

Heart inflammation - a complication of Covid 19 infection or vaccination?

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Abstract. Severe acute respiratory syndrome (SARS CoV₂) is an unparalleled challenge for the global medical community. Although the main clinical manifestation is pulmonary, with variations ranging from asymptomatic to mild flu-like illness to severe pneumonia and acute respiratory distress syndrome with potential fatality.

The essential mechanism consists of the binding of the virus to ACE₂ receptors through a viral envelope protein (protein S or SPIKE) followed by the appearance of a serum protease TMPRSS2 which mediates the binding of the virus at the cellular level. Because ACE₂ is a cell membrane peptidase in the lungs, heart, blood vessels, kidneys, brain and gastrointestinal tract, COVID19 infections can occur at any of these levels.

All ACE₂-expressing cells are at risk of infection.

Currently, viral pericarditis associated with both SARS CoV₂ infection and vaccination against this virus is becoming more and more common, regardless of the vaccine used.

Since April 2021 in the US there have been over 1000 reports in VAERS of myocarditis and post-vaccination pericarditis m RNA Covid-19 (BioNTech, Modern).

Although the frequency of myocarditis and pericarditis was rare post-vaccination - 0.0018% of cases reported between December 2020 and July 2021 - the number of cases is certainly much higher, these complications being underdiagnosed, and therefore incorrectly managed and treated^[1].

In fact, government organizations also considered these complications, on June 23, 2021 the safety committee of the US Centers for Disease Control and Prevention stated that there is a likely association between Pfizer - BioNTech and Moderna vaccines and myocarditis and pericarditis in some young people (16 -24 years), but that the benefits clearly outweigh the risks^[2]

As a result of all these signals, the US Food and Drug Administration said it will add this risk to the mRNA vaccine fact sheets, although it considers that such complications are "extremely rare" and that "most cases have been mild"^[3].

Keywords. cardiac inflammation, vaccination, Covid-19 infection, post-vaccination symptoms, adverse reactions

1. Introduction

Severe acute respiratory syndrome (SARS CoV₂) is an unparalleled challenge for the world medical community. Although the main clinical manifestation is pulmonary with variations from asymptomatic to mild flu-like disease to severe pneumonia and acute respiratory distress syndrome with lethal potential.

The essential mechanism consists of the binding of the virus to the ACE2 receptors through a protein of the viral envelope (protein S or SPIKE) followed by the appearance of a serum protease TMPRSS2 that mediates the binding of the virus at the cellular level. Because ACE2 is a cell membrane peptidase in the lungs, heart, vessels, kidneys, brain and gastrointestinal tract, Covid19 infections can occur at any of these levels.

All cells expressing ACE2 are at risk of infection.

Currently, viral pericarditis associated with both SARS CoV2 infection and vaccination against this virus, regardless of the vaccine used, is increasingly common.

Starting from April 2021 in the USA there were over 1000 reports in VAERS of post-vaccination myocarditis and pericarditis mRNA Covid-19 (BioNTech, Moderna).

Although the frequency of myocarditis and pericarditis was rare post-vaccination - 0.0018% cases reported between December 2020 and July 2021 - the number of cases is certainly much higher, these complications being underdiagnosed, and as a result incorrectly managed and treated. [1]

Moreover, governmental organizations also took into account these complications, on June 23, 2021 the safety committee of the Centers for Disease Control and Prevention in the USA declared that there is a probable association between the Pfizer - BioNTech and Moderna vaccines and myocarditis and pericarditis in some young people (16 -24 years), but that the benefits clearly outweigh the risks [2]

As a result of all these signals, the US Food and Drug Administration has stated that it will add this risk to the information sheets for mRNA vaccines, although it considers that this type of complication is "extremely rare" and that "most cases were mild"[3]

For these reasons, we had the curiosity to see what the symptoms are in heart inflammation after infection with Covid 19 or after vaccination against Covid 19.

2. Material and method

We included in the study patients who presented themselves at the cardiology office of OCH Constanta between 01.03.2021 - 01.07.2021, presenting cardiac symptoms that started after the infection of COVID-19 (documented either by PCR - Covid19 or computer tomography) or after vaccination .

We had 37 patients, of different ages, whom were divided into 2 groups:

- patients with cardiac symptoms that started after SARS-CoV2 infection, respectively
- patients with cardiac symptoms that started after vaccination (regardless of the vaccine used)

Out of the 37 patients with cardiac symptoms, only 5 claimed that these symptoms started after vaccination, the rest having a secondary onset of SARS-CoV2 infection.

3. Theory/calculation

The following were evaluated in these patients:

- age
- sex
- initial symptoms (palpitations, chest pain or dyspnea)
- the time of appearance of post-infection symptoms, respectively post-vaccination
- duration of maintenance of this symptomatology
- electrocardiographic, echocardiographic, computed tomography and biochemical changes in the patients in whom they occurred

To be mentioned that Holter EKG monitoring was performed on a number of 3 patients.

Table 1. Age of patients

Age	Number of patients	Percentage
20-25 years	4	10,81%
25-30 years	6	16,21%
30-35 years	8	21,62%
35-40 years	5	13,51%
40-45 years	5	13,51%
45-50 years	2	5,40%
50-60 years	3	8,10%
>60 years	4	10,81%
Total	37	100%

Most patients in our study were female, thus

Table 2. Patient gender

Gender	Number of patients	Percentage
Feminine	21	56,75%
Masculine	16	43,24%
Total	37	100%

The probability of anxiety is higher in female patients, which is why a large part of the symptoms, such as palpitations, can be attributed to this pathology.

Onset symptomatology:

Table 3. The symptomatology of post-infection COVID-19 patients

Symptoms	Number of patients	Percentage
Palpitations	29	78,37%
Dyspnea on exertion	17	45,94%
Precordial pain	11	29,72%
Headache	15	40,54%
Myalgia	14	37,83%
Arthralgia	14	37,83%
Low fever (37,3-38°C)	10	27,02%
Fever (> 38°C)	4	10,81%

Although there may also be gastrointestinal damage in COVID-19 infections, none of the patients presented with intestinal-type symptoms (diarrhea, nausea, vomiting).

Patients who presented cardiac symptoms following vaccination

Table 4. Symptoms started after vaccination

Symptoms	Number of patients	Percentage
Palpitations	3	60%
Dyspnea on exertion	1	20%
Precordial pain	2	40%
Headache	3	60%
Myalgia	2	40%
Arthralgia	1	20%
Low fever (37,3-38°C)	2	40%
Fever (> 38°C)	2	40%
Nausea	1	20%
Vomiting	1	20%
Diarrhea	1	20%

We did not take into account patients without post-vaccination symptoms because they have no motivation to see a doctor, which is why we consider that the institutional study could be expanded, following the reporting of adverse reactions at the national level, so that we have a complete picture of post-vaccination reactions in Romania. Associated, pre-existing pathologies in the patients included in the study:

Table 5. Pre-existing pathologies in the patients included in the study

Pre-existing pathologies	Number of patients	Percentage
Bronchial asthma	2	5,4%
Exertion angina	8	21,62%
Thyroid dysfunction	1	2,70%
Ischemic heart disease	6	16,21%
Nephrolithiasis	3	8,10%
Hepatic steatosis	11	29,72%
Obesity (BMI> 30 kg/m2)	13	35,13%

We mention that a number of 12 patients (32.43% of all patients included in the study) did not have any previously diagnosed impairment, being young, in full physical and mental health until the time of infection/vaccination with COVID-19.

Of the 37 patients included in the study, 5 (13.51%) presented post-vaccination symptoms, the remaining 32 patients (86.48%) having symptoms that started following SARS-CoV2 infection.

The average duration of symptoms from the confirmation of SARS-CoV2 infection was 9.2 days on average, and in the case of vaccinations, the symptoms started less than 24 hours post-vaccination.

In our study, we also had a case of pericarditis (2.70% of cases), which started in a young, male patient, aged 37.

In this patient, the symptoms started 21 days after the diagnosis of the infection with COVID 19, with rapid palpitations, progressive dyspnea up to low exertion dyspnea, quasi-permanent retrosternal pain and low fever (37.3-37.8 oC). It should be mentioned that during the acute period he presented only anosmia, the symptoms starting a week after he came out of isolation.

The symptomatology was typical of this condition.

Pericarditis actually represents inflammation of the pericardium, being classified - depending on its evolution - into chronic pericarditis (with a long duration, > 6 weeks) or acute pericarditis, whose duration is short, less than 6 weeks.

Acute pericarditis (< 6 weeks)	Chronic pericarditis (> 6 weeks)
<ul style="list-style-type: none"> • Fibrinous (dry) • Exudative (fluid) 	<ul style="list-style-type: none"> • Constrictive (most common) • Adhesives • Effusive

The etiology of pericarditis can be:

1. Infectious:

- Viral
- Bacterial
- Fungus
- Parasitic
- Tuberculous

Infectious pericarditis is the most common, and is usually preceded by febrile episodes. The most often encountered infectious etiologies of pericarditis are viral ones, with adenoviruses, coxsackie virus or echoviruses.

2. Non-infectious:

- Post myocardial infarction
- In aortic dissection (blood accumulation in the pericardium-hemopericardium)
- In renal failure (uremic pericarditis)
- Pericardial metastasis (neoplastic pericarditis) in primary tumors with different locations
- Autoimmune diseases

The symptoms of pericarditis depend on the rapidity of fluid accumulation between the sheets of the pericardium (the faster it is, the more pronounced the symptoms) and include:

- Sensation of suffocation
- Precordialgias characterized by chest tightness
- Dyspnea (not associated with effort, quasi-permanent)
- Dysphagia
- Hiccups (due to secondary irritation of the phrenic nerve)

In this patient, the following were performed:

Paraclinical explorations that revealed:

- non-specific inflammatory syndrome (elevations of ESR, C-reactive protein and fibrinogen)
- leukocytosis on the blood count
- no specific antibodies were performed for the etiological agent (Covid-19) because it was immediately after the infection
- Troponin T was not elevated in this patient. This cardiac necrosis marker was also collected because it is frequently elevated in SARS CoV2 cases even without secondary cardiac damage

Troponin rise in SARS CoV2 infection can have several causes:

- The most frequent non-ischemic myocardial damage through different mechanisms (severe hypoxia, systemic inflammation, stress-induced cardiomyopathy)
- Rarely typical viral myocarditis ^[4]

The electrocardiogram showed all the evolutionary changes of pericarditis:

- Stage I – upper concave ST segment elevation, without mutual elevation and PR segment elevation and corresponds, from a clinical point of view, to the initial stage with pain
- Stage II – the ST segment returns to the baseline and the T wave flattens
- Stage III – the T waves become negative and the Q wave is absent
- Stage IV - T waves return to normal (evolving in weeks or even months).

Radiologically, no changes were evident.

Transthoracic echocardiography has visualized a thin layer of pericardial fluid, but although this can detect even small amounts of pericardial effusions, up to 20 ml, and is the examination of choice in the diagnosis of pericarditis regardless of the cause, in this case, due to the small amount of liquid, it was also decided to perform a CT scan, considering that the ultrasound alone is not conclusive.

The computed tomographic examination confirmed the diagnosis of pericardial effusion, but its etiology remained to be confirmed.

We considered the etiology in this case to be SARS-CoV2 infection from the very beginning, although Troponin was not elevated, based on clinical and imaging data. Moreover, the specialized literature also shows that the cardiac damage (based on Troponin I elevations, EKG changes and cardiac ultrasound with specific changes) in patients infected with SARS CoV 2 varies around 7.2% [5] and arrhythmias have become evident in 16.7% of patients, our patient falling into this situation.

The evolution of the patient under treatment confirmed the diagnosis of Pericarditis after SARS-CoV2 infection, because by administering Colchicine, the symptoms decreased in 48 hours, and 7 days after the initiation of treatment, the amount of pericardial fluid.

Regarding pericarditis or pericardial effusion in SARS CoV2 infection, the etiological treatment must include:

Colchicine 0.5 mg x 2/day – 3 months in acute infection, 6 months in recurrent infection

Corticosteroids (Prednisone) 0.2-0.5 mg/kg/day for up to a month in advanced cases

NHIG 400-500 mg/hkc/day – 5 days, with the possibility of repeating in a month

Anakinra 2-100 mg/kg/day for 3-6 months

NSAID therapy (Aspirin 75-100 mg 3 times/day or Ibuprofen 600-800 mg x 3/day or Indomethacin 25-50 mg x3/day) administered for 1-2 weeks or until symptoms disappear and PCR normalization is potentially harmful.

Azathioprine in a dose < 2 mg/kg/day (duration > 6 months) – unknown

When corticosteroids and anakinra are used, it is necessary to monitor possible opportunistic bacterial infections

However, the treatment of pericarditis should not be interrupted [6]

The patient's prognosis was good

4. Conclusions

- ✓ The heart and vessels are potential targets for covid 19, although we currently have no data to support the direct infection and replication of SARS CoV2 in cardiac cells.
- ✓ The sequelae of COVID 19 include:
 - pulmonary complications, such as pulmonary fibrosis
 - cerebrovascular (hemorrhagic or ischemic)
 - hematological (hypercoagulability and lymphopenia)
 - cardiac (cardiomyopathies or arrhythmias)[7,8]

While some of these complications may persist chronically after the acute infection, most appear in the acute or subacute period.

- ✓ Late complications associated with post COVID 19 recovery may include chronic fatigue and memory deficits as part of a spectrum in so-called "long haulers" patients [9] Although it has been hypothesized that COVID 19 causes pericardial inflammation through a direct cytotoxic effect or through immune-mediated mechanism, for now we only know that it triggers an exaggerated systemic inflammatory response in certain patients, a response that has not yet been elucidated[10]
- ✓ It is possible that COVID-19, similar to other viral infections, causes an inflammatory response, leading to pericarditis and pleural effusion.
- ✓ CDC data showed that after 3,625,574 doses administered to men aged 18-24, there were 233 reports of myocarditis and pericarditis when it would have been expected to be between 2-25 cases [11]
- ✓ After 5237262 doses administered to women in this age group, 27 cases were observed (all <18 years).
- ✓ The first reports about heart inflammation after the Pfizer vaccination appeared in Israel at the end of April;
- ✓ Great Britain reported:
 - 53 cases of myocarditis and 33 cases of pericarditis (including 1 death) after vaccination with BioNTech,
 - 42 cases of myocarditis (and 1 death) and 77 cases of pericarditis after vaccination with Oxford-Astra Zeneca
- ✓ 3 cases of myocarditis and 1 of pericarditis after the Moderna vaccine[12]

- ✓ In the USA, among boys between 12-17 years old, researchers claim that for every 1 million doses of vaccine there could be 56-69 cases of myocarditis, but 5700 cases of COVID, 215 hospitalizations, 71 patients who will require inclusion in the ATI departments and 2 deaths.
- ✓ Prasard believes that the USA should suspend all vaccination in children <8 years and administer a single dose to men <25 years

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