

CLINICAL NOTE

Massive spontaneous hemothorax in patients with neurofibromatosis type 1

Pedro José Gil Vázquez, Andrés del Amor Arroyo Tristán, Jesús Martínez Baños, Juan Torres Lanzas

Spontaneous hemothorax is an uncommon event that can occur in patients with a history of neurofibromatosis type 1 because of intrathoracic vascular malformations that predispose to aneurysms or bleeding from thoracic tumors. Only 53 cases of this rare association have been reported in the literature since 1975. We described 2 cases: one patient was a 73-year-old man with a right hemothorax secondary to an intercostal neurofibroma; the other was a 35-year-old woman with a left hemothorax secondary to a neurofibroma that compromised the internal mammary artery. Our review of the literature found that 61.8% of cases involved women with a mean age of 43.9 years. There was a certain tendency toward left-sided (56.4%) hemothorax, and the intercostal space was the most common site of bleeding. Treatment was most often surgical (58.2%) in reported cases, although selective artery embolization is also a valid choice. Exitus occurred during 30.9% of the reported episodes, and survival was higher in patients who were treated with surgery or arterial embolization than in those in whom only a thoracic drain was placed or who received no invasive treatment ($P=0.02$).

Keywords: Hemothorax. Neurofibromatosis. Aneurysm. Arterial embolization, percutaneous.

Hemotórax masivo espontáneo en pacientes con neurofibromatosis tipo 1

El hemotórax espontáneo es una entidad poco frecuente que en los pacientes con antecedentes de neurofibromatosis tipo 1 (NF1) puede ser debido a malformaciones vasculares intratorácicas que predisponen a formaciones aneurismáticas o bien a sangrado de tumores torácicos. Esto ocurre en muy raras ocasiones, con solo 53 casos reportados en la bibliografía desde 1975. Presentamos dos casos: el primero, un varón de 73 años con hemothorax derecho secundario a un neurofibroma intercostal; el segundo, una mujer de 35 años con hemotórax izquierdo secundario a un neurofibroma que lesionaba la arteria mamaria interna. Revisando la bibliografía, el 61,8% son mujeres con una edad media de 43,9 años, y con cierta predisposición a la localización en el hemitórax izquierdo (56,4%). El paquete intercostal es el más frecuentemente involucrado en el sangrado. La cirugía ha sido el tratamiento realizado con mayor frecuencia (58,2%), si bien la embolización a través de arteriografía selectiva es un tratamiento válido. Un 30,9% fallecieron durante el episodio y aquellos tratados con cirugía o embolización arteriográfica tienen una mayor supervivencia que aquellos pacientes a los que no recibieron tratamiento invasivo o bien solo se les colocó un drenaje torácico ($p = 0,02$).

Palabras clave: Hemotórax. Neurofibromatosis. Aneurisma. Embolización arterial percutánea.

Introduction

Massive spontaneous intrathoracic bleeding is rare and is usually associated with aortic aneurysms and ruptured pleural adhesions after spontaneous pneumothorax¹. They can also be secondary to aneurysms of the intercostal arteries and tumour pathology. In these cases, they are associated with pathologies such as neurofibromatosis type 1 (NF1), Kawasaki disease and coarctation of aorta².

Clinical cases**Case 1**

A 35-year-old woman with NF1 and surgery to remove a mediastinal schwannoma. In the postoperative period of acute appendicitis, chest pain, dyspnoea and anaemia appeared, associated with left pulmonary hypoventilation and pleural effusion on the chest radio-

graph. He presented hemodynamic instability and cardiorespiratory arrest, so left posterolateral resuscitation thoracotomy was performed, appreciating active bleeding of aberrant vessels in the left internal mammary artery. Four rib fragments were resected (4th to 7th), and the internal mammary artery was ligated. He presented good evolution and was discharged.

Case 2

A 73-year-old man with NF1 went to the emergency room for right chest pain and dyspnoea. He had right pulmonary hypoventilation and hypotension (87/49 mmHg). Computed tomography (CT) showed an aneurysm in the fifth right intercostal artery that was embolized. Subsequently he presented dyspnoea and instability. Thoracic drainage was performed and about 1,200 cc of blood was obtained. Video-assisted thoracoscopy was performed, which showed bleeding from the intercostal tumour that was ligated. Since he was still hemodynamically unstable, he was re-operated

Authors affiliation:
Servicio Cirugía General y Aparato Digestivo. Hospital Clínico Universitario Virgen de la Arrixaca, El Palmar, Murcia, Spain.

Contribution of authors:
All authors have confirmed their authorship in the author's responsibilities documents publication agreement and assignment of rights to EMERGENCIAS.

Corresponding author:
Pedro José Gil Vázquez
Servicio Cirugía General
Hospital Universitario
Virgen de la Arrixaca
Ctra. Madrid-Cartagena, s/n
30120 Murcia, Spain

E-mail:
pedro.jgv88@gmail.com

Article information:
Received: 5-7-2017
Accepted: 21-9-2017
Online: 15-3-2018

Editor in charge:
Fernando Rosell Ortiz, MD, PhD.

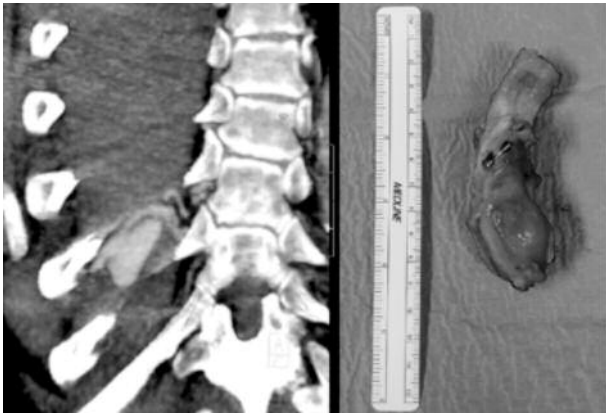


Figure 1. Aneurysm of the intercostal artery in a patient with neurofibromatosis type 1 (NF1). Computed tomography (left) and surgical piece (right).

through a right posterolateral thoracotomy, with excision of the lesion near the rib (Figure 1). In the postoperative period, he presented an acute pulmonary oedema secondary to the massive transfusion of blood products, so he died in the first week after surgery.

Discussion

A bibliographic search was carried out by three authors and independently in the main databases of health sciences (PubMed, Web of Knowledge, Scopus, Google Scholar), using the keywords "hemothorax", "spontaneous hemothorax", "Neurofibromatosis" and "Von Recklinghausen" interposing the "AND" connector. No limits have been set regarding magazine, publication date or language. All articles describing cases of spontaneous hemothorax in NF1 have been included, regardless of the nature of the hemothorax (clinical note, description of cases, description of technique...). From these articles a series of variables have been collected (year of publication, sex, age, location of the hemothorax, artery responsible, vascular injury, presence or absence of tumour, histology, treatment and survival). This type of search, despite the systematic used, may have limitations, such as the non-detection of relevant articles. However, the scarcity of results brings us closer to the idea of how exceptional these cases are (Table 1).

NF1 or Von Recklinghausen disease consists of the growth of neuroectodermal tumours in the peripheral nervous system, with an autosomal dominant inheritance, consisting of the mutation of chromosome 17q11.2 with variable penetrance³. It usually comes with multiple skin tumours and visible brown spots, hamartomas on the iris, as well as tumours in internal organs. These tumours can also be malignant⁴.

Arterial lesions in NF1 due to weakness of the vessel wall are rare, around 3.6%⁵. Massive hemothorax is a rare complication⁶ and is usually due to tumour bleeding, as an aneurysm in the intercostal artery is very infrequent^{2,7}. Sometimes, intercostal bleeding, due to bruising

or hemostatic maneuvers, can compress the spinal cord and give neurological symptoms as paraplegia⁸.

In the bibliography we have found 52 cases of spontaneous hemothorax in patients with NF1 (Table 1) (61.8% women, mean age 43.9 years), with left predisposition (56.4%). The arteries most often involved are the intercostals (41.8%), followed by the subclavian (25.5%) and the internal mammary (10.9%). Surgery has been the treatment of choice (32 cases), although it is true that in recent years there has been a trend toward arterial embolization⁸⁻¹³. Seventeen patients (30.9%) died (10 after surgery and 2 after embolization). 71.4% of the patients who did not receive hemostatic treatment died. Given the characteristics of the series of cases collected, isolated cases, with disparate information and very dispersed over time, no opinions can be inferred on the results of the different treatments performed. From a purely descriptive point of view, it seems that patients treated with surgery or embolization have a longer survival than those who did not receive invasive treatment or only had a thoracic drainage. There are also no differences between surgery and embolization, although embolization is usually reserved for patients with hemodynamic stability. Recurrence of the hemothorax between days and months after embolization is described^{14,15}, since the responsible lesion has not been excised.

The treatment of choice in the face of a massive hemothorax is surgery⁵, through thoracotomy or videothoracoscopy, in order to identify the cause of the bleeding and perform the maneuvers necessary for hemostasis. In recent years, the possibility of endovascular treatment has appeared, allowing embolization of the lesions responsible for bleeding, usually associated with other maneuvers, such as chest drainage in order to evacuate the residual hemothorax. It is a minimally invasive and safe solution that can be carried out when it is not necessary to preserve arterial flow⁵. However, when there is hemodynamic instability, the first therapeutic option must be emergency and aggressive surgery¹. In addition, we must bear in mind that hemostasis, as in the case of embolizations, does not always imply the resolution of the condition, since the patient is a critical patient who can perform multiple complications, such as renal failure or pulmonary edema due to resuscitation maneuvers.

In conclusion, before a patient with NF1 and hemodynamic instability, a hypovolemic shock should be ruled out because, although rare, massive spontaneous hemothorax can be the cause of the condition.

Conflicting interests

The authors declare no conflict of interest in relation to this article.

Financing

The authors declare the non-existence of external financing of this article.

Table 1. Previous publications of spontaneous hemothorax in neurofibromatosis type 1 (NF1)

Author	Year of publication	Sex	Age	Hemothorax location	Responsible artery	Vascular lesion	Tumour	Histology	Treatment	Survival
Butchart <i>et al.</i> ¹	1975	Male	41	Right	Intercostal	Not-examined	No	–	Surgery	Survival
Larrieu <i>et al.</i> ²	1982	Female	44	Right	Intercostal	No	Yes	Schwannoma	Surgery	Survival
Brady <i>et al.</i> ³	1984	Female	37	Right	Subclavian	No	Yes	Neurofibroma	No treated	Alive
	1984	Female	26	Left	Intercostal	Yes	No	Fibrovascular tissue	Surgery	Survival
Lim <i>et al.</i> ⁴	1990	Male	18	Left	Intercostal	No	Yes	Neurofibrosarcoma	Surgery	Survival
Fuyuno <i>et al.</i> ⁵	1995	Male	17	Left	Internal mammary	No	Yes	Schwannoma	Surgery	Alive
Teitelbaum <i>et al.</i> ⁶	1998	Female	34	Left	Subclavian	Aneurysm	No	–	Embolization	Survival
Griffiths <i>et al.</i> ⁷	1998	Female	63	Left	Not confirmed	No	No	–	No treated	Alive
Kipfer <i>et al.</i> ⁸	2001	Female	42	Right	Intercostal	Aneurysm	No	–	Embolization	Survival
Domínguez <i>et al.</i> ⁹	2002	Female	44	Left	Intercostal	Aneurysm	No	–	Embolization	Survival
Pezzetta <i>et al.</i> ¹⁰	2003	Female	29	Left	Not confirmed	No	No	–	Thoracic drainage	Survival
Baldo <i>et al.</i> ¹¹	2003	Male	33	Right	Subclavian	Yes	Yes	Neurofibroma	Surgery	Alive
Miura <i>et al.</i> ¹²	2005	Male	55	Right	Intercostal	Aneurysm	No	–	Surgery	Survival
		Female	43	Left	Intrathoracic	No	Yes	Neurofibroma	No treated	Alive
		Female	37	Left	Subclavian	No	Yes	Neurofibroma	Surgery	Alive
		Female	48	Left	Subclavian	Yes	No	–	Surgery	Alive
		Female	31	Right	Intercostal	Yes	No	–	Surgery	Survival
		Female	38	Left	Subclavian	Yes	No	–	Surgery	Survival
		Female	48	Left	Intrathoracic	Aneurysm	No	–	Surgery	Survival
		Female	57	Left	Intercostal	Yes	No	–	Surgery	Survival
		Female	55	Left	Intercostal	Yes	No	–	Surgery	Survival
		Female	48	Left	Intrathoracic	Aneurysm	No	–	Surgery	Survival
		Male	61	Left	Subclavian	Aneurysm	No	–	Thoracic drainage	Alive
		Female	59	Left	Intercostal	No	Yes	Neurofibroma	Surgery	Survival
		Male	46	Right	Intercostal	Aneurysm	No	–	Embolization	Survival
Vaziri <i>et al.</i> ¹³	2006	Female	30	Right	Internal mammary	No	Yes	Ganglioneuroma	Surgery	Survival
Arai <i>et al.</i> ¹⁴	2007	Male	38	Left	Subclavian	Aneurysm	No	–	Embolization	Alive
		Female	72	Left	Intercostal	Aneurysm	No	–	Embolization	Survival
		Male	49	Left	Intercostal	Aneurysm	No	–	Embolization	Survival
Imamura <i>et al.</i> ¹⁵	2007	Male	40	Right	Intercostal	Aneurysm	No	–	Embolization	Survival
Conlon <i>et al.</i> ¹⁶	2007	Male	40	Right	Internal mammary	Aneurysm	No	–	Surgery	Survival
Urso <i>et al.</i> ¹⁷	2007	Male	63	Right	Internal mammary	Aneurysm	No	–	Surgery	Alive
Radeschi <i>et al.</i> ¹⁸	2007	Female	36	Right	Not confirmed	No	Yes	Neurofibroma	Thoracic drainage	Survival
Fedoruk <i>et al.</i> ¹⁹	2007	Female	48	Left	Subclavian	No	Yes	Neurofibroma	Surgery	Survival
Fernández-Flores <i>et al.</i> ²⁰	2008	Male	28		Internal mammary	No	Yes	Neurofibroma	No treated	Alive
		Female	42	Left	Subclavian	Yes	No	–	Embolization	Alive
Sandhu <i>et al.</i> ²¹	2008	Female	42	Left	Subclavian	Yes	No	–	Embolization	Alive
Faruque <i>et al.</i> ²²	2009	Female	31	Left	Subclavian	No	Yes	Neurofibroma	Surgery	Survival
Aizawa <i>et al.</i> ²³	2010	Male	48	Right	Intercostal	Yes	No	–	Surgery	Survival
Kim <i>et al.</i> ²⁴	2011	Female	32	Left	Others	Aneurysm	No	–	Surgery	Alive
		Female	32	Left	Intercostal	Yes	No	–	Surgery	Alive
Miyazaki <i>et al.</i> ²⁵	2011	Female	59	Right	Subclavian	Yes	–	Surgery	Survival	
Kaneda <i>et al.</i> ²⁶	2011	Female	66	Left	Others	No	Yes	Meningocele	Surgery	Survival
Misao <i>et al.</i> ²⁷	2012	Male	40	Right	Intercostal	Yes	No	–	Embolization	Survival
Fukuda <i>et al.</i> ²⁸	2012	Male	47	Right	Intercostal	Yes	No	–	Embolization	Survival
Hongsakul <i>et al.</i> ²⁹	2013	Female	46	Left	Intercostal	Yes	Yes	Meningocele	Embolization	Survival
Pulivarthi <i>et al.</i> ³⁰	2014	Female	49	Right	Not confirmed	No	Yes	Neurofibroma	Surgery	Survival
Yusuf <i>et al.</i> ³¹	2014	Female	43	Right	Others	No	Yes	Meningocele	Surgery	Survival
Rodríguez-Guzmán <i>et al.</i> ³²	2014	Male	53	Right	Subclavian	Yes	No	–	Embolization	Survival
Fördring <i>et al.</i> ³³	2014	Female	39	Left	Not confirmed	No	Yes	Neurofibroma	Surgery	Alive
Hoonjan <i>et al.</i> ³⁴	2014	Male	43	Left	Others	No	No	–	Embolization	Survival
Mydin <i>et al.</i> ³⁵	2015	Female	56	Right	Subclavian	Aneurysm	No	–	Embolization	Survival
Bommart <i>et al.</i> ³⁶	2015	Male	44	Left	Intercostal	Aneurysm	No	–	Surgery	Alive
Case 1*	2007	Female	35	Left	Internal mammary	No	Yes	Neurofibroma	Surgery	Survival
Case 2*	2015	Male	73	Right	Intercostal	Aneurysm	Yes	Neurofibroma	Surgery	Alive

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*Cases presented in this article.

Ethical Responsibilities

All authors have confirmed the maintenance of confidentiality and respect for patients' rights in the author's responsibilities document, publication agreement and assignment of rights to EMERGENCIAS.

Patients have confirmed their consent for their personal information to be published.

Article not commissioned by the Editorial Committee and with external peer review

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