



# Blue Rubber Bleb Nevus Syndrome because of 12 Years of Iron Deficiency Anemia in a Patient by Double Balloon Enteroscopy; A Case Report and Review of Literature

Arash Dooghaie Moghadam<sup>1</sup>, Mohammad Bagheri<sup>1</sup>, Pegah Eslami<sup>1</sup>, Ermia Farokhi<sup>2</sup>, Amir Nezami Asl<sup>3</sup>, Karim Khavaran<sup>3</sup>, Shahrokh Irvani<sup>4,3</sup>, Sandra Saeedi<sup>3</sup>, Azim Mehrvar<sup>4</sup>, Masoud Dooghaie-Moghadam<sup>5</sup>

## ABSTRACT

Blue rubber bleb nevus syndrome (BRBNS) is a rare disorder comprised of venous malformation mostly involving the skin and gastrointestinal (GI) tract but can also involve other visceral organs. The most predominant site of GI tract involvement is the small bowel. In patients with GI lesions, treatment depends on the severity of bleeding, and extent of involvement. Conservative therapy with iron supplementation and blood transfusion is appropriate in cases with mild bleeding but in severe cases endoscopic and surgical interventions would be beneficial. Also, medical therapy with sirolimus significantly reduces bleeding. A 20-year-old woman was referred to our hospital after transfusion of six units of packed cell because of several episodes of lower GI bleeding within the past three months in the form of melena and a single episode of hematochezia. Her last hemoglobin level before admission was 10mg/dl. She underwent various unsuccessful investigations since she was eight years old to find the origin of refractory iron deficiency anemia. In upper endoscopy, five bleeding polypoid lesions were discovered in the jejunum. Lesions were excised by snare polypectomy. Over a six-month follow-up period, no signs of lower GI bleeding were noted and the patient had a normal hemoglobin level.

## KEYWORDS:

Blue rubber bleb nevus syndrome, Double balloon enteroscopy, Submucosal dissection, Endoscopy, Anemia, Small bowel

Please cite this paper as:

Dooghaie Moghadam A, Bagheri M, Eslami P, Farokhi E, Nezami Asl A, Khavaran K, Irvani, Sandra Saeedi S, Mehrvar A, Dooghaie-Moghadam M. Blue Rubber Bleb Nevus Syndrome because of 12 Years of Iron Deficiency Anemia in a Patient by Double Balloon Enteroscopy; A Case Report and Review of Literature. *Middle East J Dig Dis* 2021;13:153-159. doi: 10.34172/mejdd.2021.219.

## INTRODUCTION

Blue rubber bleb nevus syndrome (BRBNS) is an uncommon disorder comprised of multiple venous malformations mostly in the skin and gastrointestinal (GI) system but can also involve other organs such as the muscles, lung, eye, kidney, joints, and nervous system.<sup>1-3</sup> Cutaneous lesions have various appearance ranging from a blue-purple papule to a large vascular tumor.<sup>4</sup> Intestinal lesions can cause abdominal pain, intussusception, volvulus, infarction and GI bleeding.<sup>4</sup> BRBNS is more prevalent in childhood and adolescence but also lesions can be observed at birth.<sup>5,6</sup> Occurrence is mostly sporadic but autosomal dominant inheritance has been suggested previously.<sup>7</sup>

1. Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2. Liver Transplantation Research Center, Tehran University of Medical Sciences, Tehran, Iran
3. Gastroenterology and Hepatobiliary Research Center, AJA University of Medical Sciences, Tehran, Iran
4. Research Center for Cancer Screening and Epidemiology, AJA University of Medical Sciences, Tehran, Iran
5. Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran

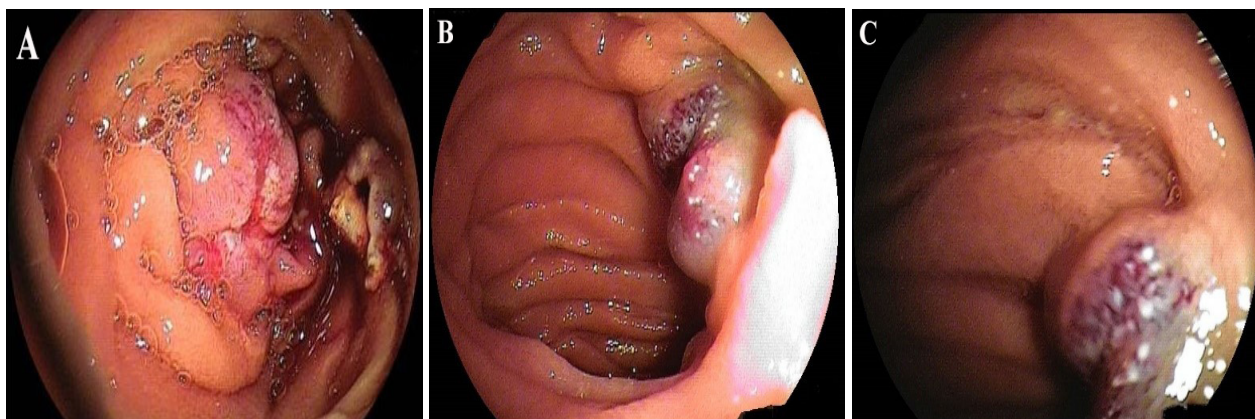
### \* Corresponding Author:

Masoud Dooghaie-Moghadam, MD  
North Kargar Street, Shariati Hospital,  
Digestive Diseases Research Institute  
Tel: + 98 21 82415000  
Fax: + 98 21 82415400  
Email: drmasoudm@gmail.com

Received: 08 Nov. 2020  
Accepted: 03 Mar. 2021



© 2021 The Author(s). This work is published by Middle East Journal of Digestive Diseases as an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0/>). Non-commercial uses of the work are permitted, provided the original work is properly cited.



**Fig.1:** Venous malformations located in jejunum observed during double balloon enteroscopy

Lower GI bleeding is a common manifestation of this syndrome ranging from an obscure lower GI bleeding to a massive life threatening bleeding.<sup>8</sup> Treatment options depend on the extent of and severity of involvement and bleeding. Conservative treatments can be a method of choice in mild bleeding but in severe forms, surgical and endoscopic interventions are necessary.<sup>5,9,10</sup> Double balloon enteroscopy has an important diagnostic-therapeutic role in small intestine pathologies. This method can be used to observe and excise BRBNS intestinal lesions.<sup>11</sup> We reported a 20-year-old woman with BRBNS manifested with obscure GI bleeding. Double balloon enteroscopy was used for diagnosis and finally the lesion was excised by snare polypectomy.

#### CASE REPORT

A 20-year-old woman was referred to our hospital after transfusion of six units of packed cell because of several episodes of lower GI bleeding from three months ago in form of melena and a single episode of hematochezia. Her last hemoglobin level before admission was 10 mg/dl. She underwent various unsuccessful investigations since she was eight years of age to find the origin of refractory iron deficiency anemia. Previously, she did not have a history of GI bleeding (melena and hematochezia), nausea or vomiting, diarrhea or constipation, abdominal pain, fever, significant weight loss, NSAIDs usage, or any comorbidities. In physical exam the patient was pale. No skin lesion was revealed. In our medical

center upper and lower endoscopy did not show any pathologies. Thus, we decided to perform an oral double balloon enteroscopy. Sedation initiated with pethidine 50 mg and diazepam 10 mg and was then adjusted according to the patient's demand. Vital signs were normal and stable during the procedure. Five bleeding polypoid vascular lesions were discovered in the jejunum (figure 1). The size of the largest lesion was 15×15 mm. After injecting epinephrine in lesions to bulge them, all of them were resected by snare and referred to a pathologist. Histopathology reported multiple hemangiomas. Two weeks later, the patient underwent oral double balloon enteroscopy again with the same sedation protocol. No signs of bleeding were found and hemoglobin level rose. After six months of follow-up, no signs of lower GI bleeding were noted and the patient had a normal hemoglobin level.

#### DISCUSSION

BRBNS is a rare syndrome presented with venous malformations mostly involving the skin and GI tract but can affect other organs such as the muscles, joints, eye, lung, kidney and nervous system.<sup>3</sup> Pathophysiology of the disease is not fully understood and is still unclear. Most of the cases are sporadic but autosomal dominant inheritance has been suggested previously.<sup>7</sup> It has been reported that stem cell factor/c-kit signaling system may cause vascular overgrowth.<sup>12</sup> Stimulation of mammalian target of rapamycin complex (mTOR) and mutations in TEK gene can also lead to angiogenesis in patients with

BRBNS.<sup>13,14</sup> Our patient did not undergo genetic analysis because of poor socioeconomical level. BRBNS, Maffucci syndrome, Osler–Weber–Rendu syndrome and Klippel–Trenaunay–Weber syndrome are differential diagnoses of skin and GI hemangiomas and accurate diagnosis is important.<sup>15,16</sup> Cutaneous lesions have three types: soft easy compressing bluish papules which quickly refill after compression, large vascular masses that can affect adjacent structures, and macular bluish lesions with irregular border. These lesions are not usually painful or bleed spontaneously. Lesions can be observed at birth but mostly present in childhood and adolescence. Excision or laser ablation is the method of choice in cutaneous lesions.<sup>3,17</sup> GI lesions can be observed in all parts of the GI tract from the mouth to anus. Lesions range from 1 to 10 cm. The small intestine is the most commonly involved site. Various GI presentations can be seen. Patients may have upper or lower GI bleeding for a long period of time. Lower GI bleeding is the most common symptom ranging from obscure to massive bleeding leading to anemia.<sup>3,18</sup> Some other rare complications may occur such as perforation, intussusception, intestinal torsion and infarction,<sup>16,19</sup> or hematological complications such as Disseminated intravascular coagulation and thrombocytopenia.<sup>3,6,20</sup> Mortality in patients with BRBNS was mostly reported in severe GI involvement such as intussusception, perforation and volvulus.<sup>21–23</sup>

Barium swallow, upper and lower Endoscopy, nuclear imaging, abdominal CT scan and MRI can be beneficial in diagnosis of GI tract lesions. Barium swallow can elucidate polypoid lesions in the upper GI tract but cannot differentiate vascular malformations from other types of lesions. Colonoscopy is an accurate method in discovering colonic lesions as well as video capsule endoscopy and double balloon enteroscopy that could be used as an ideal diagnostic measure for small intestine evaluation. The former is a non-invasive method that can record a video whole intestine specially, small intestine and the latter is an invasive method for evaluation of small intestine pathologies. MRI is beneficial in finding lesions located in organs such as spleen and liver. Scintigraphy is another non-invasive diagnostic method to find the source of GI bleeding when endoscopic procedures are unable to find the source of bleeding. Aggregation of radio nucleotide in venous malformations can reveal the GI lesions.<sup>18,24</sup>

Treatment of GI lesions depend on the extent and severity of involvement. In mild bleedings, iron supplementation therapy and appropriate diet can compensate Iron Deficiency Anemia (IDA). In some occasions blood transfusion is necessary.<sup>5</sup> Pharmacological treatment by corticosteroids, INF $\alpha$  and  $\beta$ -blockers have been tried before but did not significantly affect bleeding.<sup>25</sup> On the other hand, chronic subcutaneous octreotide has been reported to be effective in decreasing patients' demand for blood transfusions.<sup>26</sup> Recently, low dose sirolimus is beneficial in reducing GI bleeding in patients with BRBNS and can be an alternative to blood transfusions. Sirolimus inhibits mTOR complex which is associated with angiogenesis. Thus, it can decrease the size of GI venous malformations.<sup>27,28</sup> Before performing an invasive surgical operation, precise evaluation of the number of lesions and extent of involvement is necessary. Surgical excision such as partial gastrectomy, partial small bowel resection is preferred in focal GI involvement, although in cases with widespread GI involvement is not the method of choice. Moreover, in some complications including torsion, intussusception or perforation, surgical intervention is necessary.<sup>25</sup> Extensive resection increases the risk of short gut syndrome in these patients.<sup>21</sup> In patients with multi-organ involvement, medical therapy with sirolimus should be considered.<sup>29</sup> Endoscopic treatments are another invasive method of excising GI lesions by means of sclerotherapy, laser photocoagulation, band ligation, Argon plasma coagulation (APC), snare mucosectomy and endoscopic submucosal dissection.<sup>30</sup> Several studies suggested to avoid endoscopic procedures such as APC in the small intestine because of its thin wall and risk of perforation, while other authors reported that endoscopic procedures such as polypectomy and band ligation increased the risk of perforation and ulceration in transmural lesions.<sup>31,32</sup> Therefore, surgical full thickness wedge resection seems to be a better option.<sup>33</sup> We reviewed English articles containing endoscopic treatments in cases with BRBNS reported in last 5 years in table 1.

## CONCLUSION

According to the results of our review and also our case presentation, in the case of patient with prolonged Iron Deficiency Anemia, Blue Rubber Bleb Nevus Syndrome can be considered as differential diagnosis, however BRBNS is a rare disease and also Double balloon enteroscopy

**Table 1: Review of Endoscopic Treatments in Cases with BRBNS**

Patient number	Reference	Sex	Age at diagnosis	Site of involvement	Treatments	Type of endoscopy treatment	Follow-up results
1	21	M	4	Skin-GI-Angiokeratoma of left thigh	Endoscopic	APC- Band ligation- Sclerosing agent	Blood transfusions requirement decreased
2	21	F	15	GI	Endoscopic	APC	Blood transfusions requirement decreased
3	21	M	1	Skin-GI-Muscle	Endoscopic-Surgery	APC	Asymptomatic
4	21	M	5	Skin-GI	Endoscopic-Surgery	APC	Stable
5	21	M	12	Skin-GI	Endoscopic-Surgery	Intra-operative enteroscopy with snare mucosectomy- APC	Anemia- Iron infusion dependent
6	21	M	1	GI- CNS- Eyes	Endoscopic-Sirolimus	APC	Asymptomatic
7	21	F	2	GI- Skin- Joints- Angiokeratoma of second left toe and right thigh	Endoscopic-Surgery- Sirolimus	APC	Scarce response to endoscopic and surgical treatment
8	21	F	7	GI- Skin- Joints- Parotid Glands- Left kidney	Endoscopic-Surgery- Thalidomide- Interferon alpha-2a- Prednisolone- Propanolol- Octreotide	Intraoperative enteroscopy with surgical wedge excision of small bowel lesions	Still blood transfusion dependent- Interferon alpha-2a side effects
9	21	F	5	Skin- GI- CNS- Spine- Muscles- Joints	Endoscopic-surgery- Thalidomide- Tranexamic acid- Sirolimus	Sclerosing agent- Intraoperative enteroscopy with surgical wedge excision of small bowel	Active Intussusceptions- Thalidomide side Effects- Good response to sirolimus, relapse when the drug was stopped, required surgery- Occasional blood per rectum, no blood transfusion requirement
10	21	M	1	Skin- GI- Lungs	Endoscopic-Surgery- Prednisolone	Sclerosing agent	Blood transfusions requirement decreased
11	34	M	21	Skin- liver- GI	Endoscopy-Surgery- Octreotide- Sirolimus	Sclerosing agent- APC- ligature with envelope	Maintains an excellent control of anemia and gastrointestinal bleeding
12	35	F	13	GI	Endoscopy-Surgery	Sclerosing agent	Failure of endoscopic management and bleeding recurred, surgery was planned

Patient number	Reference	Sex	Age at diagnosis	Site of involvement	Treatments	Type of endoscopy treatment	Follow-up results
13	17	F	19	Skin- GI- Pleura- Liver- Spleen- Ovary	Endoscopy- Surgery- Beta blocker	Band ligation- APC- intra operative endoscopy	No bleeding and anemia for 5 years after endoscopy and surgery
14	36	M	19	Skin- GI	Endoscopy- Surgery- Siro- limus	Sclerosing agent- APC	Anemia resolved and patient's weight increased
15	37	M	9	Skin- GI	Endoscopy	Sclerosing agent- APC	Asymptomatic
16	30	F	18	GI	Endoscopy	Endoscopic submucosal dissection	No bleeding happened
17	38	F	10	Skin- GI- Cer- ebellum- Iris	Endoscopy	Sclerosing agent	She did not manifest anemia
18	39	M	13	Skin- GI	Endoscopy	Sclerosing agent	No further blood transfusion was needed
19	40	M	21	GI	Endoscopy	Endloop-snare	No bleeding of perforation during 6 months of follow up
20	41	F	19	Skin- GI	Endoscopy	Snare mucosectomy	No recurrence of the hemangiomas in the patient's stomach 6 months after endoscopic treatment
21	42	F	24	Skin- GI	Endoscopy	Sclerosing agent	The patient had no obvious drop in hemoglobin during the process
22	43	F	21	GI	Endoscopy	En-bloc endoscopic mucosal resection (EMR) using a symmetric snare- APC	There was no bleeding recurrence in two years of follow-up
23	44	F	34	GI	Endoscopy- surgery	Intra operative endoscopy with band ligation	Good clinical condition and did not need further blood transfusions.
24	45	F	15	Skin- GI	Endoscopy- surgery	Intra operative endoscopic band ligation	After 6 months she had no discomfort

can play crucial role in the diagnosis and treatment of these patients.

#### ETHICAL APPROVAL

There is nothing to be declared.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

#### REFERENCES

1. Domini M, Aquino A, Fakhro A, Tursini S, Marino N, Di Matteo S, et al. Blue rubber bleb nevus syndrome and gastrointestinal haemorrhage: which treatment? *Eur J Pediatr Surg* 2002;**12**:129-33. doi: 10.1055/s-2002-30172.
2. Hasosah MY, Abdul-Wahab AA, Bin-Yahab SA, Al-Rabeaah AA, Rimawi MM, Eyon YA, et al. Blue rubber bleb nevus syndrome: extensive small bowel vascular lesions responsible for gastrointestinal bleeding. *J Paediatr Child Health* 2010;**46**:63-5. doi: 10.1111/j.1440-1754.2009.01619.
3. Jin XL, Wang ZH, Xiao XB, Huang LS, Zhao XY. Blue rubber bleb nevus syndrome: a case report and literature review. *World J Gastroenterol* 2014;**20**:17254-9. doi: 10.3748/wjg.v20.i45.17254.
4. Nahm WK, Moise S, Eichenfield LF, Paller AS,

- Nathanson L, Malicki DM, et al. Venous malformations in blue rubber bleb nevus syndrome: variable onset of presentation. *J Am Acad Dermatol* 2004;**50**:101-6. doi: 10.1016/s0190-9622(03)02468-x.
5. Haiping P, Guoqing L, Zhongshu Y. Blue rubber bleb naevus syndrome. *Eur J Surg* 2001;**167**:628-30. doi: 10.1080/110241501753171263.
  6. Menegozzo MAC, Novo FdCF, Mori ND, de Oliveira Bernini C, Utiyama EM. Postoperative disseminated intravascular coagulation in a pregnant patient with Blue Rubber Bleb Nevus Syndrome presenting with acute intestinal obstruction: Case report and literature review. *Int J Surg Case Rep* 2017;**39**:235-8. doi: 10.1016/j.ijscr.2017.08.026.
  7. Gallo SH, McClave SA. Blue rubber bleb nevus syndrome: gastrointestinal involvement and its endoscopic presentation. *Gastrointest Endosc* 1992;**38**:72-6. doi: 10.1016/s0016-5107(92)70339-3.
  8. Li Z, Yuan H, Yu D, Victor N, Chen Y, Feng J, et al. The surgery for blue rubber bleb nevus syndrome. *Ann Med Surg* 2016;**5**:93-6. doi: 10.1016/j.amsu.2015.12.062.
  9. Choi KK, Kim JY, Kim MJ, Park H, Choi DW, Choi SH, et al. Radical resection of intestinal blue rubber bleb nevus syndrome. *J Korean Surg Soc* 2012;**83**:316-20. doi: 10.4174/jkss.2012.83.5.316.
  10. Wong CH, Tan YM, Chow WC, Tan PH, Wong WK. Blue rubber bleb nevus syndrome: a clinical spectrum with correlation between cutaneous and gastrointestinal manifestations. *J Gastroenterol Hepatol* 2003;**18**:1000-2. doi: 10.1046/j.1440-1746.2003.03083.x.
  11. Hernandez OV, Blancas M, Paz V, Moran S, Hernandez L. Diagnosis and treatment of blue rubber bleb nevus syndrome with double balloon enteroscopy and endoscopic ultrasound. *Dig Endosc* 2007;**19**:86-9. doi: 10.1111/j.1443-1661.2007.00672.x
  12. Mogler C, Beck C, Kulozik A, Penzel R, Schirmacher P, Breuhahn K. Elevated expression of c-kit in small venous malformations of blue rubber bleb nevus syndrome. *Rare Tumors* 2010;**2**:e36. doi: 10.4081/rt.2010.e36.
  13. Yuksekkaya H, Ozbek O, Keser M, Toy H. Blue rubber bleb nevus syndrome: successful treatment with sirolimus. *Pediatrics* 2012;**129**:e1080-e4. doi: 10.1542/peds.2010-3611.
  14. Soblet J, Kangas J, Nätyнки M, Mendola A, Helaers R, Uebelhoer M, et al. Blue Rubber Bleb Nevus (BRBN) Syndrome Is Caused by Somatic TEK (TIE2) Mutations. *J Invest Dermatol* 2017;**137**:207-16. doi: 10.1016/j.jid.2016.07.034.
  15. Tang X, Gao J, Yang X, Guo X. A 10-year delayed diagnosis of blue rubber bleb nevus syndrome characterized by refractory iron-deficiency anemia: A case report and literature review. *Medicine* 2018;**97**:e10873. doi: 10.1097/MD.00000000000010873.
  16. Nakajima H, Nouse H, Urushihara N, Fukumoto K, Yamoto M, Miyake H, et al. Blue Rubber Bleb Nevus Syndrome with Long-Term Follow-Up: A Case Report and Review of the Literature. *Case Rep Gastrointest Med* 2018;**2018**:8087659. doi: 10.1155/2018/8087659. eCollection 2018.
  17. Martinez CAR, Rodrigues MR, Sato DT, Silveira Júnior PP, Gama RF, Mattavelli CB, et al. Blue rubber bleb nevus syndrome as a cause of lower digestive bleeding. *Case Rep Surg* 2014;**2014**:683684. doi: 10.1155/2014/683684.
  18. Ur Rashid M, Muhammad Khan M, Ullah W, Hussain I, Hurairah A. Blue rubber bleb nevus: a rare cause of GI bleeding—review of management. *BMJ Case Reports* 2019;**12**:e231561. doi: 10.1136/bcr-2019-231561.
  19. Browne AF, Katz S, Miser J, Boles Jr ET. Blue Rubber Bleb Nevi as a cause of intussusception. *J Pediatr Surg* 1983;**18**:7-9. doi: 10.1016/s0022-3468(83)80263-2.
  20. Dobru D, Seuceha N, Dorin M, Careianu V. Blue Rubber Bleb Nevus Syndrome: Case Report and literature review. *Rom J Gastroenterol* 2004;**13**:237-40.
  21. Isoldi S, Belsha D, Yeop I, Uc A, Zevit N, Mamula P, et al. Diagnosis and management of children with Blue Rubber Bleb Nevus Syndrome: A multi-center case series. *Dig Liver Dis* 2019;**51**:1537-46. doi: 10.1016/j.dld.2019.04.020.
  22. Lee C, Debnath D, Whitburn T, Farrugia M, Gonzalez F. Synchronous multiple small bowel intussusceptions in an adult with blue rubber bleb naevus syndrome: Report of a case and review of literature. *World J Emerg Surg* 2008;**3**:3. doi: 10.1186/1749-7922-3-3.
  23. Ocampo-Garza J, Salas-Alanís JC, Ponce-Camacho MA, Rosales-Solis GM, Miranda MI, Elizondo-Riojas G, et al. Fatal Outcome from Brain Vascular Lesions in a Neonate with Blue Rubber Bleb Nevus Syndrome. *Pediatr Dermatol* 2016;**33**:e29-31. doi: 10.1111/pde.12718.
  24. Aravindan U, Ganesan R, Kannan MT. Surgery for Blue Rubber Bleb Nevus Syndrome—a Case Report. *Indian J Surg* 2018;**80**:272-4. doi: 10.1007/s12262-017-1715-y.
  25. Fishman SJ, Smithers CJ, Folkman J, Lund DP, Burrows PE, Mulliken JB, et al. Blue rubber bleb nevus syndrome: surgical eradication of gastrointestinal bleeding. *Ann Surg* 2005;**241**:523-8. doi: 10.1097/01.sla.0000154689.85629.93.
  26. Gonzalez D, Elizondo BJ, Haslag S, Buchanan G, Burdick JS, Guzzetta PC, et al. Chronic subcutaneous octreotide decreases gastrointestinal blood loss in blue rubber-bleb nevus syndrome. *J pediatr Gastroenterol Nutr* 2001;**33**:183-8. doi: 10.1097/00005176-200108000-00017.
  27. Wang KL, Ma SF, Pang LY, Zhang MN, Hu LY, Liu MJ, et al. Sirolimus alternative to blood transfusion as a life saver in blue rubber bleb nevus syndrome:

- A case report. *Medicine* 2018;**97**:e9453. doi: 10.1097/MD.00000000000009453.
28. Yuksekkaya H, Ozbek O, Keser M, Toy H. Blue rubber bleb nevus syndrome: successful treatment with sirolimus. *Pediatrics* 2012;**129**:e1080-4. doi: 10.1542/peds.2010-3611.
  29. Fox VL. New therapies for vascular anomalies of the gastrointestinal tract. *Minerva pediatr* 2018;**70**:303-7.
  30. Chen W, Chen H, Shan G, Yang M, Hu F, Li Q, et al. Blue rubber bleb nevus syndrome: our experience and new endoscopic management. *Medicine* 2017;**96**:e7792. doi: 10.1097/MD.00000000000007792.
  31. Ng WT, Wong YT. Blue rubber bleb nevus syndrome: more lessons to be learnt. *Eur J pediatr Surg* 2007;**17**:221-2. doi: 10.1055/s-2007-965392.
  32. Ng WT, Kong CK. Argon plasma coagulation for blue rubber bleb nevus syndrome in a female infant. *Eur J Pediatr Surg* 2003;**13**:137-9. doi: 10.1055/s-2003-39582.
  33. Kopacova M, Tacheci I, Koudelka J, Kralova M, Rejchrt S, Bures J. A new approach to blue rubber bleb nevus syndrome: the role of capsule endoscopy and intra-operative enteroscopy. *Pediatr Surg Int* 2007;**23**:693-7. doi: 10.1007/s00383-006-1843-0.
  34. Fernandez Gil M, Lopez Serrano P, Garcia Garcia E. Successful management of anemia with sirolimus in blue rubber bleb nevus syndrome: case report and update. *Rev Esp Enferm Dig* 2019;**111**:643-7. doi: 10.17235/reed.2019.6250/2019.
  35. Aravindan U, Ganesan R, Thamarai Kannan M. Surgery for Blue Rubber Bleb Nevus Syndrome-a Case Report. *Indian J Surg* 2018;**80**:272-4. doi: 10.1007/s12262-017-1715-y.
  36. Cardoso H, Dias JA, Silva M, Vilas-Boas F, Trindade E, Tavares M, et al. Education and Imaging. Gastrointestinal: Successful treatment with sirolimus of a patient with blue rubber bleb nevus syndrome. *J Gastroenterol Hepatol* 2016;**31**:519. doi: 10.1111/jgh.13178.
  37. Malafaia MC, Heissat S, Jacob P, Le Gall C, Ruiz M, Saurin JC, et al. Blue rubber bleb nevus syndrome: endoscopic treatment with sclerotherapy during double-balloon enteroscopy in a 9-year-old boy. *Endoscopy* 2019;**51**:E98-E100. doi: 10.1055/a-0840-3214.
  38. Kumei T, Toya Y, Shiohata T, Kakuta F, Yanai S, Kawasaki K, et al. Gastrointestinal: Endoscopic injection sclerotherapy for duodenal vascular malformation in blue rubber bleb nevus syndrome. *J Gastroenterol Hepatol* 2019;**34**:963. doi: 10.1111/jgh.14590.
  39. Li A, Chen FX, Li YQ. An Unusual Cause of Recurrent Melena. *Gastroenterology* 2019;**157**:311-2. doi: 10.1053/j.gastro.2019.04.009.
  40. Jin J, Pan J, Zhu L. Therapy for hemangiomas of blue rubber bleb nevus syndrome in the small intestine with single balloon endoscopy. *Dig Endosc* 2015;**27**:780. doi: 10.1111/den.12522.
  41. Wu C, Tan Q, Zhang Q, Hu B. Successful Endoscopic Resection of Blue Rubber Bleb Nevus Syndrome in the Stomach Using a Snare. *Am J Gastroenterol* 2017;**112**:1494. doi: 10.1038/ajg.2017.169.
  42. Wang Z, Yang X, Wu L, Shi H, Lu Y, Yuan B, et al. Blue rubber bleb nevus syndrome: treatment of lesions in the small intestine with repeated injection of lauro-macroglol. *Gastrointest Endosc* 2015;**81**:1274-5. doi: 10.1016/j.gie.2014.08.013.
  43. Rubio-Mateos JM, Tojo-Gonzalez R, Perez-Cuadrado-Robles E. Endoscopic mucosal resection by double-balloon enteroscopy can be an alternative in small bowel venous malformations. *Dig Endosc* 2018;**30**:789. doi: 10.1111/den.13224.
  44. Arena M, Viridis M, Morandi E, Viaggi P, Pisani A, Opocher E, et al. Blue rubber bleb nevus syndrome: combined surgical and endoscopic treatment. *Endoscopy* 2015;**47**:E372-3. doi: 10.1055/s-0034-1392635.
  45. Yang X, Wei M, Wang Z. A Rare Cause of Recurrent Hematochezia. *Gastroenterology* 2016;**150**:568-9. doi: 10.1053/j.gastro.2015.12.010.