Introducing a new entity: chemotherapy-induced arrhythmia

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The relationship between chemotherapy and arrhythmias has not been well established. We reviewed the existing literature to better understand this connection. We reviewed published reports on chemotherapy-induced arrhythmias in English using the PubMed/Medline and OVID databases from 1950 onwards as well as lateral references. Arrhythmias were reported as a side effect of many chemotherapeutic drugs. Anthracyclines are associated with atrial fibrillation (AF) at a rate of 2–10%, but rarely with ventricular tachycardia (VT)/fibrillation. Taxol and other antimicrotubular drugs are safe in terms of pro-arrhythmic side effects and do not cause any consistent rhythm abnormalities. Arrhythmias induced by 5-fluorouracil, including VT, are mostly ischaemic in origin and usually occur in the context of coronary spasm produced by this drug. Cisplatin—particularly with intrapericardial use—is associated with a very high rate of AF (12–32%). Melphalan is associated with AF in 7–12% of cases, but it does not appear to cause VT. Interleukin-2 is linked to frequent arrhythmia, mostly AF. We summarized the available data on chemotherapy-induced arrhythmia, particularly AF and VT. Studies with prospective data collection and thorough analyses are needed to establish a causal relationship between certain anticancer drugs and arrhythmia.

Keywords

Chemotherapy • Arrhythmia • Atrial fibrillation • Ventricular tachycardia

Introduction

Many cardiology consultations in cancer centres are generated by arrhythmias, which occur in two major settings: after surgery and after chemotherapy. Although post-operative arrhythmias—mostly atrial fibrillation (AF)—are a recognized entity, the relationship between chemotherapy and arrhythmias is not well established. Even in review papers, arrhythmia is not commonly listed among typical chemotherapeutic-induced cardiotoxic effects.1 Data on arrhythmias are scattered in the oncology literature, in papers analysing outcomes and adverse effects of cancer drugs in oncology and haematology journals; however, these sources usually fail to attract the attention of a cardiology readership. Therefore, the purpose of this review was to collect and summarize the evidence of possible connections between different classes of chemotherapeutic agents and cardiac arrhythmias.

Methods

We reviewed published reports on chemotherapy-induced arrhythmia in English using the Pubmed/Medline and OVID databases from 1950 onwards as well as lateral references. We searched the databases using the key words ‘arrhythmia’, ‘ventricular tachycardia’, and ‘atrial fibrillation’ combined with ‘chemotherapy’, ‘associated with chemotherapy’, or ‘chemotherapy-induced’. We also ran searches on typically used chemotherapeutic agents.

General considerations

It is only rarely that arrhythmias are studied in a controlled fashion before and after chemotherapy. On the other hand, they are routinely reported as adverse events in clinical trials. Cancer itself creates an arrhythmogenic milieu. In one study of colorectal cancer, AF occurred more than twice more frequently in cancer patients than in controls2 despite the exclusion of all confounding factors, including the chemotherapy itself. As baseline studies reflecting participants’ status prior to beginning chemotherapy are frequently missing, it is difficult to make a determination as to whether these arrhythmias reflect the baseline state of the patient or are truly a manifestation of the side effects/toxicity of chemotherapeutic drugs. For example, recording Holter monitors before and after chemotherapy with various agents of different classes, Hersh et al.3 demonstrated that, although the proportion of patients with arrhythmias was high (64%), it did not differ from their baseline. Had pre-treatment evaluation not been

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done, these arrhythmias might have been attributed incorrectly to the adverse effects of chemotherapeutic agents.

Another difficulty comes from the fact that, as a rule, more than one chemotherapeutic agent is used in each patient. Multiple chemotherapeutic drugs are administered simultaneously, making it difficult to decide which one caused this adverse effect. For example, two out of eight patients developed AF while being treated with an intensified high-dose regimen of idarubicin, melphalan, and cyclophosphamide—any of which could be associated with the arrhythmia. Likewise, in another study, AF developed in 3 of 31 patients with malignant glioma treated with ‘eight-drugs-in-one-day’ chemotherapy (methylprednisolone, vincristine, procarbazine, hydroxyurea, cisplatin, cytosine arabinoside, and imidazole carboxamid). The rate of AF (10%) appears rather high; however, it is impossible to say which of the drugs caused the arrhythmia.

Therefore, we tried to be selective and include only reports where the connection between chemotherapeutic drugs and arrhythmias was well documented. On another notice, practically all referenced articles are written by non-cardiologists. As a consequence, general terms like ‘supraventricular arrhythmia’ rather than specific terms are commonly used. Whenever possible, we found the exact kind of arrhythmias, but sometimes nothing more specific could be found in the source.

**Findings based on individual drugs**

**Anthracyclines**

Anthracyclines (AC) are cytostatic antibiotics. They inhibit DNA and RNA synthesis by intercalating between base pairs of the DNA/RNA strand and preventing the replication of rapidly growing cancer cells.

The cardiotoxicity of AC has been well studied. Acute toxicity, with transient effects developing during or immediately after the first dose, manifests as arrhythmias, a pericarditis–myocarditis syndrome, or acute heart failure. However, the most common cardiotoxicity, occurring months after the beginning of treatment, is left ventricular systolic dysfunction with possible arrhythmias. For the purpose of this review, we focused on early toxicity, with arrhythmias as an initial sign of the cardiac side effects of chemotherapy.

The pro-arrhythmic effect of AC was observed in a culture of cardiomyocytes where doxorubicin induced rhythm abnormalities that could be prevented by beta-blockers. In canine Purkinje fibres, adriamycin prolonged the action potential in a dose-dependent manner. The effect was consistent with direct inhibition of the transient inward current and/or an indirect reduction via reduced activity of sodium–calcium exchange.

The effects of AC on rat electrocardiograms included widening of the QRS complex, increased voltage, and prolonged QT. Acute intravenous doxorubicin elicited premature ventricular contractions (PVCs) and ventricular tachycardia (VT) in mice in a dose-dependent fashion.

The reported rate of ECG changes in patients treated with AC varies from 6 to 38.6%. They commonly include non-specific ST-T changes and a modest increase in supraventricular and ventricular ectopic beats. Steinberg et al. reported a 3% rate of arrhythmia, mainly PVCs, in the first hour after doxorubicin infusion and 24% in the first 24 h after infusion. However, in other observations, the increase of extrasystoles was non-significant.

A prospective study including 29 patients revealed varying arrhythmias on Holter monitors in 19 patients (65.5%), including supraventricular extrasystoles (41.4%), PVCs (31.0%), and paroxysmal AF (10.3%). In one case, transient Mobitz II and complete atrioventricular block occurred. In another series of 39 patients, 9 experienced arrhythmias (3 atrial arrhythmias, 2 ventricular arrhythmias, and 4 atrioventricular block episodes). Other reports also described symptomatic second- and third-degree AV blocks.

Atrial fibrillation appears to be a rather common complication of AC. Kilickap et al. recorded paroxysmal AF in 10.3% of 29 patients during the first course of doxorubicin-based chemotherapy.

Although several cases of torsades de pointes were reported, concomitant presence of hypokalaemia diminishes the validity of this observation. A marked QT prolongation followed by ventricular fibrillation (VF) was observed in two patients; recurrent monomorphic VT causing cardiac arrest was reported once, as well as cardiac arrest with documented VT/VF occurred in another one. Arrhythmia was suspected, but not documented in sudden death in four unmonitored patients on AC. Others reported sudden cardiac death resulting from VT/VF shortly after the completion of AC or a combination of AC/paclitaxel.

In summary, association of AC with AF appears to be consistent, whereas the association with VT/VF was rarely observed and documented. Table 1 summarizes most of the representative studies reporting the rate of AF and VT/VF in different classes of chemotherapeutic agents.

**Antimicrotubule agents**

Antimicrotubule drugs include vinca alkaloids and taxanes (e.g. paclitaxel and docetaxel). They block cell division by stabilizing microtubules. Paclitaxel is an extract from the rare Pacific yew tree; poisoning from such extracts has previously resulted in VT, VF, and sudden death.

Paclitaxel induces arrhythmias and bradycardia at doses approximately 10 times higher than therapeutic. In the isolated perfused heart of the guinea pig, paclitaxel induced conduction abnormalities and reduced coronary flow and left ventricular systolic pressure. In frog and rabbit hearts, taxanes slowed the heart rate, produced AV block, and then caused asystole. In dogs, ECG changes progressed through widening of the QRS to polymorphic PVCs and eventually to VF and death.

The cardiac events consistently reported among patients using paclitaxel include frequent asymptomatic sinus bradycardia (29%) and first-degree atrioventricular block (25%) More advanced heart block and conduction abnormalities occur infrequently and are often asymptomatic.

In the National Cancer Institute database, only 4 patients of approximately 3400 had second- and third-degree heart block. There were also nine cases of ventricular arrhythmias, and eight cases of atrial arrhythmias. Almost all patients with non-sustained
VT (NSVT) received paclitaxel in combination with cisplatin. Overall, VT and VF occurred in only 0.26% patients, and atrial arrhythmias occurred even less frequently. Therefore, routine cardiac monitoring is not required for patients without history of arrhythmia.29,33

Antimetabolites

Antimetabolites provide antitumour effect by interfering with DNA synthesis. Methotrexate-related cardiotoxicity may manifest as premature atrial contractions (PACs), PVCs, VT/VF, and sinus bradycardia with junctional escape beats.36

5-Fluorouracil

An overall incidence of fluorouracil cardiotoxicity represented mostly by ischaemic events induced by coronary vasospasm or direct drug-mediated cytotoxic effects ranges from 1.2 to 18% of patients.37,38 Cardiac adverse effects include ischaemic myocardial infarction, reversible myocardial ischaemia, supraventricular, and ventricular arrhythmias as well as bradycardia.

5-Fluorouracil (5-FU) therapy has been associated with prolongation of the QT interval and an increase in PACs and PVCs.39–41 In 2 of 25 patients receiving 5-FU, the duration and dispersion of the P-wave on the ECG increased,42 and transient asymptomatic bradycardia below 50 bpm was observed in 6 of 207 patients.43 While being treated with 5-FU and cisplatin, 5 of 72 patients developed arrhythmias, including 3 with AF and 2 with frequent supraventricular ectopic beats.44 Among 100 consecutive patients receiving 5-FU, 2 developed multiple PVCs.45 Eskilsson et al.46 described AF after treatment with 5-FU and cisplatin, occurring in 5 of 76 patients and indicating the third most common manifestation of cardiac toxicity of this combination, after chest pain and ST-T changes. They also reported frequent PACs, VF, and sudden cardiac death (one patient each). In total, they recorded AF in 5 of 76 patients (6.6%).

As myocardial ischaemia appears to dominate the picture of cardiac toxicity of 5-FU, many arrhythmias occur in the setting of ischaemia and represent more ischaemic than chemotherapeutic complications,47 like polymorphic PVCs, ventricular arrhythmias, and cardiac arrest in the context of marked ST elevation.41,47 Repolarization changes (ST-segment deviation; T-wave inversion) occurred in 65%, and decreased voltage in 22% of the patients who presented with cardiac events.46 In summary, patients treated 5-FU are prone to coronary spasm, myocardial ischaemia, and myocardial infarction, with all arrhythmias typical for this clinical context. Arrhythmias without ischaemic events are rare.

Capecitabine

Capecitabine is used in the treatment of breast and colon cancer. Cardiotoxicity associated with capecitabine is similar to that of

### Table 1 Atrial fibrillation and ventricular tachycardia associated with chemotherapy

<table>
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<tr>
<th></th>
<th>n</th>
<th>AF</th>
<th>VT</th>
<th>Comments</th>
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<tr>
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<td>33</td>
<td>2 (6%)</td>
<td>6 (2.2%)</td>
<td>NSVT</td>
</tr>
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<td>3 (10.3%)</td>
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<tr>
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<td>4 (8.2%)</td>
<td>VT/VF</td>
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<td>6 (0.18%)</td>
<td>NSVT</td>
</tr>
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<td>Taxol</td>
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<tr>
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<td>7 (15.2%)</td>
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<tr>
<td>Cisplatin</td>
<td>44</td>
<td>7 (15.2%)</td>
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<tr>
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<td>9 (0.26%)</td>
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</tr>
<tr>
<td>5-FU and cisplatin</td>
<td>72</td>
<td>3 (4.2%)</td>
<td>4 (1.1%)</td>
<td>Sudden death</td>
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<td>5-FU and cisplatin</td>
<td>367</td>
<td>5 (6.5%)</td>
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<td>1 VF, 1 sudden death</td>
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<td>NSVT</td>
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<td>Melphalan</td>
<td>36</td>
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<td>1 (0.2%)</td>
<td>NSVT</td>
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<td>16 (8%)</td>
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<tr>
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<td>2 (0.5%)</td>
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<td>Depsipeptide</td>
<td>15</td>
<td>3 (20%)</td>
<td>2 NSVT and sudden death</td>
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</table>

AF, atrial fibrillation; VT, ventricular tachycardia; VF, ventricular fibrillation; NSVT, non-sustained ventricular tachycardia.
5-FU. In 153 patients treated with capecitabine and oxaliplatin in two prospective trials for advanced colorectal cancer, 10 patients (6.5%) developed cardiac events, 3 of which were VF requiring defibrillation, VT that terminated spontaneously on discontinuation of intravenous capecitabine, and 1 sudden cardiac death. The remaining patients experienced ischaemic events.49

**Gemcitabine**

Gemcitabine is used for the treatment of solid tumours. It has direct toxic effect on the sinus node and atrioventricular conduction system.50–52 Cardiac arrhythmias, without further specification, were reported in 12.2% of patients treated with gemcitabine, although no control group was available.53 Ventricular tachycardia with cardiac arrest54,55 and AF were both found in association with gemcitabine.51,52,56 In one pancreatic cancer patient, AF followed the administration of gemcitabine on six occasions. Each episode took place within 18 to 24 h after every infusion of the chemotherapeutic agent, despite amiodarone prophylaxis, which was started after the second episode, although no precipitating factors could be identified.51

When patients with metastatic non-small-cell lung cancer received gemcitabine or gemcitabine plus vinorelbine, 4 of the 49 patients developed atrial flutter or AF.53 The combined regimen of carboplatin plus paclitaxel and gemcitabine with amifostine was associated with AF in 1 of 17 patients.57

**Cytarabine**

Cytarabine is used primarily for the chemotherapy of haematological malignancies. Cardiotoxicity is rare, but includes bradycardias, sometimes requiring the discontinuation of the cytarabine infusion and the administration of atropine.58

**Alkylating agents**

Alkylating agents include chlorambucil, cyclophosphamide, busulfan, cisplatin, and melphalan. They cause the cross-linking of DNA strands, abnormal base pairing, or DNA strand breaks and thereby prevent the cell from dividing. They are generally used in the treating of slow-growing cancers.

**Cisplatin**

Cisplatin is thought to be associated with AF59 and paroxysmal supraventricular tachycardia.60,61 Marked sinus bradycardia was reported, including a patient with a heart rate of 35 bpm that recurred during each of six cycles of cisplatin.62,63

Intrapерicardial and intrapleural administration of cisplatin for metastatic lesions resulted in AF in 12–32%64–67 of patients and NSVT in 8%. Direct irritation of the pericardium could be responsible for part or all of these cases.

**Melphalan**

AF is a well-documented complication of melphalan. Among 40 patients older than 60 years of age, AF after melphalan was present in 9.68 Furthermore, melphalan used prior to a bone marrow transplant was associated with AF in 6.6–8.3%.69,70 patients. No AF occurred in the group of 36 patients who received a bone marrow transplant without melphalan. All patients had structurally and functionally normal hearts according to echocardiography and did not have ischaemia on stress testing.71 Another study of 17 patients over 65 years old and received high-dose melphalan as well as 17 younger patients (controls) who received the same treatment found that 2 patients in each age group developed AF.72 Therefore, melphalan association with AF is established—occurs in a significant proportion of patients regardless of age. It would not be unreasonable to monitor patients on high-dose melphalan.

**Cyclophosphamide**

Acute cardiac toxicity is a well-known, potentially fatal side effect of high-dose cyclophosphamide therapy; however, arrhythmia usually occurs in the context of perimyocarditis and congestive heart failure73,74—although isolated AF has been reported.75 Pentoctatin, an adenosine deaminase inhibitor, increases the acute cardiotoxicity of high-dose cyclophosphamide and might result in fatal arrhythmias and acute cardiomyopathy.76

Ifosfamide is structurally similar to cyclophosphamide and can also be associated with arrhythmias. High-dose ifosfamide therapy is associated with early cardiac toxicity, usually in the setting of decreased kidney function, which manifests through malignant arrhythmias that may require anti-arrhythmic drugs or cardiovascular. Arrhythmias associated with ifosfamide therapy included PACs, supraventricular tachycardia,77 AF, atrial flutter, PVCs, and VT. Most of these arrhythmias occurred in patients who developed cardiomyopathy.78

**Tyrosine kinase inhibitors**

Tyrosine kinase inhibitors are newer members of chemotherapeutic drugs. They are important targets in cancer therapy because they play a significant role in the modulation of growth factor signalling.

Trastuzumab is a monoclonal antibody that acts upon the human epidermal growth factor receptor-2. It is used in breast cancer in patients whose tumours over-express this receptor. Trastuzumab therapy is associated with asymptomatic left ventricular systolic dysfunction but is not considered arrhythmogenic.79 Ventricular tachycardia with presyncope was reported in a patient with a preserved ejection fraction after 6 months of trastuzumab. Ventricular ectopy resolved gradually after discontinuation of trastuzumab, with no other changes in medications.80 Olin et al.81 described a patient on trastuzumab with mild left ventricular dysfunction who sequentially developed AF, accelerated junctional rhythm, and atrial tachycardia.

Sunitinib, cetuximab, and alemtuzumab were reported to be associated with AF in one case report each.82–84 Rituximab is associated with many infusion reactions, including arrhythmias like AF, PVCs, and VT reversible upon the discontinuation of the drug.85,86

**Miscellaneous chemotherapeutic agents**

**Arsenic trioxide**

Arsenic is currently used for intractable haematological malignancies. In terms of pro-arrhythmic effects, it inhibits the rapid component of the delayed rectifier potassium current (I_KA) or the slow component of the potassium current (I_KS) and activation of the adenosine triphosphate-sensitive potassium current (I_KATP).
In guinea pig right ventricular papillary muscles, arsenic trioxide prolonged action potential duration.\(^8^7\)

ECG signs of arsenic poisoning include QRS widening, prolonged QT interval, QT depression, and T-wave flattening. Sinus tachycardia, PVCs, and NSVT have been observed as well.\(^8^8\) QT prolongation occurred in 38.4% of patients on arsenic, with 26.5% developing QTc of \(\geq 500\) ms; only one developed torsades.\(^8^9\) Patients with pre-existing heart disease, hypokalaemia, and women, predictably, were at higher risk. QT prolongation was significant but reversible; it increased by 30–60 ms in 36.6% of treatment courses and by \(>60\) ms in 35.4% of patients. In patients receiving multiple courses, QTc intervals returned to pretreatment levels before the second course.\(^8^9\)

Prolonged QT intervals were observed in all eight patients who received arsenic. PVCs were noticed during 8 of 12 courses of therapy. Four patients developed NSVT. Accelerated idioventricular rhythm\(^9^0\) and torsade de pointes with VT have also been reported.\(^8^9,9^1,9^2\) Not surprisingly, sudden deaths occur among patients on arsenic trioxide.\(^9^3\) Of 10 patients with acute promyelocytic leukaemia, 3 died suddenly during the first cycle of treatment—2 off monitor, with autopsies showing no obvious cause of death, whereas the third developed asystole on the monitor, with QT intervals ranging from 439 to 508 ms several days before the event; no autopsy performed.\(^9^4\) Atrioventricular block after arsenic trioxide treatment for refractory acute promyelocytic leukaemia is very rare. In one patient, the block was at the A-H level and manifested as complete AV block and Wenckebach second-degree type 3:2 block. It was reversible after discontinuation of the drug.\(^9^5\)

Many authors believe that patients taking arsenic trioxide should have frequent ECG monitoring.\(^9^0,9^1\) Patients who develop a QTc of \(>500\) ms or symptoms such as palpitations or syncope should be hospitalized and closely monitored using cardiac telemetry. Concomitant risk factors like electrolyte imbalances should be immediately corrected,\(^8^8,9^0,9^6,9^7\) and arsenic trioxide therapy should be suspended to reassess QTc.\(^8^8\)

**Thalidomide**

Thalidomide, once widely administered as a sedative and withdrawn from the market because of teratogenic effects, is currently used for some solid tumours.

Thalidomide therapy is associated with sinus bradycardia,\(^9^8\) observed in up to 27% of patients.\(^9^9\) Third-degree AV block with hypotension and loss of consciousness was reported in one patient who had started thalidomide 2 weeks prior, had normal baseline AV conduction, and was not taking other medications.\(^1^0^0\) The mechanism may be inhibition of intrinsic sinus-node pacemaker activity. No increase in PR, QRS, or QTc intervals has been documented. Sustained VT has also been reported.\(^1^0^1\) Cardiotoxicity is a potentially serious adverse effect of thalidomide treatment; therefore, close clinical and electrocardiographic monitoring should be performed.\(^1^0^1\)

**Histone deacetylase inhibitors**

Histone deacetylase inhibitors like depsipeptide alter gene expression and modulate cell cycle arrest and apoptosis. They are associated with prolonged QTc interval, asymptomatic VT, and sudden cardiac death attributed to possible fatal ventricular arrhythmia. One study involving 15 patients receiving depsipeptide was terminated prematurely due to an unexpected high number of serious cardiac adverse events. A sudden death, two episodes of asymptomatic VT, and three occurrences of QT prolongation were recorded.\(^1^0^2\) Depsipeptide has also been associated with AF. Cardiotoxicity seems to be related to the rate of depsipeptide infusion; a 4 h infusion is much better tolerated than a 10 min bolus.

Panobinostat is another histone deacetylase inhibitor. It has also been associated with QTc prolongation. The incidence and severity of this QT prolongation vary dramatically—from 6 to 33%—as a function of the dose and schedule.\(^1^0^3\)

**Amsacrine**

Amsacrine is an antileukaemia drug whose mode of action is somewhat similar to that of the AC in that it acts—as at least partially—as a DNA-intercalating agent. It has been associated with ECG abnormalities (including QT prolongation),\(^1^0^4\) atrial and ventricular arrhythmias,\(^1^0^5\) sudden death, and heart failure. Amsacrine appears to affect depolarization and repolarization of the heart, but the mechanisms by which it does so remain unknown. Weiss et al.\(^1^0^6\) analysed 5340 patients treated with amsacrine: only 5 (0.7%) developed arrhythmia. However, in published and unpublished case reports, the authors found 34 patients with VT/VF or cardiac arrest, including 14 patients who died either on infusion or within 4 h after it was stopped, as well as 3 episodes of AF. Some of these patients had recurrences of arrhythmia with repeated doses.

**Interleukin-2**

Interleukin-2 (IL-2) is a glycoprotein produced by activated lymphocytes that induces T-cell proliferation. It has significant antitumour activity in metastatic renal cell carcinoma and malignant melanoma.

IL-2 has been associated with bradycardia, AF,\(^1^0^7,1^0^8\) supraventricular tachycardia, and VT.\(^1^0^9,1^1^0\)

One study involving 93 patients found that 20 developed cardiac arrhythmias, including SVT in 10 (11%), AF in 4 (4.3%), PVCs in 5, and VT-requiring cardioversion in 1.\(^1^1^1\) Meanwhile, an analysis of 317 patients treated with 423 courses of IL-2 therapy found that 8% of the courses were associated with AF, 1.7% were associated with a prolonged atrial arrhythmia and hypotension, and 0.2% were associated with a NSVT.\(^1^1^2\)

**Conclusions**

In this review, we tried to summarize the data on arrhythmia in chemotherapy from the existing literature and to attract attention of cardiologists to this problem. The data presented provide more questions than answers. Because the arrhythmia during chemotherapy usually occurs in cancer centres, clinically relevant data on treatment, duration, risk of embolic events, and particularly ischaemic strokes are practically missing from the literature.

Although the data are limited, several classes of cancer chemotherapeutic agents appear to be associated with cardiac arrhythmias. Anthracyclines, melphalan, and IL-2 appear to be
associated with the development of AF. Monitoring would be prudent in patients receiving these drugs, especially in those who had documented ECG abnormalities or arrhythmias during past exposure to a given chemotherapeutic regimen.

Taxol and other antimitotubular drugs are safe in terms of pro-arrhythmic side effects and do not cause any consistent rhythm abnormalities beyond sinus bradycardia and mild conduction disorders such as first-degree atrioventricular block. Likely no routine monitoring for arrhythmia is necessary.

Arrhythmias induced by 5-FU, including VT, are mostly ischaemic in origin and usually occur in the context of coronary spasm produced by this drug. It is not, therefore, an arrhythmia problem, but rather prediction and prevention of coronary spasms in high-risk population undergoing chemotherapy.

Cisplatin—particularly intrapericardial administration—is associated with a very high rate of AF, likely due to direct irritation of the pericardium, and warrants monitoring.

Sudden death with documented or suspected ventricular arrhythmias has been reported with almost all classes of chemotherapeutic drugs but rarely. Dispeptide was the only drug which demonstrated a high rate of VT, but the number of patients was so small\textsuperscript{15,102} that more observations are necessary for definitive conclusions.

In general, chemotherapy-induced arrhythmia is an existing but poorly recognized and studied entity. Studies with prospective collection and thorough analyses will be needed to establish a causal relationship between certain anticancer drugs and arrhythmias.

Conflict of interest: none declared.

References


Chemotherapy-induced arrhythmia


