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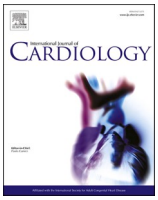

Drug-induced pericarditis: a systematic review of all published cases

Valentino Collini [a,1], Luca Siega Vignut [a,b,1], Francesco Venturelli [a,1], Massimo Imazio [a,c,*,1]

[a] Cardiology and Cardiothoracic Department, University Hospital Santa Maria della Misericordia, ASUFC, Udine and Department of Medicine, University of Udine, Italy
[b] Cardiovascular Department, Azienda Sanitaria Universitaria Giuliano Isontina (ASUGI), University of Trieste, Trieste, Italy
[c] Department of Medicine (DMED), University of Udine, Udine, Italy

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ABSTRACT

Background: No large case series nor clinical trials on drug-induced pericarditis have been reported. This study analyses data from previously reported cases to provide a comprehensive understanding of the aetiology, clinical presentation, management strategies, and outcomes of this rare and often underestimated aetiology of pericarditis.

Methods: A systematic review according to PRISMA guidelines was conducted, identifying 121 cases of drug-induced pericarditis. All references found, upon initial assessment at title and abstract level for suitability, were consequently retrieved as full reports for inclusion in this review.

Results: Among the 121 cases, 37 were related to anti-cancer, immunosuppressive, immunomodulatory drugs, 27 to anti-inflammatory drugs, 33 to central nervous system agents, 10 to cardiovascular drugs and 18 to other drugs. Median age was 45 (27, 59), 38.8 % were females, the most frequent symptom was pericardial chest pain, described in 86.8 % of patients. Many patients presented associated systemic symptoms; concomitant minor myocardial involvement was found in about half of the patients. All patients were hospitalized and withdrew the drug at the time of diagnosis. Symptoms resolved in an average of 5 ± 4 days and all patients who resumed the drug experienced a new recurrence. 18 patients underwent pericardiocentesis for cardiac tamponade, 9 underwent pericardiectomy. Four patients died during the follow-up.

Conclusions: Although uncommon, drug-induced pericarditis can be a life-threatening condition, causing cardiac tamponade or constrictive pericarditis. It is therefore crucial to increase awareness and knowledge of this rare aetiology of pericarditis to ensure prompt diagnosis and timely withdrawal of the causative drug.

1. Introduction

The knowledge of pericardial diseases has been recently improved, including prospective and retrospective cohort studies focusing on the pathogenesis, diagnosis, treatment, and outcomes [1–4]. However, population-based studies on the incidence and aetiology of pericardial diseases are scant. The incidence of acute pericarditis (AP) is estimated to be approximately 3–32 cases per 100,000 person-years [1]. Of these, the idiopathic or viral aetiology is the most frequent in developed countries, comprising about 80 % of all new diagnoses of AP, while the incidence of drug-related pericarditis remains rare, being estimated in less than 1 % of cases [1]. Historically, drugs such as procainamide, hydralazine and isoniazid have been associated with systemic lupus erythematosus (SLE), resulting in serositis and pericardial involvement presenting as pericarditis [5]. Other causative mechanisms include a spectrum of allergic reactions, the innate immunity and a direct cardiotoxic action that cause pericardial injury and associated myocarditis (i.e. myopericarditis). In some cases, mechanisms may combine, and the relative proportion of these associations remains undefined. The clinical presentation may be variable, ranging from oligosymptomatic to AP manifesting with cardiac tamponade or right heart failure due to constrictive pathophysiology. The treatment and prognosis are still unknown, as there are no studies conducted specifically for these patients. Our aim was to conduct a systematic review of all published cases of drug-induced pericarditis in order to raise awareness of this rare cause of pericarditis and describe the clinical presentation, diagnostic findings, treatment strategies and outcomes of this often-unrecognised cause of pericarditis.

* Corresponding author at: Cardiology and Cardiothoracic Department, University Hospital Santa Maria della Misericordia, ASUFC, Piazzale Santa Maria della Misericordia 15, 33100 Udine, Italy.
E-mail address: massimo.imazio@uniud.it (M. Imazio).

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2. Methods

2.1. Search strategy and data extraction

The study was accepted by PROSPERO (ID CRD420250651030) on 14 March 2025. Three independent authors (V.C., L.S.V., F.V.) create the database performing a systematic search of literature according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines using Medline (National Library of Medicine, Bethesda, MD) via PubMed and EMBASE, until June 29, 2024. A total of 359 articles were identified that mention MeSH terms "pericarditis OR myopericarditis" AND "hypersensivity OR drug-induced". We included only case reports and case series ($n = 188$), then we excluded all cases where the diagnosis was uncertain (or didn't full field the diagnosis of pericarditis), duplicate articles, abstracts without comprehensive case descriptions. According to the 2015 European Society of Cardiology guidelines for the diagnosis and treatment of pericardial diseases, AP was diagnosed with the presence of two of the following criteria: chest pain, pericardial friction rub, electrocardiographic (ECG) changes (such as new widespread ST elevation or PR depression), and new or worsening pericardial effusion. Cases of pericardial effusion without pericarditis were systematically excluded and we excluded also cases of vaccination-related pericarditis. We also excluded pure myocarditis and perimyocarditis. Cases of myopericarditis (pericarditis with minor myocardial involvement, defined as concomitant elevation of biomarkers of myocardial damage without new focal or diffuse impairment of left ventricular function) were included. Subsequently, the reference list of selected articles was searched to identify any additional articles for inclusion in accordance with previously established selection criteria, and, ultimately, we included 121 cases that fulfilled the criteria. To note case series were considered only if sufficient data were clearly available for each case. Then three independent authors (V.C., L.S.V., F.V.) performed analysis and discrepancies were resolved by consensus or by a third senior author (M.I.), if necessary. Fig. 1 depicted the detailed process of article selection, data extraction, management, identification, screening and inclusion of suitable cases. The patients were finally divided into 5 classes, depending on the type of drugs that induced pericarditis: "Pericarditis related to anti-cancer, immunosuppressive, immunomodulatory drugs"; "Pericarditis related to anti-inflammatory drugs"; "Pericarditis related to central nervous system agents"; "Pericarditis related to cardiovascular drugs" and "Pericarditis related to other drugs".

2.2. Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) or median and interquartile range (IQR), according to the data distribution. The data were analysed using the Shapiro–Wilk test to verify the normal distribution. Categorical variables were presented as absolute numbers and percentages. The Student *t*-test or the Mann–Whitney *U* test was used to compare continuous variables between groups, as appropriate. Comparison of categorical variables was performed by Chi-squared analysis or the Fisher exact test, as appropriate. A p-value <0.05 was considered statistically significant.

3. Results

3.1. Overall population

Baseline characteristics and outcomes of the whole population and according to different subgroups of drugs are presented in Table 1 and Table 2. The geographical distribution of cases is shown in

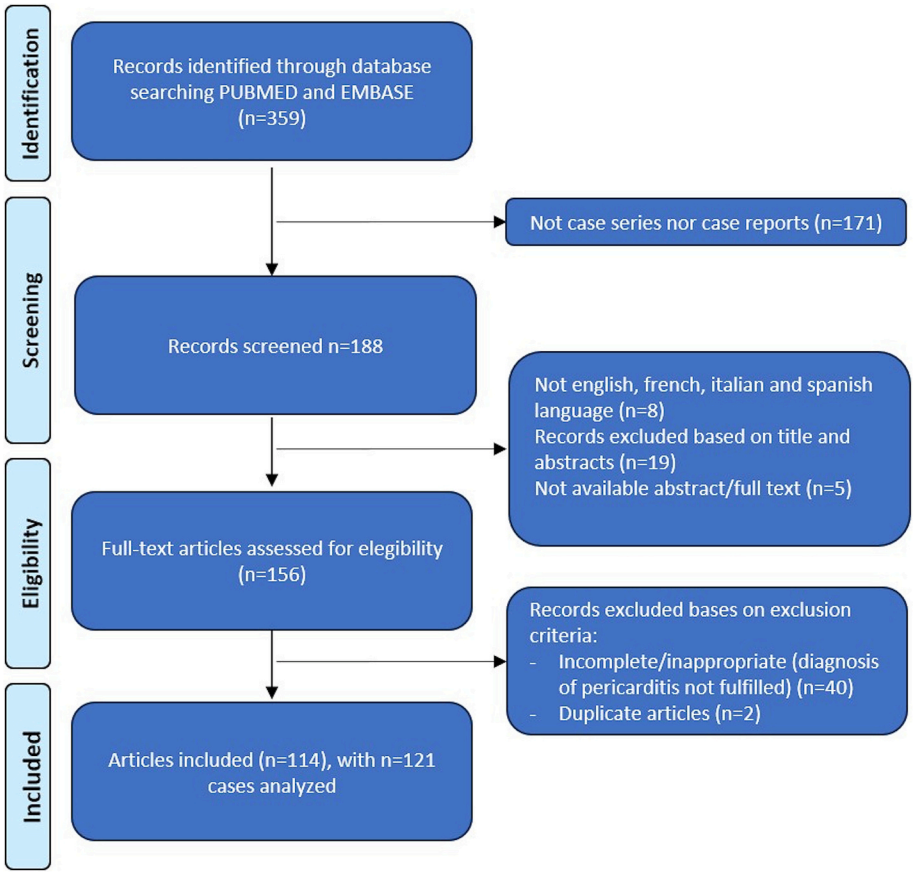

Fig. 1. Article selection, data extraction, management, identification, screening and inclusion of suitable cases.

Table 1
Baseline features of the studied population according to drugs subgroups.

	Whole population		Anti-cancer, immunosuppressive, immunomodulatory drugs		Anti-inflammatory drugs		Central nervous agents		Cardiovascular drugs		Other drugs	
	No. of patients with available data	Value	No. of patients with available data	Value	No. of patients with available data	Value	No. of patients with available data	Value	No. of patients with available data	Value	No. of patients with available data	Value
Age, yrs., median (IQR)	121	45 (27, 59)	37	49 (38, 62)	33	36 (21, 48)	23	42 (23, 67)	10	58 (49, 71)	18	49 (31, 62)
Gender, n (%)	121		37		33		23		10		18	
Female		47 (38.8)		14 (37.8)		11 (33.3)		10 (43.5)		3 (30.0)		9 (50.0)
Male		74 (61.2)		23 (62.2)		2 (66.7)		23 (56.5)		7 (70.0)		9 (50.0)
Time between start of drug therapy and onset of pericarditis, days±SD	100	316 ± 938	31	69 ± 114	27	264 ± 319	18	777 ± 1160	8	236 ± 302	16	68 ± 81
Fever, n (%)	121	61 (50.4)	37	12 (32.4)	33	18 (55.0)	23	12 (52.2)	10	7 (70.0)	18	12 (66.7)
Chest pain, n (%)	121	105 (86.8)	37	32 (86.5)	33	32 (97.0)	23	16 (69.7)	10	10 (100)	18	15 (83.3)
Dyspnoea, n (%)	121	59 (48.8)	37	18 (48.6)	33	9 (27.2)	23	18 (78.3)	10	5 (50.0)	18	9 (50.0)
Pericardial rubs, n (%)	121	30 (24.8)	37	8 (21.6)	33	9 (27.2)	23	2 (8.7)	10	5 (50.0)	18	6 (33.3)
Associated symptoms, n (%)	121		37		33		23		10		18	
Arthritis/myositis		12 (9.9)		1 (2.7)		3 (9.1)		0		2 (20.0)		6 (33.3)
Erythema		5 (4.1)		1 (2.7)		1 (3.0)		0		1 (10.0)		2 (16.6)
Pneumonia		2 (1.6)		1 (2.7)		0		1 (4.3)		0		0
Others		1 (0.8)		0		1 (3.0)		0		0		0
SLE		15 (12.4)		3 (8.1)		2 (6.1)		1 (4.3)		7 (70.0)		2 (16.6)
Widespread ST elevation, n (%)	88	45 (51.1)	27	14 (51.9)	30	18 (60.0)	12	4 (33.3)	10	3 (30.0)	9	6 (66.6)
Low voltages, n (%)	75	11 (14.7)	24	3 (12.5)	22	2 (0.9)	10	2 (10.1)	10	1 (10.0)	9	3 (33.3)
White blood cells ($x10^3$/ul), mean ± SD	59	11,391.9 ± 4233	17	10,013.1 ± 4507	19	11,942.1 ± 3791.3	7	11,524.8 ± 3106.2	7	11,215.0 ± 4635.4	9	15,366.7 ± 3276.5
CRP (mg/dl), mean ± SD	59	72 ± 71	14	66 ± 57	20	75 ± 85	8	48 ± 54	5	72 ± 11	9	146 ± 23
CRP > 5 mg/dl, n (%)	56	51 (91.1)	14	14 (100)	20	18 (90)	8	8 (100)	5	5 (100)	9	9 (100)
ESR (mm/h)	48	67 (35)	9	65 (33)	15	59 (33)	6	67 (40)	6	72 (27)	12	97 (37)
Troponin elevation, n (%)	52	28 (53.8)	18	8 (44.4)	17	12 (70.6)	8	5 (62.5)	6	0	3	3 (100)
ANA elevation, n (%)	53	21 (39.6)	9	4 (44.4)	16	4 (25)	8	3 (37.5)	8	7 (87.5)	12	3 (25.0)
PE, n (%)	121	91 (75.2)	37	27 (72.9)	33	24 (72.7)	23	15 (65.2)	10	10 (100)	18	15 (83.3)
Moderate/large, n (%)		38 (41.8)		12 (44.4)		6 (25.0)		6 (40.0)		5 (50.0)		9 (60.0)
Mild, n (%)		53 (58.2)		15 (55.6)		18 (75.0)		9 (60.0)		5 (50.0)		6 (40.0)
Pleural effusion, n (%)	121	41 (33.9)	37	10 (27.0)	33	8 (24.2)	23	10 (43.5)	10	7 (70.0)	18	6 (33.3)
Therapy	121		37		33		23		10		18	
Colchicine, n (%)		19 (15.7)		9 (24.3)		3 (9.1)		2 (9.1)		2 (20.0)		3 (16.6)
Aspirin/NSAIDs, n (%)		38 (31.4)		17 (47.2)		14 (42.4)		5 (21.7)		2 (20.0)		0
Corticosteroids, n (%)		45 (37.2)		18 (48.6)		13 (39.4)		3 (13.0)		5 (50.0)		6 (33.3)

SD = standard deviation; SLE = systemic lupus erythematosus; WBC: White blood cells; CRP = C-reactive protein; ESR = Erythrocyte sedimentation rate; ANA = Antinuclear antibodies; PE = pericardial effusion; NSAIDs = non-steroidal anti-inflammatory drugs.

Table 2
Clinical outcomes of the studied population according to drugs subgroups.

	Whole population		Anti-cancer, immunosuppressive, immunomodulatory drugs		Anti-inflammatory drugs		Neurologic/ antipsychotic drugs		Cardiovascular drugs		Other drugs	
	No. of patients with available data	Value	No. of patients with available data	Value	No. of patients with available data	Value	No. of patients with available data	Value	No. of patients with available data	Value	No. of patients with available data	Value
Mean follow-up, days±SD	79	131 ± 189	26	155 ± 223	22	71 ± 79	15	103 ± 112	7	316 ± 303	9	98 ± 91
Need of hospitalisation, n (%)	121	121 (100)	37	37 (100)	33	33 (100)	23	23 (100)	10	10 (100)	18	18 (100)
Resolution of symptoms after drug withdrawal, days±SD	102	5 ± 4	37	5 ± 5	26	3 ± 2	14	5 ± 5	7	3 ± 3	18	9 ± 5
Recurrence of symptoms after restarting the drug, n (%)	22	22 (100)	8	8 (100)	6	6 (100)	4	4 (100)	1	1 (100)	3	3 (100)
Cardiac tamponade, n (%)	121	18 (14.9)	37	9 (24.3)	33	3 (9.1)	23	2 (8.6)	10	1 (10.0)	18	3 (16.7)
Constrictive physiology at admission, n (%)	121	16 (13.2)	37	4 (10.8)	33	1 (3.2)	23	10 (43.5)	10	1 (10.0)	18	0
Constrictive pericarditis, n (%)	121	9 (7.4)	37	1 (2.7)	33	0	23	7 (30.4)	10	1 (10.0)	18	0
Death related to pericarditis, n (%)	121	4 (3.3)	37	3 (8.1)	33	0	23	0	10	1 10.0)	18	0

SD = standard deviation.

Supplementary Fig. 1. Almost all cases were reported in Europe and the USA (59.5 and 37.2 % of cases, respectively). The study includes 121 patients, with a median age of 45 (27, 59) years, 38.8 % females. Among the 121 patients, pericarditis related to anti-cancer, immunosuppressive, immunomodulatory drugs was the most reported aetiology (30.6 % of patients), followed by anti-inflammatory drugs (27.3 % of patients), central nervous system agents (19.0 % of patients), cardiovascular drugs (8.3 % of patients) and other drugs (14.8 % of patients). All patients met the criteria for the diagnosis of AP: pericardial chest pain, pericardial rubs, pericardial effusion and ST-segment elevation on ECG were described respectively in 105 (86.8 %), 30 (24.8), 91 (75.2) and 45 (51.1 %) patients. Many patients presented associated systemic symptoms: fever, C-reactive protein (CRP) elevation, pleural effusion were detected in 61 cases (50.4 %), 51 cases (91.1 %), and 41 cases (33.9 %), respectively. Concomitant minor myocardial involvement was found in about half of patients. All patients withdrew the drug at the time of diagnosis. Anti-inflammatory therapy was started in 54 (44.6 %) patients, mainly with prednisone (37.2 % of patients). The mean follow up was 131 ± 189 days, all patients were hospitalized. Symptoms resolved after and average of 5 ± 4 days after discontinuation of the drug, and all patients who resumed the drug experienced a new recurrence. 18 patients underwent pericardiocentesis for cardiac tamponade, 9 underwent pericardiectomy. Four patients died during the follow-up.

3.2. Pericarditis related to anti-cancer, immunosuppressive, immunomodulatory drugs

This aetiology was diagnosed in 37 patients, representing the most commonly identified condition. The class that most frequently triggered pericarditis were antimetabolites (particularly 5-Fluorurucil, Azacitidine and Cytarabine), followed by Immune Checkpoint Inhibitors (ICI) (e.g. Nivolumab and Pembrolizumab), while among the older alkylating agents, pericarditis may be most frequently induced by Cyclophosphamide and Busulfan.

Of note, pericarditis occurred after multiple doses of alkylating agents, while ICIs can lead pericarditis even after the first infusion, with an average time to onset after 4 cycles of ICI therapy. About immunosuppressive agents, pericarditis was reported most frequently in patients treated with leflunomide and methotrexate. The median age at presentation was 49 (38, 62) years. Chest pain and dyspnoea were the most common symptoms (86.5 % and 48.6 %, respectively). When compared with other drug-related forms, this group showed the lowest incidence of fever (32.4 % of patients; overall $p = 0.01$). At the time of admission, widespread ST elevation was observed in up to 51.9 % of cases, all patients presented an elevated CRP. Pericardial effusion was observed in 72.9 % with the highest prevalence of cardiac tamponade compared to the overall population (24.3 % of patients, $p = 0.04$). Anti-inflammatory therapy with aspirin/nonsteroidal anti-inflammatory drugs (NSAIDs) was administered in 17 (47.2 %) patients and steroid therapy in 18 (48.6 %) cases. One patient died during the AP attack from septic shock, one patient died from metastatic cancer and one from anthracycline-related heart failure after hospital discharge.

3.3. Pericarditis related to anti-inflammatory drugs

In 33 patients, pericarditis was related to anti-inflammatory drugs used to treat inflammatory bowel disease. Pericarditis was most frequently related to traditional aminosalicylates, especially mesalazine (23 patients) and sulfasalazide; however, new drugs such as infliximab and balsalazide can also cause pericarditis. This usually occurs within 2–4 weeks after the start of therapy, but also after several months of treatment, particularly in patients taking corticosteroids. These patients had the lowest age at presentation (36 (21, 48) years, overall $p < 0.01$). Almost all patients presented with chest pain, while patients complained of dyspnoea (27.2 %; overall $p < 0.01$) less frequently than in other conditions. These patients had the highest, although not statistical, prevalence of myocardial involvement (70.6 % of cases, overall $p = 0.53$) and the lowest prevalence of antinuclear antibodies (ANA) (25 %

of patients, overall $p = 0.08$). At admission, 3 patients underwent pericardiocentesis, while no further events were reported after hospital discharge with a median follow-up of 71 ± 79 days.

3.4. Pericarditis related to central nervous system agents

Pericarditis was associated with central nervous system drugs in 23 patients, of which 11 were clozapine related. Almost all other cases are attributable to antiparkinsonian drugs including bromocriprine, methylsergide, carbegolide, and pergolide and rarely related to drugs used to treat multiple sclerosis (Alemtuzumab and Natalizumab). Patients had a median age of 42 (23, 67) years and reported fever, chest pain and dyspnoea in 52.2 %, 69.7 % and 78.3 % of cases, respectively. CRP was always elevated, while 62.5 % of patients showed contextual myocardial involvement. This aetiology had the highest prevalence of constrictive physiology at admission (43.5 % of cases, overall $p < 0.01$) and the highest prevalence of constrictive pericarditis (30.4 %, overall $p < 0.01$) after a mean follow-up of 103 ± 112 months. This is particularly due to antiparkinsonian drugs, for which pericarditis typically occurs after several years of intake.

3.5. Pericarditis related to cardiovascular drugs

10 cases were associated with cardiovascular drugs. Almost all the cases were secondary to taking procainamide or the older antihypertensive drugs such as minoxidil, methyldopa and hydralazine; while among the new drugs one case was reported as being related to captopril.

These patients were older than the other subgroups (58 (49, 71) years, overall $p = 0.008$), and all patients complained of chest pain. At the time of admission, the prevalence of fever (70.0 %, overall $p = 0.17$) and pericardial rubs (50.0 %, overall $p = 0.04$) was higher than the other conditions. The characteristic feature of this group is that 70 % of cases arises in the context drug-induced lupus erythematosus (DILE) with a higher prevalence of ANA, pericardial effusion and pleural effusion than in the overall population (87.5 %, 100 %, 70 %, respectively). One patient died on admission from cardiac tamponade, while after a mean follow-up of 316 ± 303 days one patient developed constrictive pericarditis.

3.6. Pericarditis related to other drugs

Pericarditis was associated with other drugs in 18 patients, mostly related to anti-infective drugs (mainly isoniazid followed by penicillins and tetracyclines). The cases non-antibiotic related were secondary to intake of dantrolene, isotretinoin and zolendronic acid. Patients in this group had a median age of 49 (31, 62) years and the highest, though not statistically significant, prevalence of women (50 %; overall $p = 0.62$). At presentation, the most commonly reported symptoms were chest pain and fever. Compared to the other groups, these patients had a higher CRP (146 ± 23) mg/dl, overall $p < 0.01$). Three patients required urgent pericardiocentesis for cardiac tamponade, whereas no other major complications were documented.

4. Discussion

To our knowledge this is the first study based on published cases that provides data on the clinical presentation, diagnostic findings, treatment, and outcome of patients with drug-induced pericarditis.

The first case reports date back to the 1960s–70s and were almost exclusively concerning old antihypertensive and antiarrhythmic drugs (e.g. hydralazine and procainamide) [6,7]. Subsequently, in the 1990s, the vast majority of reports were against anti-inflammatory bowel drugs, especially regarding sulfazalasine (5-aminosalicylate and sulfapyridine). Given its adverse effects sulfasalazine was replaced by 5-aminosalicylic acid alone (also known as mesalazine or mesalamine), however warnings continued [8,9]. Finally, in recent years, reports have been mainly about anti-cancer drugs with particular interest in pericarditis related to ICI and on newer anti-inflammatory drugs (e.g., anti-tumor necrosis factor (TNF) drugs)) [10,11].

Understanding the timeframe for the development of pericarditis after drug initiation is crucial for timely diagnosis and management. Surprisingly, the average time between drug initiation and diagnosis of pericarditis was almost one year, with statistically significant differences between drug classes. In fact, for anti-cancer/immunosuppressants and antibiotics is about 60 days, while for drugs acting on the nervous system it is more than 2 years. Among these, the average time to onset of pericarditis is particularly long among antidopaminergic drugs used in the therapy for Parkinson's disease. These drugs, when used at high doses and for prolonged periods of time, are known fibrosing agents and can lead to constrictive pericarditis. The mechanism is still controversial; a serotonergic mechanism promoting vasoconstriction and subsequent fibrosis has been hypothesized to play an aptene role, and thus trigger an immunological response; while a pharmacological interaction mechanism is also possible (also given the high metabolism at cytochrome P450 3A4) [12,13].

The pathophysiology and clinical features are different among the different classes. Historically, the old antihypertensive drugs gave pericardial damage several months after the first intake, and in most cases, the pericarditis was part of a group of diseases, characterizing DILE [14]. DILE has clinical features (e.g., arthralgia, myalgia, fever, rash, hepatosplenomegaly, lymphadenopathy, and pleuritis) similar to SLE, however tends to be milder and renal or central nervous system involvement are rare. The pathogenesis is still unclear and appears to be related to demethylation of DC4+ T cells, which makes them autoreactive, thus promoting hyperproduction of autoantibodies. Diagnosis is suspected when there are lupus-like symptoms with the exclusion of other autoimmune disorders and when the resolution of symptoms is reached after the withdrawal of the drug [14]. Recognizing DILE is of paramount importance since new drugs such as TNF alpha inhibitors can also promote it [15].

The mechanism of damage related to ICIs is different, with most cases occurring within few weeks to 3 months as a result to a loss of peripheral tolerance of autoreactive T cells. This is due to ICI-mediated disruption of negative regulators of immune activation, such as CTLA-4, PD-1, and PD-L1, which have cardioprotective effects against immune-mediated damage after stress. Therefore, inhibition by ICIs may make pericardial cells more susceptible to injury [16,17]. The mechanism of damage of anti-inflammatory bowel drugs is not fully elucidated, it seems to be related to a humoral hypersensitivity mechanism (in which antibodies produced against mesalazine cross-react with pericardial tissue, leading to inflammation), however IgE-mediated or cell-mediated hypersensitivity have also been considered. The diagnosis of pericarditis in this case is often very challenging, because symptoms can be mitigated by the concomitant use of corticosteroids as bowel disease therapy and because pericarditis could also be secondary to the bowel disease. There are no distinguishing cynical features: the concomitant worsening of bowel disease makes plausible the hypothesis of pericarditis related to the disease, whereas the disappearance of pericarditis after drug withdrawal (and the reappearance after reuptake) suggest drug-related cause [18].

In any case of a suspected drug-related pericarditis, the diagnosis requires a careful anamnesis and the exclusion of other more frequent causes. Suspicion must always be present, especially in cases of pericarditis with systemic involvement (e.g. when fever, pleuritis, arthralgias and a high ANA titer are present). In order to estimate and confirm the drug-adverse reaction, the clinician can be supported by the Naranjo score, a 10-question survey which, depending on the total score, makes the adverse reaction doubtful (0 points), possible (1 to 4 points), probable (5–9 points), very likely (≥ 9 points) [19].

To note the therapy for acute idiopathic pericarditis is based on the empirical anti-inflammatory combination therapy with NSAIDs plus

colchicine [1], while, when these drugs are contraindicated or there are specific indications, corticosteroids should be considered at low to moderate doses plus colchicine [20]. On the other hand, for drug-induced pericarditis, the prognosis seems excellent in most cases, with a rapid reduction and cessation of symptoms after an abrupt discontinuation of the drug even without starting the anti-inflammatory therapy. In fact, dividing the population into four groups: untreated (31.4 %), NSAIDs monotherapy (15.7 %), NSAIDs plus colchicine (15.7 %), and prednisone monotherapy (37.2 %), there were no significant differences in the occurrence of complications. In complicated cases (e.g. with a moderate to large pericardial or pleural effusion, with constrictive signs or with constriction) a course of anti-inflammatory therapy is required. When toxicity is secondary to ICIs, especially if there is a concomitant myocardial involvement, a prompt course of corticosteroid therapy (even by an initial intravenous route) is indicated. Probably for this reason, half of the patients in the "Pericarditis related to anti-cancer, immunosuppressive, immunomodulatory drugs" group were treated with corticosteroids. Even in the "cardiovascular drug-induced pericarditis" group, half of the patients received corticosteroids as first-line therapy, probably due to the high percentage of patients with polyserositis (pleural and pericardial effusion) at presentation.

Regarding outcomes, the first point of interest is that all patients were hospitalized, and this is probably due to the fact that only the most challenging cases are typically described in case reports. Despite this possible publication bias, mortality during follow-up was only 3.3 % (4 patients), and only one died from pericarditis related-death (cardiac tamponade at admission).

The most frequent complication is pericardial effusion, which is found in almost 3 out of 4 patients, while in idiopathic pericarditis it is found in about half of the patients. Moreover, in almost half of the cases it is moderate or severe, requiring pericardiocentesis in 14.9 % of our patients. It should be noted that pericarditis and pericardial effusion are not synonymous and that drug-induced pericardial effusion is often present even in the absence of pericarditis and potentially recognises different causes (anticoagulant drugs etc.), which will not be addressed in this review.

The other fearsome complication is constrictive pericarditis described in much higher percentages than idiopathic pericarditis (7.8 % vs. < 1 %). As previously mentioned, almost all the cases described are secondary to prolonged intake of antidopaminergic drugs and arise due to their known fibrosing power.

4.1. Proposed algorithm for the diagnosis and management of drug-induced pericarditis

A proposed algorithm for the diagnosis and management of drug-induced pericarditis is explained in. Rapid and reliable diagnosis is essential: the most frequent aetiologies of pericarditis must be excluded and, if drug-induced pericarditis is possible, the drug must be abruptly discontinued. If pericarditis begins with severe features, the patient must be hospitalized, anti-inflammatory therapy started and complications treated. If the pericarditis is not complicated, the patient can be treated as an outpatient with careful follow-up within 1–2 weeks. In any case, if the expected recovery is not achieved, it is advisable to repeat a careful differential diagnosis and search for alternative causes of pericarditis.

4.2. Study limitations

The main limitation of this report is that all data were taken from published cases, and this did not allow us to verify their accuracy and completeness. The average follow-up is about four months, and this may have led to an underestimation of recurrences. Furthermore, there may be a publication bias since typically only the most severe cases are published. It should be noted that the results mainly reflect the characteristics of patients admitted to hospitals in North America, Europe, and Japan (85.1 %), while only 2 cases are referred from the African continent. This may have created an under-representation of certain aetiologies, for instance of pericarditis related to isoniazid, a widespread antibiotic used in Africa in the treatment of tuberculosis.

5. Conclusions

This is the first study describing the clinical presentation, diagnostic findings, treatment strategies and outcomes of drug-induced pericarditis, based on published cases. It also proposes an algorithm for diagnosis and treatment that is based on two fundamental cornerstones: the need for an accurate drug history and the prompt discontinuation of the suspected drug. Making clinicians aware of the existence of this rare and often unrecognised aetiology of pericarditis is therefore crucial to discontinue the drug early and avoid major complications. Large registries are needed to increase knowledge of this rare condition.

CRediT authorship contribution statement

Valentino Collini: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Luca Siega Vignut:** Writing – review & editing, Writing – original draft, Visualization, Validation, Formal analysis, Data curation. **Francesco Venturelli:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Massimo Imazio:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

All authors deny conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2025.134000.

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