV	2.5×45.0, 2.2×15.5
4	62	F	lt-CFV	2.9×11.3
5	35	M	rt-CFV	1.2×8.9
6	35	F	rt-CFV	2.0×8.4
7	45	F	lt-CFV-FV	2.5×3.0

Size of thrombus given as maximum diameter×length. Thrombi in case 1 and 4 were organized. CFV, common femoral vein; DFV, deep femoral vein; PTV, posterior tibial vein; FV, femoral vein.

Table 3 Comparison of characteristics between patients with DVT and those without DVT

	DVT group (n=7)	non-DVT group (n=9)
Male	3	4
Female	4	5
Maximum thickness of soleus muscle (mm)	6.9±1.2*	10.0±3.1
Maximum diameter of soleal vein (mm)	1.6±0.6	1.5±0.4
Maximum diameter of femoral vein (mm) (lt)	4.5±1.2*	6.0±1.0
Motor developmental history		
walking	0	3
standing with support	2	3
crawling and sitting	3	1
bedridden	2	2

*P<0.05, Data presented as mean±SD. DVT, deep vein thrombosis.

Discussion

We asymptomatically detected 7 of the 16 cases (43.8%) of DVT in the lower extremities in patients with SMID

confined to bed and with decreased mobility of the lower limbs, and there is prolonged bed rest and undergoing medical care including tube feeding and respiratory management such as tracheostomy based on our previous reports.[3,4] In addition, in the region of thrombus formation with DVT, mostly the femoral vein and the common femoral vein central to popliteal veins were involved, and we did not detect DVT in the soleal vein, which was previously reported as the initial site of DVT in the lower extremities.[6,10–12]

In SMID, thrombus formation is causally considered related to disturbance of mobility owing to a prolonged bedridden state, and most sites of DVT are femoral and common femoral veins centrally, not the soleal veins as commonly initial site of DVT. These findings indicate major differences between general adult and SMID in the course of DVT development.

In the thickness of soleus muscles in our present study, there were 7.3 ± 1.5 mm in all of SMID notably thinner compared with 19.7 ± 4.0 mm in that of soleus muscles for the literature data[8] and there was significantly thinner in DVT group compared with non-DVT group.

In cerebral palsy causative for SMID, there are mostly quadriplegia and diplegia with intense leg paralysis, and motor paralysis of the lower limbs has caused to deformities and contractures of legs.[13,14]

These results showed that such more profound motor damages are likely to develop DVT and SMID with more severe motor disabilities and may possibly have the failure of coagulation and fibrinolytic system.

The mean diameter of soleal veins in SMID is 1.6 ± 0.5 mm, which is very small compared with 6.7 ± 1.8 mm, which is that for the literature data in healthy adult.[9] Development of soleus muscles is necessary part to be able to walking[15] and part enable to venous return at standing position by the action of muscle pumps.[9,16–18] In bedridden SMID, they developed bodily kicking movements on supine position at bed rest, and we received the impression that their gastrocnemius well developed than soleus muscles in the study patients. On supine position at bed rest, muscle pumping function is not necessary to prompt venous flow of the lower extremities. The soleus muscle and gastrocnemius are mainly involved in pumping function of lower legs, and it is unclear to what degree each muscle contributes to the pumping muscle function.[9,17,18] In adults, the soleus muscle is larger in volume than gastrocnemius, and so, a maximum part of the circumference is just adjacent to the median lower legs. As the thickness of soleus muscles defined as maximum site is measured in approximately near to the middle of lower extremities, the measurement of thickness of soleus muscles at central part of lower legs is not likely problem. Meanwhile, we found that the maximum circumference of the lower legs is central to the middle of the leg because of a well-developed gastrocnemius in a large part than that of soleus muscle in SMID. It is questionable that the thickness of the soleus muscles is regularly measured at the maximum circumference of lower extremities. However, as the thickness of the muscles is uniformly smaller in SMID, it is no problem that the maximum site of thickness of muscles is defined as the middle part of lower legs. The risk factors of DVT in SMID are still unclear, and we think that these are not a little enlarged multiple lymph nodes in the groin in present study patients. We have further considered in the future the findings that the maximum diameter of femoral veins in DVT group is significantly smaller. There are mostly femoral veins centrally in the region with DVT for SMID, and there are possible advanced mechanisms that any life modes including diaper use, frequencies of bed-bath, positioning different types from healthy adult may involve in thrombophlebitis in the area of the groin and come into DVT formation.

The clarification of risk factors to DVT onset is an important problem that needs to be addressed in the future. Treatment for asymptomatic DVT in SMID has not reached consensus. We administer warfarin by regulating the dosage at PT-INR (prothrombin time-international normalized ratio) values of approximately 1.5 by completely considering the risk and benefit for the risk factors to lower extremity dysfunction, and we have carefully followed up the clinical course with examination of D-dimer and venous ultrasonography of lower extremities serially.[3,4] But it is not necessarily easy to control the PT-INR at target ranges and it is difficult to get blood samples because of increase in muscle tone in SMID, and therefore, we have therapeutic management of warfarin for VTE with much difficulty at present. Hence, it is very important to establish the therapeutic principle of VTE applied to characteristic features of DVT in SMID. Contrarily, the new oral anticoagulant drugs Xa inhibitors covered by insurance to VTE are reportedly regulated of dosage easily and effective and safety to VTE treatment.[19–21] These new drugs are possibly applied to the management of VTE in SMID, and it is necessary for further consideration in the future.

Also, as patients with SMID have poor development of the muscles of the lower leg, especially the soleus muscle, it is scarce evidence of any indication for the use of elastic stockings in patients with SMID.

To use the elastic compression stockings for chronic thrombosis improves venous reflux to the microcirculation owing to compression of the lower leg muscles, enables over a long time period, and is more effective combined with physical therapy of extension upward of the lower legs.[6] In SMID with poor development of veins of lower legs, the effects of knee-high socks type elastic stockings remain doubtful, and we consider to apply the

stockings over the entire lower leg to DVT with SMID.

Current therapeutic guidelines for VTE is adapted to adult person with acquired walking ability[6] and is not corresponded to SMID in bedridden state with restricted mobility due to underlying diseases such as cerebral palsy from a young age. From these results, we investigate carefully VTE with complications of the circulatory and vascular systems in SMID, and it is necessary to prepare new guidelines for VTE to SMID adapted the typical pathogenesis.

Conclusion

Poor development in the intramuscular veins of lower legs in SMID compared with the general adult is possibly related to the difference in the mechanism for development of DVT. According to the current established guidelines for VTE that has applied to the adult having ability walking and not to SMID with restricted mobility due to underlying diseases such as cerebral palsy from a young age. In the light of present our study, it is necessary for formulation of newly preventive specific guidelines for DVT corresponding to characteristic clinical conditions of SMID.

Disclosure Statement

Hiromitsu Ohmori and coauthors have no conflicts of interest to disclose.

Additional Note

We presented the overview of our manuscript at the Annual Meeting of Japanese Society of Phlebology (June 2016, Aomori, Japan).

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