ORIGINAL REPORT

Children Treated for Slow-flow Vascular Malformations: Overall Description and Focus on Complications Such as Cellulitis

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Some patients with slow-flow vascular malformations (SFVMs) develop recurring cellulitis. The main objective of this study was to describe SFVMs in children. Other objectives were to determine the frequency of cellulitis episodes, and the factors associated with the occurrence of cellulitis. This retrospective, longitudinal, single-centre study included all children with SFVMs being managed at Lille University Hospital between 1994 and 2020. Data were collected using a standardized questionnaire. After a descriptive analysis, the variables associated with the onset of cellulitis were analysed; 133 patients (median age at diagnosis: 72 months; 53% girls) were included. SFVMs were: venous (81%), lymphatic-venous (10%), capillary-venous (5%), and lymphatic (4%). Nine children had presented at least 1 episode of cellulitis (7%, 95% CI: 4–12) and 29 episodes were reported (median: 3, interquartile range: 2–4; median age at the first episode: 3.5 years). Cellulitis occurred more frequently in young children, with lymphatic and syndromic forms of SFVM, large SFVMs, affecting skin folds, and without long-term SFVM treatment. In conclusion, the occurrence of cellulitis in patients with a SFVM is rare. However, after the first episode, it frequently becomes recurrent, particularly in some patients with identified risk factors, who may require antibiotic prophylaxis.

Key words: cellulitis; children; risk factors; vascular malformations.

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SIGNIFICANCE

Slow-flow vascular malformations are rare inherited diseases in children. Infectious skin complications (cellulitis) may arise and vary according to the type of slow-flow vascular malformation. These skin infections are rare but represent a diagnostic and therapeutic challenge and may be recurrent in some of these children. The frequency and risk factors for cellulitis have been identified here. Early detection of these children at risk of recurrent cellulitis would be useful to propose specific management and perhaps early long-term treatment or even antibiotic prophylaxis to avoid the onset and/or recurrence of cellulitis.

Vascular anomalies are a heterogeneous group of poorly understood lesions that affect on average 5–10% of children (1). In 1996, the classification of vascular anomalies was adopted by the International Society for the Study of Vascular Anomalies (ISSVA), and was then revised in 2014. Two groups were distinguished: vascular tumours and superficial vascular malformations (2).

Superficial vascular malformations may involve capillaries, veins, or lymphatic vessels and are haemodynamically inactive, contrary to arteriovenous malformations. Our study focused specifically on capillary, venous, and lymphatic malformations occurring in children, known as slow-flow vascular malformations (SFVMs) (2, 3). These malformations, which are all congenital, may be diagnosed antenatally, at birth, or be clinically apparent later in life and diagnosed during childhood or adulthood (3, 4). Syndromic forms of such SFVMs exist, some of which are caused by known genetic mutations such as somatic mutations in the PIK3CA, TIE 2, or other genes (3–6).

Patients with SFVMs require regular follow-up with specialists, and sometimes specific treatment may be necessary (4, 7, 8). Complications may arise and vary depending on the type of SFVM: acute episodes of oedema usually due to intra-lesional bleeding, thrombosis, and skin infections (3, 8–10). These infections are rare but represent diagnostic and therapeutic challenges (3, 10). Indeed, these patients sometimes present recurring episodes of skin infections (9). However, there are very few data in the literature concerning the importance of this phenomenon and the management of skin infections, especially cellulitis, in these children. The management of episodes of non-necrotizing bacterial cellulitis and recurrent cellulitis in children with SFVMs is in line with general paediatric recommendations, with the implementation of long-term prophylactic treatments in some cases. The role and the rarity of the underlying condition in the occurrence of such infectious complications make it difficult to provide specific practice recommendations for these patients. Therefore, it seemed important to give an overview of cellulitis episodes in children being mo-

nitored for SFVMs. The question of the presence of risk factors or susceptibility to skin infections arises in these children, to anticipate the onset and recurrences of these infections and to enable more appropriate management.

The primary objective of the study was to describe the population of children being monitored for SFVMs in our institution. The secondary objectives were to describe the episodes of cellulitis in these children, the frequency of recurrences, and to identify factors associated with the onset of cellulitis.

MATERIALS AND METHODS

Design and inclusion criteria

We conducted a retrospective, single-centre, descriptive and analytical study, which included all children being monitored for an SFVM at Lille University Hospital between 1 January 1994 and 10 August 2020. The study report complied with the Standards for Reporting Diagnostic Accuracy Studies guidelines. All children under the age of 18 at the time of diagnosis of an SFVM, being followed at Lille University Hospital during the study period, were included. The types of SFVMs included were: common venous malformations, lymphatic malformations, lymphatic-venous malformations, and segmental capillary-venous malformations, with involvement of the upper and/or lower limbs. The episodes of cellulitis were included if the patient was under 18 years old at the time of diagnosis of the infection. The non-inclusion criteria were: patients with an SFVM involving only the head and neck, and patients diagnosed with a familial venous malformation (glomangiomatosis).

Definitions

Our study focused specifically on SFVMs. The various vascular malformations included were defined based on the ISSVA classification (2, 3). The size of the SFVM was reported as a percentage of the affected limb. A small lesion size was defined as less or equal to 50%, while a large lesion size was strictly greater than 50% of the affected limb. In the management of patients with SFVMs, it is recommended that D-dimer levels be measured to help diagnose possible localized intravascular coagulation, which is very often associated with these malformations and with infectious complications (1, 4). We defined a normal D-dimer level as <500 ng/mL, according to usual practice (11–13). Infections of the skin and soft tissues are anatomically classified according to the affected tissues: cellulitis is defined by dermal and hypodermal involvement. The infection is bacterial, although obtaining pathogen identification is uncommon. The diagnosis is clinical, based on the presence of an inflammatory area on the skin, which is red, hot, painful, of abrupt onset, rapidly spreading, and unilateral. A well demarcated, raised peripheral border of the inflammatory area may also be present. Bullous peeling of the skin and localized purpura may be present, but do not necessarily indicate severity.

Collected data and data collection procedure

The variables collected were: demographic data (date of birth, age at diagnosis, gender), the types and descriptions of the SFVMs (syndromic forms, diagnosis made *in utero*, year of diagnosis, localization and size of the malformation, possible extension to the perineum or thorax, deep tissue involvement), possible treatment of the SFVMs (compression therapy, drainage physical therapy, indication for sclerotherapy, surgical indication, long-term treatments), data concerning the infection(s) (number of infections, dates of management, patient's age at diagnosis, time in days between onset and diagnosis of skin infection, localization of infection, associated symptoms reported by the parents, presence of systemic signs including fever, prior consultation with a general practitioner, description of the cellulitis, presence of localized intravascular coagulation, results of laboratory tests, type of treatment, complications if any, time between recurring infections), indication for antibiotic prophylaxis after treatment (if so, name of the indicated drug, route of administration, and duration), foreseeable functional sequelae. The principal investigator collected these data using a standardized questionnaire. Patients being treated at Lille University Hospital for SFVMs were registered in a database in the Cardiovascular Functional Explorations Department at Lille University Hospital, Heart-Lung Institute.

Ethical considerations and medico-legal aspects

As recommended by law, an information letter was sent to each patient included in this study, informing them of the research work and giving them, or their parents for young children, the opportunity to refuse to have their data collected for this study. Data collection concerning the patients with SFVMs was in strict compliance with France's MR-004 reference methodology, established by the French National Data Protection Commission. The study was approved by Lille University Medical Centre's data protection authority (reference: DEC19-440).

Statistical analyses

This was a descriptive study, first of the total population and of the population having presented at least 1 episode of cellulitis. Second, we carried out a descriptive study of the episodes of cellulitis. Quantitative variables were described using means and standard deviations or using medians and interquartile range (IQR) in the case of non-Gaussian distributions. The normality of distributions was verified graphically and using the Shapiro–Wilk test. Qualitative variables were described in terms of

frequencies and percentages. Finally, some qualitative variables of interest were compared between patients with and without cellulitis using Fisher's exact test. Age between these 2 groups was compared using the Mann–Whitney *U* test. The significance level was set at 5%. Statistical analyses were performed using SAS software (version 9.4; SAS Institute, Cary, NC, USA) by the Lille University Hospital Methodology Platform and Biostatistics team.

RESULTS

During the study period, 249 patients were treated at Lille University Hospital for an SFVM, and 133 patients (median age: 72 months, IQR: 24–125; girls: 53%) had all the inclusion criteria. Nine had presented at least 1 episode of cellulitis (**Fig. 1**). Of these 133 children, 19 (14%) had syndromic forms, including 4 with an *in utero* diagnosis: 7 Klippel–Trenaunay syndromes, 4 PIK3CA gene mutations, 4 highly probable PIK3CA mutations that were not yet identified, 1 TIE 2 gene mutation, 1 GNAQ gene mutation, 2 unidentified syndromic forms with undergoing genetic analyses. The different types of SFVMs were: venous (81%), lymphatic-venous (10%), capillary-venous (5%), and lymphatic (4%) (**Table I**).

The majority of patients with SFVMs had non-drug treatments, most frequently compression therapy ($n=76$, 57%), and long-term drug treatments (71%), most often an antiplatelet agent, i.e., oral acetylsalicylic acid at 2 mg/kg/day. This long-term treatment was sometimes stopped for one or multiple reasons: poor tolerance, thrombosis, pain, indication for surgery or sclerotherapy, efficacy or inefficacy of the treatment, poor compliance. Therefore, for some patients, multiple lines of treatment were introduced (Table SI).

Of the 9 children who presented at least 1 episode of cellulitis during the study period (7%, 95% CI: 4–12), 5 had a syndromic form (2 had identified PIK3CA gene mutations, 2 had possible PIK3CA gene mutations, 1 was unidentified). All children with a lymphatic malformation had recurrent episodes of cellulitis. The median age at diagnosis of the first cellulitis episode was 3.5 years (IQR: 8 months–5.7 years). The characteristics of these patients and their SFVMs are detailed in **Table II**. Over the course of the study, 29 episodes of cellulitis were reported in these 9 patients (**Table III**). One patient initially presented with a coagulation disorder, incipient disseminated intravascular coagulation (DIC), without consumption of fibrinogen, which required initial admission into a paediatric intensive care unit. Most patients being treated for cellulitis were admitted to hospital ($n=22$, 76%). The management of the 29 episodes of acute cellulitis is presented in Table III. Prophylactic antibiotic treatment was prescribed after an infectious episode for 4 patients, who had presented either recurrent cellulitis or at least 1 episode of severe sepsis (Fig. S1).

When comparing children with and without at least 1 episode of cellulitis, variables significantly associated

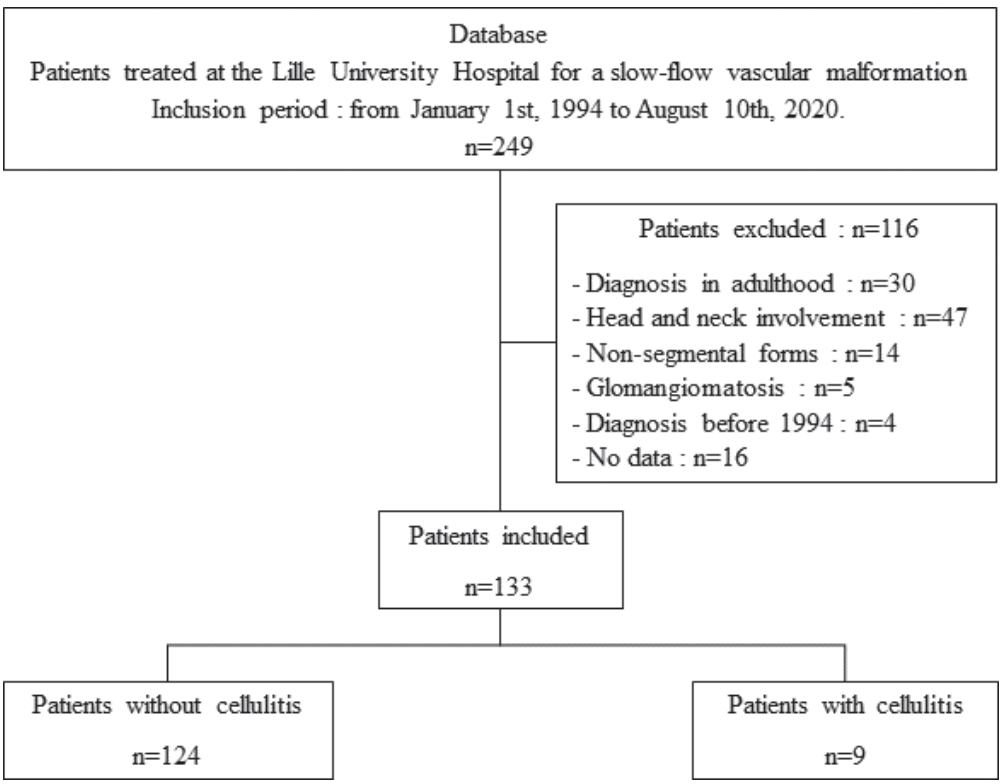

Fig. 1. Children treated at the Lille University Hospital for a slow-flow vascular malformation.

Table I. Description of the total population with details of the slow-flow vascular malformations (*n* = 133)

Variables	
Female sex, *n* (%)	70 (53%)
Age at diagnosis, in months, median (IQR)	72 (24–125)
In utero diagnosis, *n* (%)	5 (4%)
Syndromic form, *n* (%)	19 (14%)
Type of vascular malformation, *n* (%)	
Venous malformation	108 (81%)
Lymphatic-venous malformation	13 (10%)
Capillary-venous malformation	7 (5%)
Lymphatic malformation	5 (4%)
Localization, *n* (%)	
Left upper limb	28 (21%)
Right upper limb	28 (21%)
Left lower limb	40 (30%)
Right lower limb	40 (30%)
Extension beyond affected limb, *n* (%)	17 (13%)
Perineum	12 (9%)
Thorax	9 (7%)
Acral localization, *n* (%)	36 (27%)
Involvement of skin folds, *n* (%)	83 (62%)
Popliteal	40 (30%)
Inguinal	11 (8%)
Axillary	11 (8%)
Interdigital	35 (26%)
Elbow	16 (12%)
Deep tissue involvement, *n* (%)	85 (64%)
Muscle	79 (59%)
Articulation	15 (11%)
Bone	22 (17%)
Size, as percentage of affected limb, *n* (%)	
< 25%	63 (47%)
25–50%	36 (27%)
50%	1 (1%)
50–75%	10 (8%)
> 75%	23 (17%)
Normal D-dimer base levels, *n* (%) (38 MD)	36 (38%)
Patients who presented at least 1 infection, *n* (%)	9 (7%)*

IQR: interquartile range; MD: missing data.
*95% confidence interval: 4–12.

Table II. Description of patients with a slow-flow vascular malformation, having presented at least 1 episode of cellulitis

Patients	1	2	3	4	5	6	7	8	9
Sex (M, F)	M	M	F	M	M	M	F	M	M
Year of diagnosis	2011	2012	2013	2016	2005	2013	2019	2005	2016
Age at diagnosis (months)	0	2	3	0	22	0	0	0	192
In utero diagnosis				X		X	X	X	
Syndromic form				X		X	X	X	X
Type of vascular malformation									
Venous malformation			X	X	X				
Lymphatic-venous malformation	X								
Capillary-venous malformation									
Lymphatic malformation		X				X	X	X	X
Localization									
Left upper limb			X		X	X			
Right upper limb						X			
Left lower limb						X			X
Right lower limb	X	X		X			X	X	X
Extension beyond affected limb	X	X				X	X	X	X
Perineum	X	X				X	X	X	X
Thorax						X		X	X
Acral localization			X		X	X	X	X	
Involvement of skin folds	X	X	X	X	X	X	X	X	X
Popliteal		X		X		X	X	X	
Inguinal	X	X		X		X	X	X	X
Axillary						X			
Interdigital			X		X	X	X	X	
Elbow			X			X			
Deep tissue involvement		X	X		X	X	X	X	X
Muscle		X	X		X	X	X	X	X
Articulations		X					X	X	X
Bones		X					X	X	X
Size (as % of affected limb)									
< 25%									
25–50%	X				X				X
50%									
50–75%		X	X						
> 75%				X		X	X	X	
Normal D-dimer base levels	MD	X		MD					MD
Episodes of cellulitis, *n*	6	2	1	3	1	5	5	4	2

X: sign was present; empty fields: sign was absent; MD: missing data.

with the occurrence of cellulitis were: having a lymphatic malformation ($p < 0.001$), a syndromic form of SFVM ($p = 0.003$), a large SFVM ($p = 0.007$), extending beyond the affected limb ($p < 0.001$), skin fold lesions ($p = 0.03$), no long-term SFVM treatment ($p = 0.005$), and a young age at diagnosis ($p = 0.002$) (**Table IV**).

DISCUSSION

Between 1994 and 2020, 133 children were monitored at Lille University Hospital for an SFVM, in the majority of cases for a venous malformation (81%). A syndromic form was diagnosed or suspected for 14%. Only 7% (95% CI: 4–12) of these children had at least 1 episode of cellulitis, but a total of 29 episodes was recorded over the study period, with a median of 3 episodes per patient (IQR: 2–5). The variables significantly associated with the risk of developing cellulitis were: lymphatic malformations, syndromic forms of SFVM, young age at the time of diagnosis of the malformation, extension of the lesion beyond the affected limb, involvement of skin folds, large lesion size, absence of long-term SFVM therapy.

Our patients' characteristics were similar to other reports, with venous malformations being the most frequent SFVM in patients from other vascular anomaly centres (11, 14, 15), and a mean age at diagnosis similar to another study at 70 months (range: 5–138 months) (16). However, few studies have reported the proportion of SFVMs in children with syndromic forms. In a study conducted over 9 years, the rate of syndromic forms was lower than in our study (8.2%) and corresponded to 5 patients who had Klippel–Trenaunay syndrome (17). In our study, the majority of patients (71%) were undergoing long-term SFVM therapy, most often by oral acetylsalicylic acid and compression therapy, as elsewhere (18). A systematic review of compression therapy showed that this appeared to be a commonly used treatment for patients with SFVMs (19). In a Spanish study, surgery and sclerotherapy were the main curative treatments (18).

Five of the 9 patients who had presented at least 1 episode of cellulitis had a lymphatic malformation. Four of them had a syndromic form of SFVM, diagnosed *in utero*. The median age at diagnosis of the first episode of

Table III. Presentation of cellulitis cases (*n* = 29) and their management in the 9 children followed for a slow-flow vascular malformation who presented at least 1 episode of acute cellulitis

Variables	
Place of initial management	
Emergency department	17 (59%)
General practitioner	5 (17%)
Specialist in vascular malformation	7 (24%)
Duration of symptoms before visit, days, median (IQR)	0 (0–1)
Symptoms reported by parents:	
Local symptoms	
Redness and swelling of the affected limb	24 (83%)
Pain	21 (72%)
Worsening of symptoms despite treatment	3 (10%)
Suspected thrombosis	2 (7%)
General symptoms	
Fever	20 (69%)
Diminished appetite/anorexia	5 (17%)
Respiratory signs	2 (7%)
Other symptoms (unusual behaviour, limping, oozing lesion) (1 MD)	14 (50%)
Symptoms upon admission to hospital	
Fever	22/25 (88%)
Red, inflammatory skin	26 (90%)
Bullous form	3 (10%)
Cutaneous entry point	25/28 (89%)
Tests performed	
Local ultrasound	21 (72%)
Thrombosis found	5/20 (25%)
Blood test	26 (90%)
Inflammatory syndrome found	22/26 (85%)
Blood culture done	8/23 (35%)
Positive blood culture	1/8* (13%)
Bacterial skin sample	0 (0%)
Time between 2 episodes of cellulitis, months, median (IQR)	4 (1–22.5)
Hospital admission**	22 (76%)
Antibiotics	29 (100%)
Amoxiclav	28 (97%)
Amoxicillin	3 (10%)
Ceftriaxone	3 (10%)
Amikacin	2 (7%)
Anti-MRSA agent#	2 (7%)
Others##	5 (17%)
Median duration of antibiotics, in days	16 (12–21)
Secondary antibiotic prophylaxis	4 (44%)
Local wound treatment (1 MD)	20/28 (71%)
Analgesic treatment (13 MD)	
Acetaminophen	16/16 (100%)
Tramadol	1/16 (6%)
Nalbuphine	2/16 (12%)
Morphine	1/16 (6%)
Anti-aggregating or anticoagulation treatment	25 (86%)
Aspirin (1 MD)	4/28 (14%)
Anticoagulation therapy	21 (72%)

MD: missing data; *Streptococcus pyogenes; **Because of extensive cellulitis; (*n* = 22): the presence of general signs of infection (*n* = 12): associated thrombosis (*n* = 5) or risk factors for complications, i.e., risk of thrombosis of the vascular malformation (*n* = 22): a history of cellulitis with complications (*n* = 2): or other factors like the patient's young age or poor compliance with treatment (*n* = 13). #Fucidic acid (*n* = 1); vancomycin (*n* = 1); ##cefamandole (*n* = 1): cefalexin monohydrate (*n* = 2); clindamycin (*n* = 2); cefpodoxime (*n* = 1); gentamicin (*n* = 1).

cellulitis was 3.5 years (IQR 8 months–5.7 years). There are very few studies concerning cellulitis in children with SFVMs and we found no incidence data concerning this phenomenon. However, the incidence of cellulitis appears to be much lower in the general population than in our study population. In France, the annual incidence of cellulitis was stable at between 10 and 100 cases per 100,000 inhabitants (20). In the general population of European countries, the estimated incidence of cellulitis was between 19 and 24 cases per 100,000 inhabitants (21).

All episodes of cellulitis were treated with antibiotics, in outpatient care for 7/29. Except in cases of severe sepsis, the first line of antibiotics was amoxicillin-clavulanic acid (97%), for a median duration of 16 days. This choice of antibiotic followed the recommendations for the general paediatric population (20). Although the duration of treatment seemed shorter in the general population, between 5 and 10 days (20, 21), the longer duration in children with SFVMs was based on national guidelines (22). The risk of recurrence and prolonged microbial clearance in children with SFVMs may explain the choice to prolong antimicrobial treatment in some patients with SFVMs. This was done in an Australian study on prolonged antibiotic therapy in patients monitored for a SFVM from 2001 to 2015 (23), in which an even longer course of antibiotics, of at least 3 months, seemed to be recommended for a first episode of cellulitis in patients with a SFVM.

Contrary to the Australian study, bacteriological samples were insufficiently taken in our centre, and when done they were rarely positive. This was in line with data from the general population. Cellulitis being mainly a clinical diagnosis, it was difficult to establish the actual prevalence of the responsible pathogens, as in most cases bacterial cultures were negative (24–26). In the cases where the pathogen was identified, the most common were beta-haemolytic *streptococci* and *Staphylococcus aureus* (21). Bacterial epidemiology was different in children than in adults, with frequent co-infections by *S. aureus* and group A beta-haemolytic *Streptococcus* (20). In our study, the majority of patients were hospitalized and treated with intravenous antibiotics. In the general paediatric population over the age of 1, oral antibiotics could be the first-line treatment in cases of uncomplicated cellulitis. Intravenous treatment was indicated for complicated forms or in the case of sepsis for the first days of treatment (21). Finally, hospitalization was indicated if the child was less than 1 year old (20).

Study strengths and limitations

First, this study concerned only children being monitored at one University Hospital. However, the Cardiovascular

Table IV. Univariate analysis of variables potentially associated with the occurrence of cellulitis in patients being treated for a slow-flow vascular malformation (SFVM)

	Cellulitis episodes		
Variables	No (*n* = 124)	Yes (*n* = 9)	*p*-value*
Lymphatic malformation, *n*/total *n* (%)	0/124 (0%)	5/9 (56%)	< 0.001
Syndromic form of SFVM, *n*/total *n* (%)	14/110 (13%)	5/9 (56%)	0.003
Malformation extending beyond the affected limbs, *n*/total *n* (%)	11/124 (9%)	6/9 (67%)	< 0.001
Acral localization, *n*/total *n* (%)	31/124 (25%)	5/9 (56%)	0.06
Involvement of skin folds, *n*/total *n* (%)	78/122 (61%)	9/9 (100%)	0.03
Muscle and/or articulation and/or bone involvement, *n*/total *n* (%)	78/123 (63%)	7/9 (78%)	0.49
Lesion of large size, *n*/total *n* (%)	27/124 (22%)	6/9 (67%)	0.007
Long-term SFVM therapy, *n*/total *n* (%)	88/124 (71%)	2/9 (22%)	0.005
Median age at diagnosis in months (IQR)	82 (30–131)	0 (0–3)	**0.002

*Fisher's exact test, except **Wilcoxon's test; IQR: interquartile range.

Functional Explorations Department at this hospital is the reference centre for patients with an SFVM in Northern France, a region with about 1 million children. The study had the merit of identifying all children followed for a segmental SFVM over a long period of almost 26 years. Second, the retrospective nature of our study may have constituted a bias. However, the limited number of patients with an SFVM and a cellulitis rate of less than 10% in these patients made it difficult to conduct a prospective study. Although this method did not impact the identification of all patients being monitored for SFVMs, it could have had an effect on the thoroughness of the data collected. However, as all patients had centralized regular follow-up in the reference centre, there were very few missing data. Follow-up at the reference centre also helped to confirm each diagnosis of cellulitis and ruled out differential diagnoses through systematic blood tests, ultrasound scans, and re-evaluation by the referring physicians. Third, the small number of patients who presented at least 1 episode of cellulitis did not allow us to perform a multivariate analysis of predictors of a cellulitis episode. With so few events, multivariate analysis results could be misleading even if we used a penalized regression approach. Among the factors tested in univariate analyses, 8 were associated with cellulitis episodes at p-value <0.20, including 2 complete separations. Very few data were available in the literature concerning complications like cellulitis in these patients. Similar figures were found in the Australian study, comprising 21 patients out of 620 (3.4%) in their database (2001 to 2015) (23). Contrary to this Australian study, we chose to include segmental SFVMs affecting the upper and/or lower limbs and to exclude malformations involving the head and neck. This choice also constituted a possible bias in our study. However, there are specificities concerning the management of head and neck vascular malformations that differ from those affecting the limbs, with a risk of local infection that seems different, and different predisposing factors such as frequent upper respiratory tract infections or surgical procedures for functional impairment or significant cosmetic concerns.

Study perspectives

Recommendations for the management of cellulitis in the general population and more specifically the paediatric population were clear and based on numerous studies (27–31). However, there were no specific recommendations for children with SFVMs. Our results show the importance of building on our study to manage these episodes of cellulitis in the most appropriate way possible.

The main complication of cellulitis was recurrence, which was frequent (20, 32); in the general population, 10–30% of patients presented a new episode within 6 to 36 months (32–34). Certain risk factors have been identified in adults: obesity, chronic oedema or lymphoedema, presence of a cutaneous entry point such as intertrigo (20, 32). Concerning these recurrent episodes of cellulitis and the indication for antibiotic prophylaxis, here again the recommendations were based on the general paediatric population (20) and were mainly based on expert opinions (32). In the United Kingdom and the United States, antibiotic prophylaxis was recommended if the patient presented more than 2 episodes of cellulitis in the same area within 1 year (34, 35). In France, for patients presenting risk factors, it was recommended that antibiotic prophylaxis be started if 2 episodes of cellulitis had occurred in the previous year (20).

Conclusion

Our study identified factors significantly associated with the onset of cellulitis in this population with a high rate of recurrent cellulitis. It would be interesting to confirm our results with a multicentre study and to develop recommendations for early management of these children to avoid the onset and/or recurrence of bacterial cellulitis;, especially concerning the indication for early long-term treatment or even antibiotic prophylaxis in the presence of these risk factors. A lymphatic malformation in 5 of the 9 patients with cellulitis episodes, and the presence of genetic factors such as a proven or suspected PIK3CA gene mutation in 4, also raised the question of starting early long-term SFVM treatment or antibiotic prophylaxis in these specific patients.

The authors have no conflicts of interest to declare.

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