10° CONGRESSO NAZIONALE

CAMPUS Cuore

Quello che le Linee Guida Non Dicono

Napoli
Hotel Excelsior
14-15 aprile 2023

Fulminant myocarditis unmasking Adult-onset Still's disease and Desmoplakin Cardiomyopathy

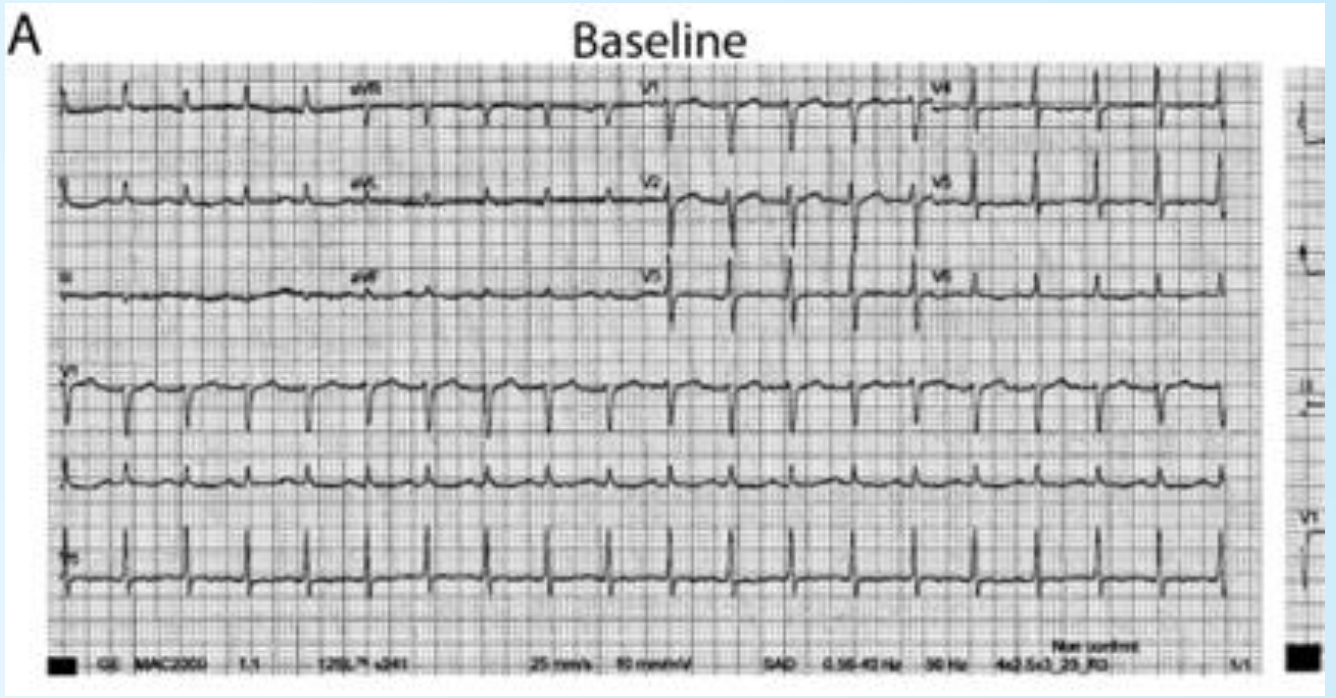
Dott. Enrica Pezzullo

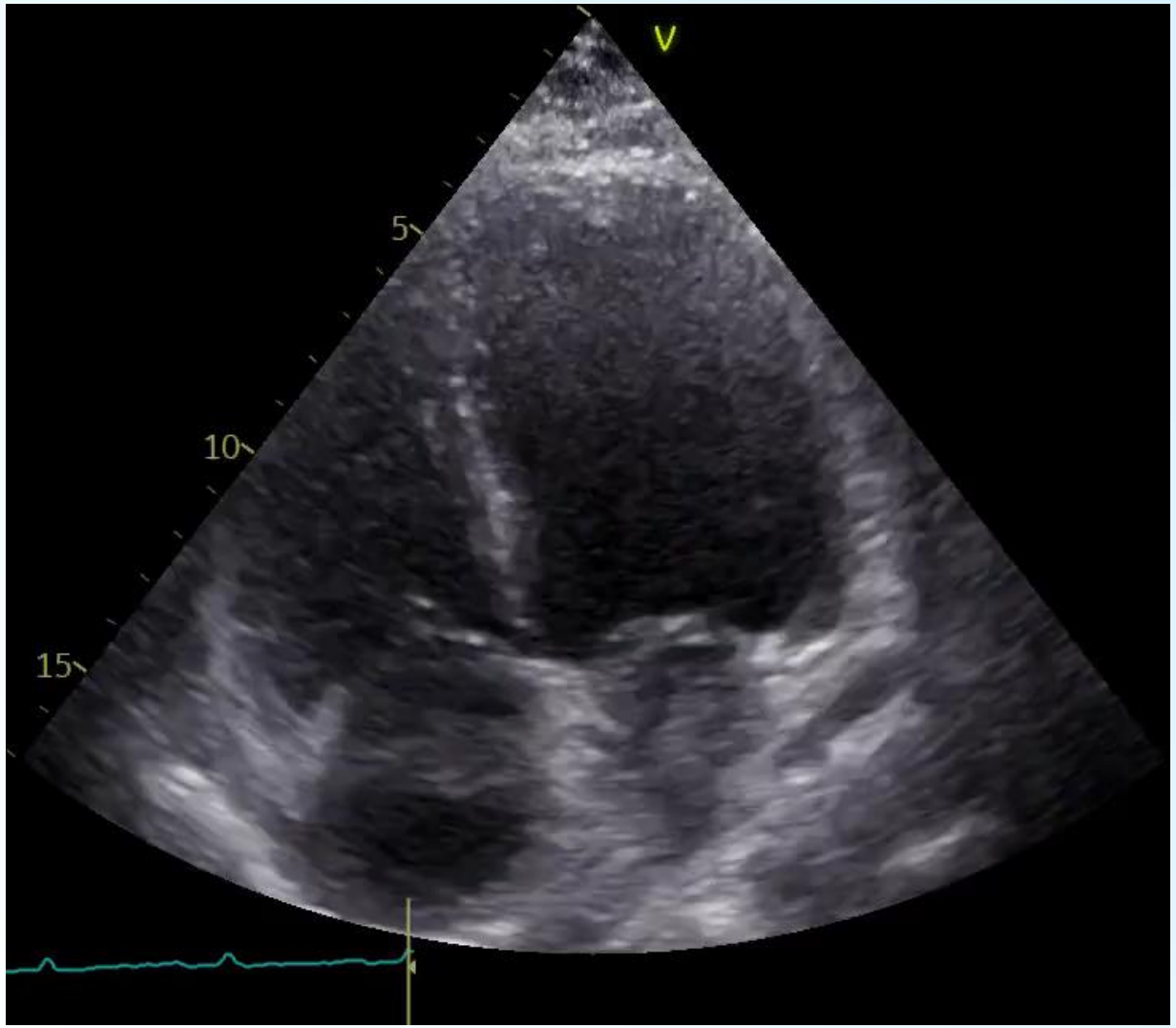
American Heart Association.

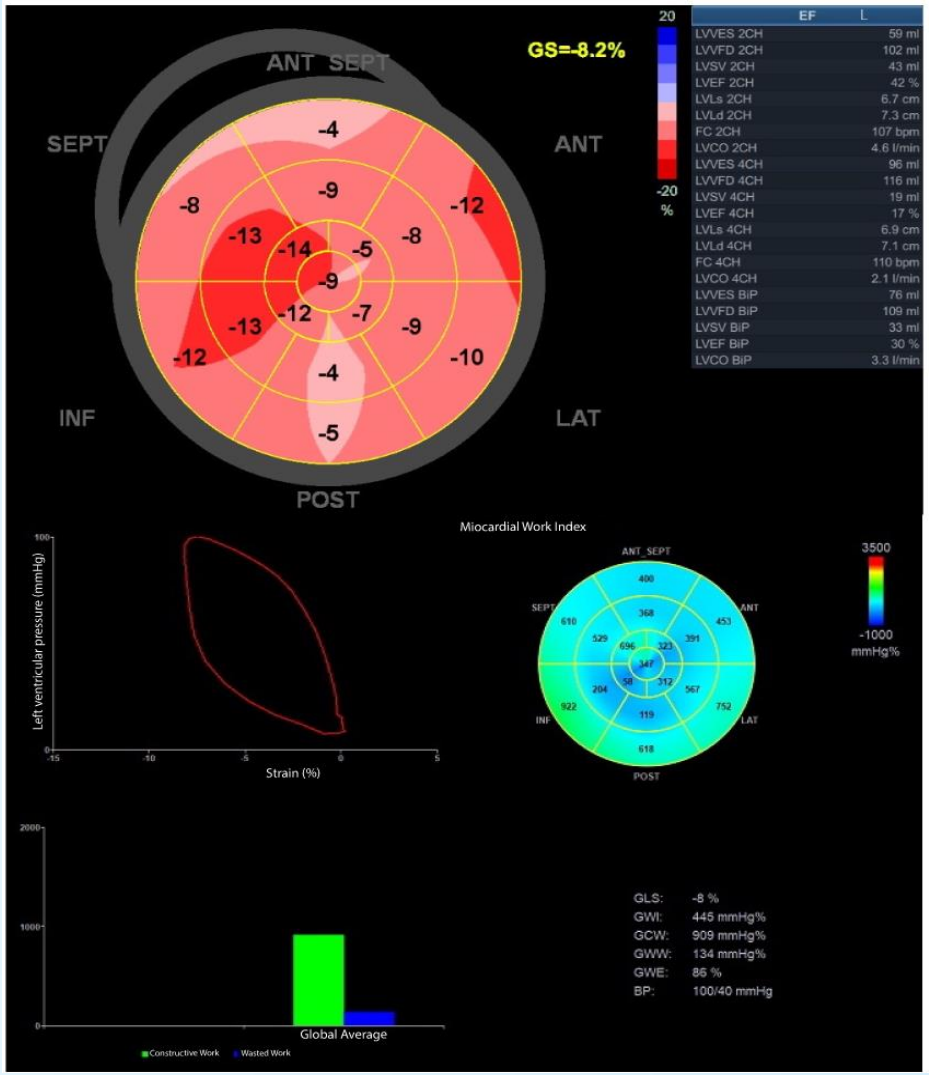
Circulation: Cardiovascular Imaging

Paziente di **24 anni.**
Familiarità per CAD, Diabete mellito ed Ipertensione arteriosa sistemica, negativa per MI e cardiomiopatie.
Obesità. Abitudine tabagica.
Non vaccinato SARS COV2
Febbre (38- 40 C°) da una settimana
Dispnea, malessere generale, sudorazione
Linfoadenopatia cervicale e sottomandibolare dolente.
Terapia antibiotica domiciliare

Parametri al ricovero:
PA 85/45 mmHg,
FC 115 bpm,
FR 45/min,
TC 37,6°C,
SpO2 96% in O2 terapia con cannule nasali a 5L/min (Fi=2 40%).







Insufficienza mitralica funzionale ed insufficienza tricuspidale di grado moderato-severo (3+/4+), PAPs 33 mmHg, VCI dilatate ed ipocollassante e lieve scollamento pericardico.

	Admission
WBC (10^3/uL) (n.v. 4.50-11) **Neutrophils (%)**	47.93 94.4
Creatinine (mg/dL, n.v. 0.6-1.1)	1.5
ALT (U/L, n.v. 0-34) **AST (U/L, n.v. 10-49)**	280 266
Ferritin (ng/mL, 30-400) **hsCRP (mg/dL, n.v. < 1)**	4325 27.3
NT-proBNP (pg/mL, n.v. 0-125) **hsTnI (pg/mL, n.v. 40.8-115.1)**	53000 568

Inizia supporto inotropo con infusion di Dobutamina e si somministra terapia antibiotica ad ampio spettro.

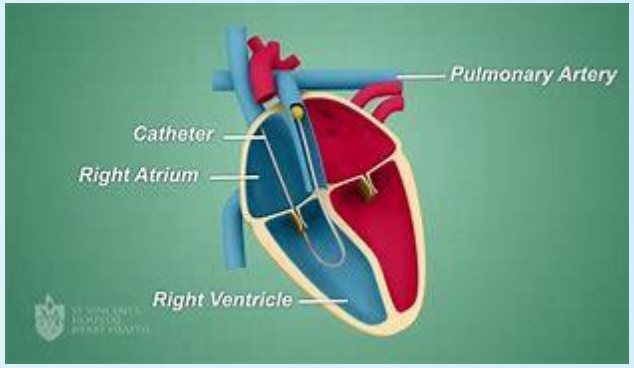
Cateterismo cardiaco destro: Shock misto

Pressione di incuneamento polmonare (PA wedge pressure): 15 mmHg

Pressione arteriosa polmonare media (mPAP): 18 mmHg

Indice cardiaco(CI): 4.2 L/min/m2

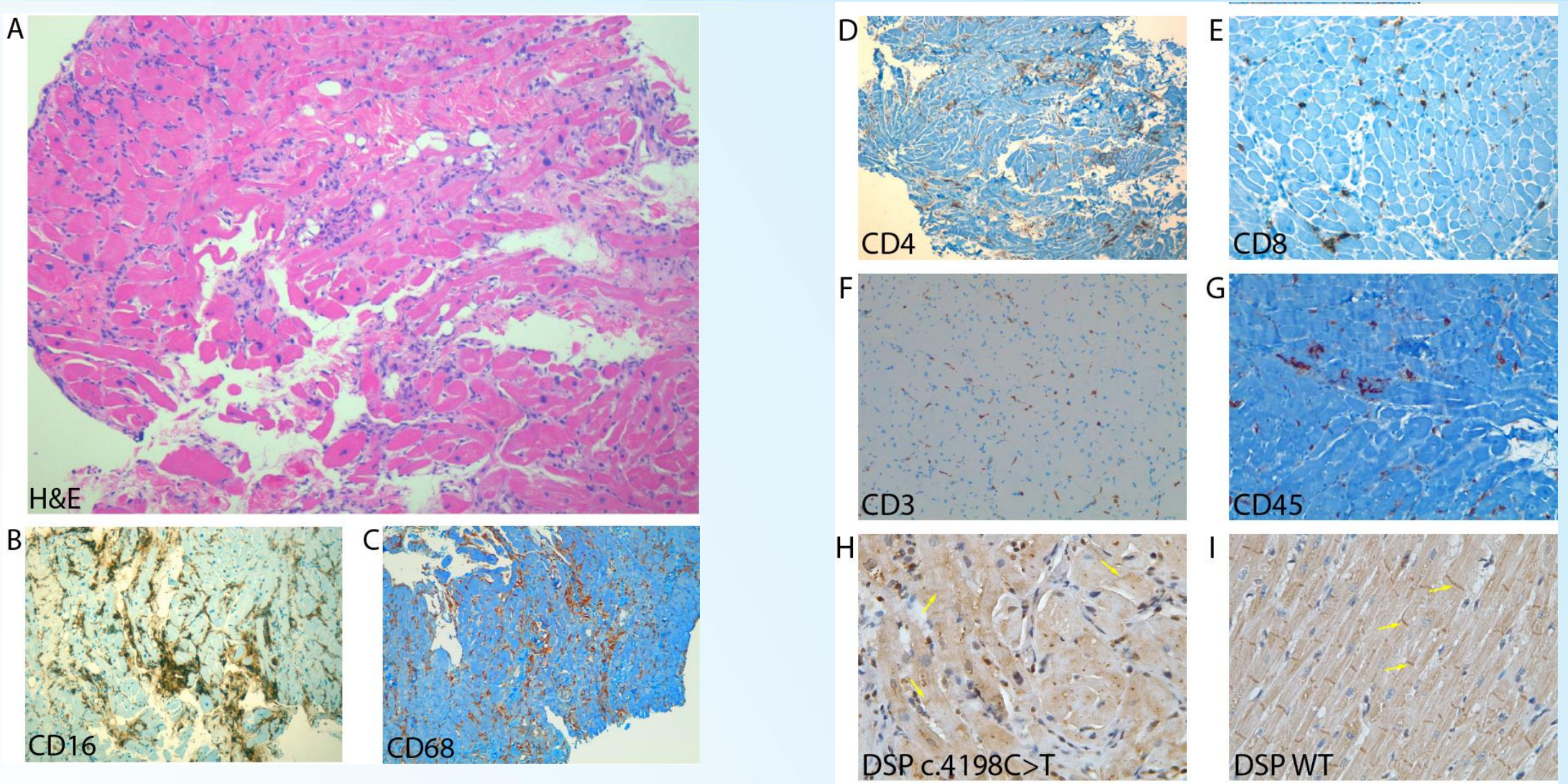
Pressione atriale destra: 10 mmHg



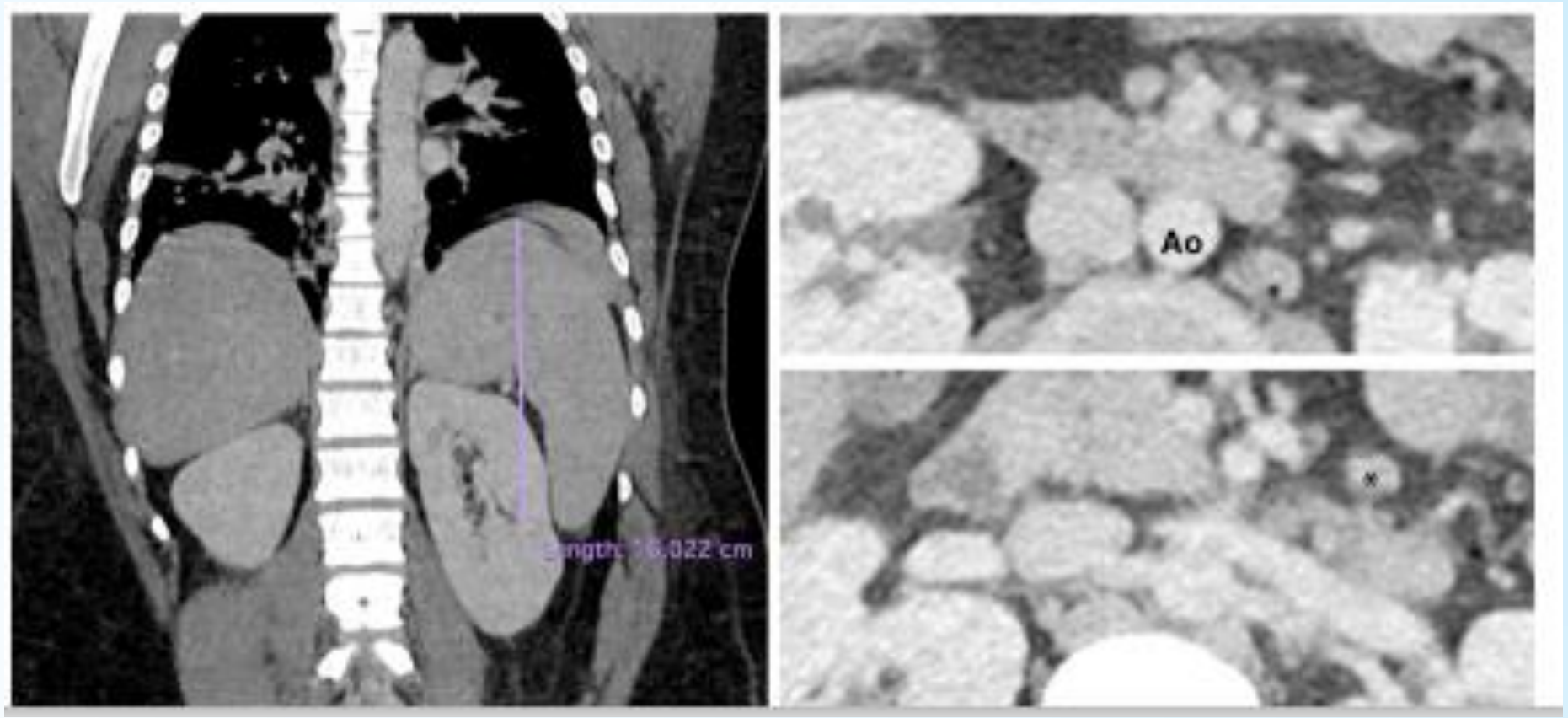
DIAGNOSI DIFFERENZIALI

COVID-19
SHOCK SETTICO
NEOPLASIA
MALATTIA LINFOPROLIFERATIVA
MIOCARDITE VIRALE

Tampone NF Real Time-PCR per SARS-CoV-2: negativo.
Emocolture: negative.
Tipizzazione linfocitaria: nella norma
Sierologia per parvovirus B19, hepatitis B or C, HIV, Toxoplasma, Mycoplasma, Coxsackievirus, Rickettsia, Bartonella, Borrelia, CMV, EBV: negativa.
Pannello autoimmunità: ANA, ANCA, ENA, Complementemia, anti-double-stranded DNA antibodies, Lupus anticoaugulant (LAC), anti-cardiolipin antibodies, anti-beta-2 microglobulin antibodies, rheumatoid factor (RF) nella norma.



Quantitative and qualitative polymerase chain reaction (PCR) results on biopsy were negative for SARS-Cov2, Cytomegalovirus, Epstein Barr virus, human herpesvirus 6, parvovirus B19, enteroviruses and adenovirus.



Linfoadenopatia paraortica, splenomegalia, epatomegalia

Adult-onset Still's disease (AOSD) with fulminant myocarditis and systemic inflammatory response syndrome (SIRS) was suspected.

The etiology is unknown; both genetic factors and a variety of infectious triggers have been suggested

Very uncommon, the annual incidence of AOSD to be 0.16 cases per 100,000 people

AOSD is considered a continuum of juvenile idiopathic arthritis, emphasizing the central role of inflammasome and cytokine storm (especially IL-1, IL-5 6, TNF-alpha).

This uncontrolled inflammatory state can represent a life-threatening condition for the patients because of disseminated intravascular coagulation, macrophage activation, thrombotic microangiopathy and myocarditis. Cardiac involvement is most frequently represented by pericarditis, associated with pericardial effusion and chest pain while myocarditis is more common in young men and can represent the onset symptom.

It is not uncommon for the first two patterns (monophasic and intermittent) to evolve into the chronic articular pattern.

- **Monophasic pattern** – Patients with monophasic AOSD have a disease course that typically lasts only weeks to months, completely resolving within less than a year in most patients. Systemic features, including fever, rash, serositis, and hepatosplenomegaly, predominate in this group.

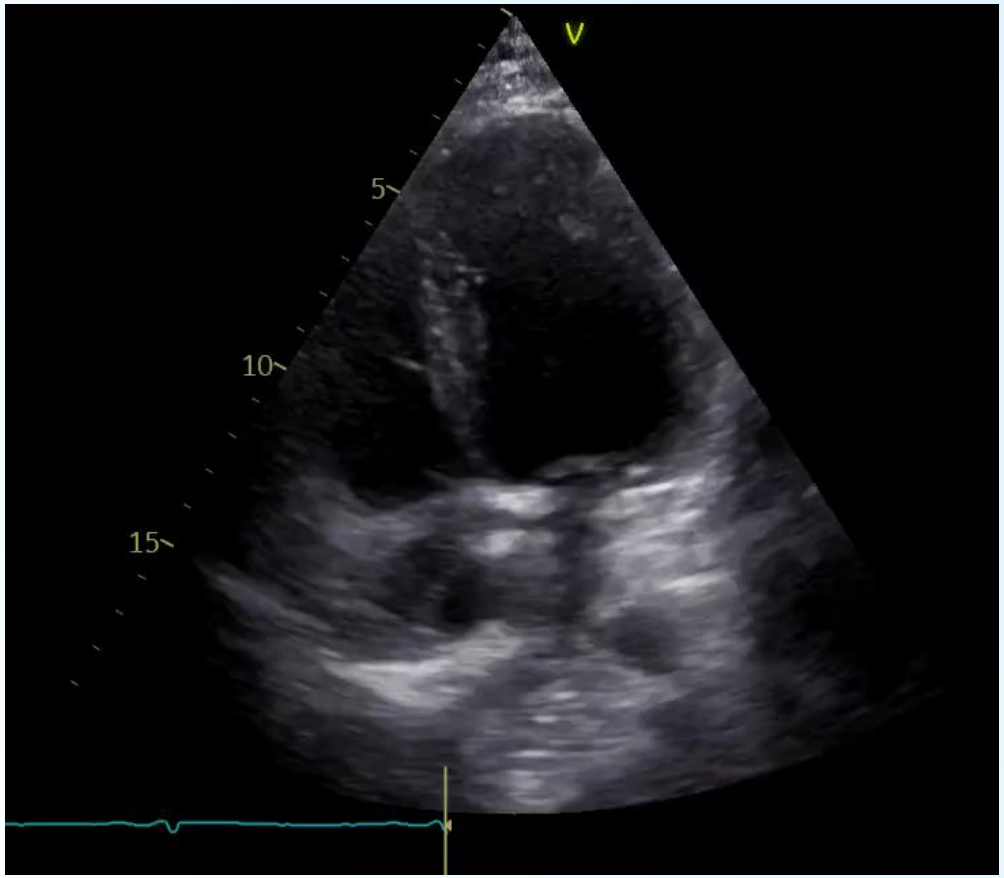
- **Intermittent pattern** – Patients with intermittent AOSD have one or more disease flares, with or without articular symptoms, with complete remissions between episodes lasting from weeks up to one or two years. Although subsequent flares cannot be predicted, they tend to be less severe and of shorter duration than the initial disease episode.

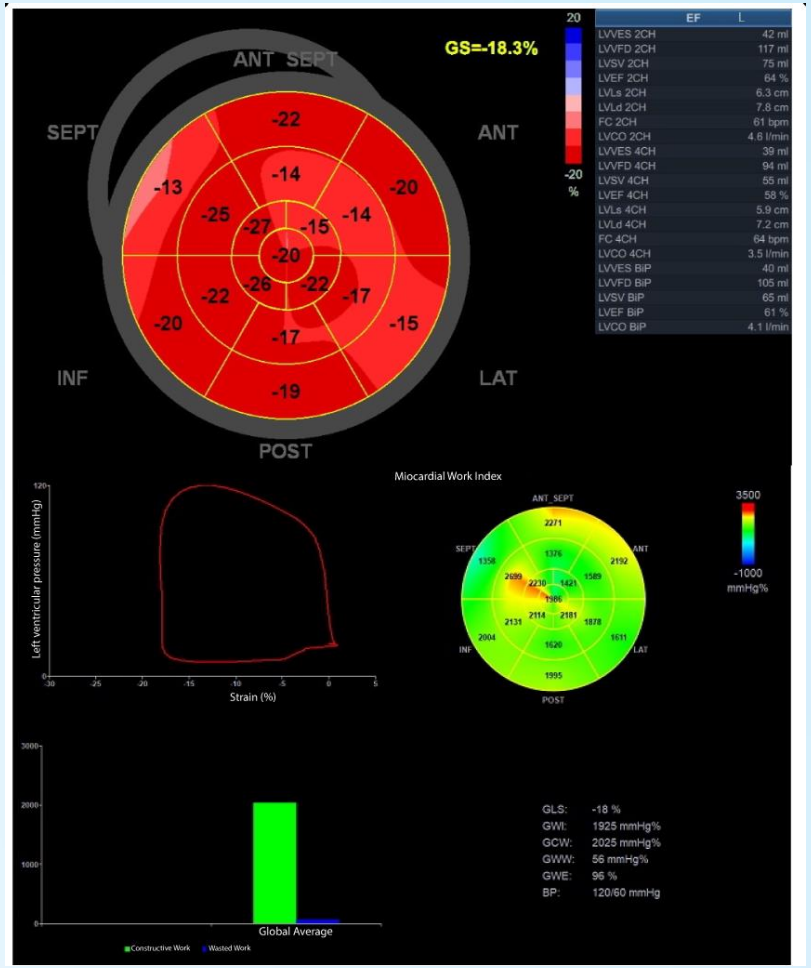
- **Chronic pattern** – Patients with chronic AOSD have persistently active disease, in which articular symptoms usually predominate. A destructive arthritis may occur in patients in this group.

YAMAGUCHI'S CRITERIA[1]		
Five or more criteria are required. Two or more criteria must be major.		
Major Criteria	Minor Criteria	Exclusion Criteria
Fever >39°C lasting 7 days or longer	Sore throat	Infections
Arthralgias or arthritis for 14 days or longer	Hepatomegaly or splenomegaly	Malignancies
Typical rash	Lymphadenopathy	Other rheumatic disease
WBC count >10,000/μL with >80% neutrophils	Abnormal aminotransferases	
	Negative rheumatoid factor and anti-nuclear antibody	

Inizia terapia con boli di Metilprednisolone 1000 mg/die per tre giorni con pronta risposta e miglioramento delle condizioni emodinamiche e cliniche generali, successiva terapia per os con prednisone e lento scalaggio.
Terapia con inibitore del recettore dell'angiotensina e della neprilisina (ARNI), beta-bloccante e antagonista recettore mineralcorticoidi

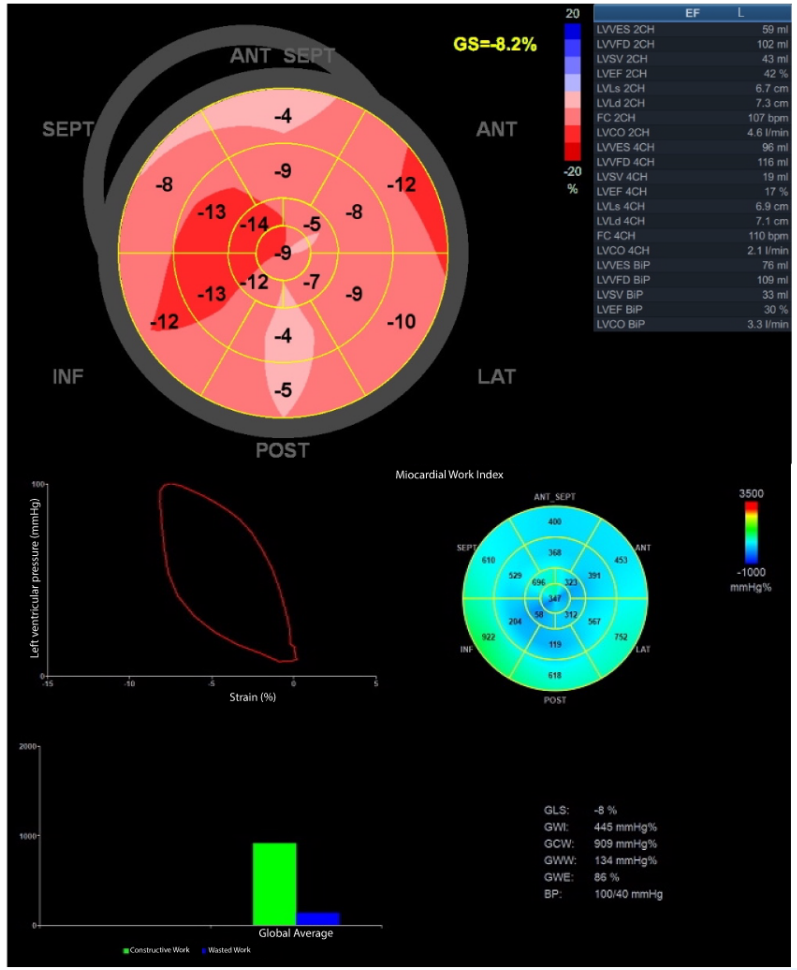
Eco pre-Dimissione





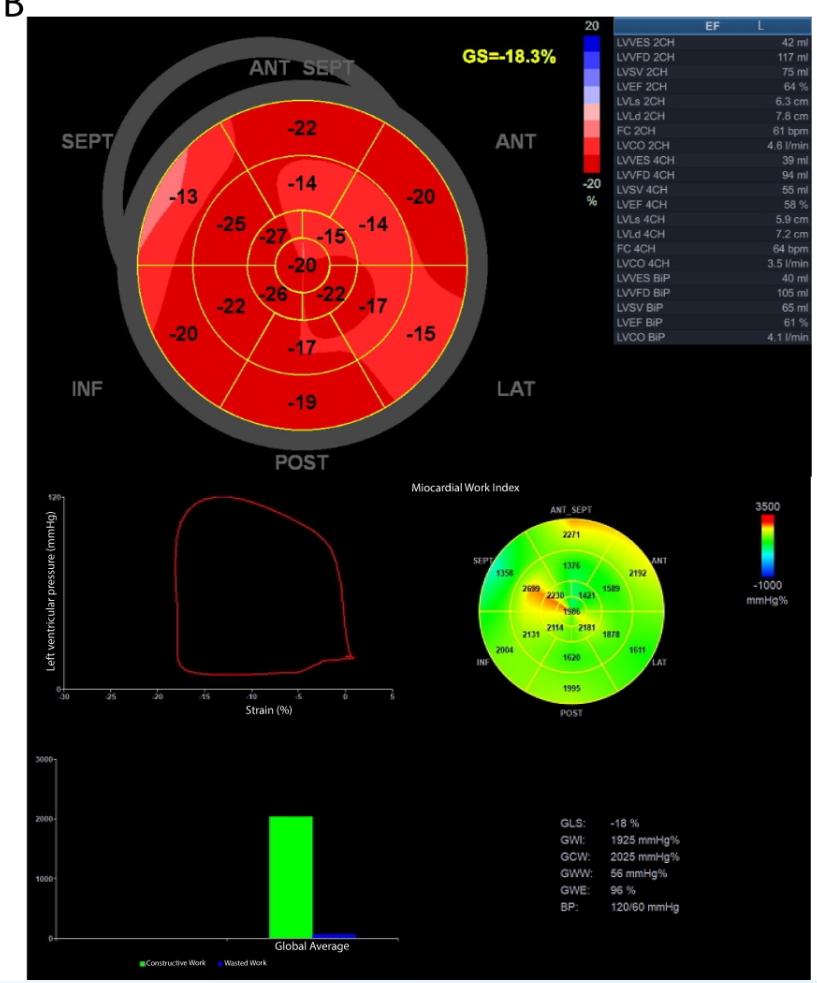
Ricovero

A



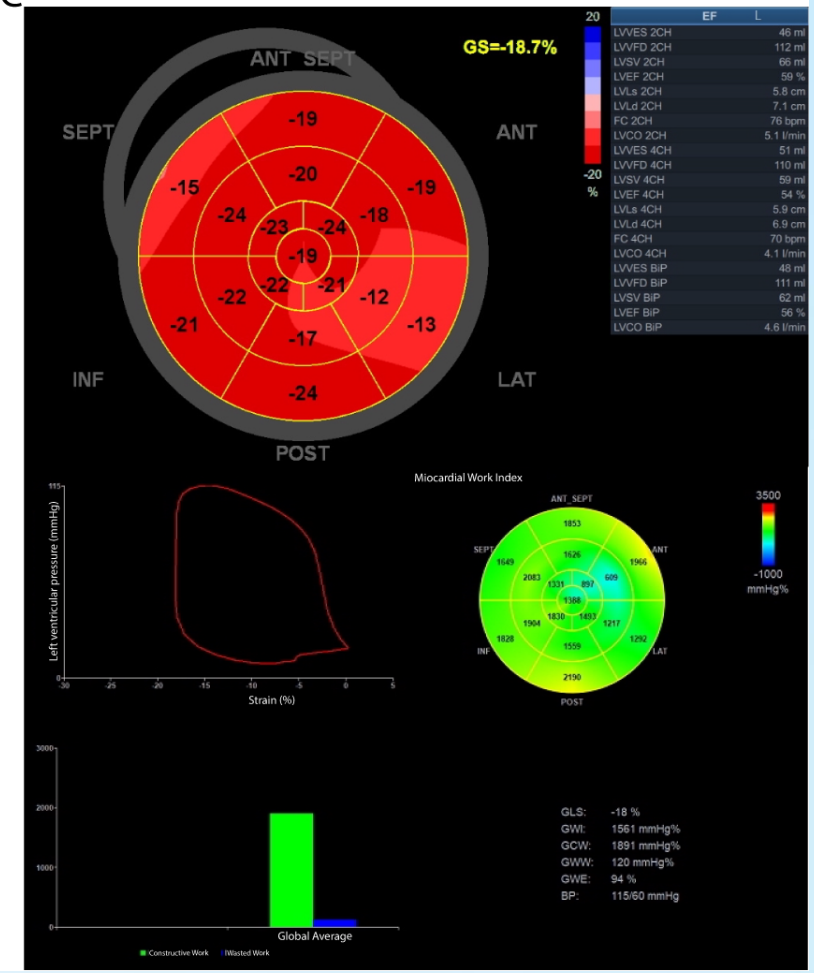
pre-Dimissione

B

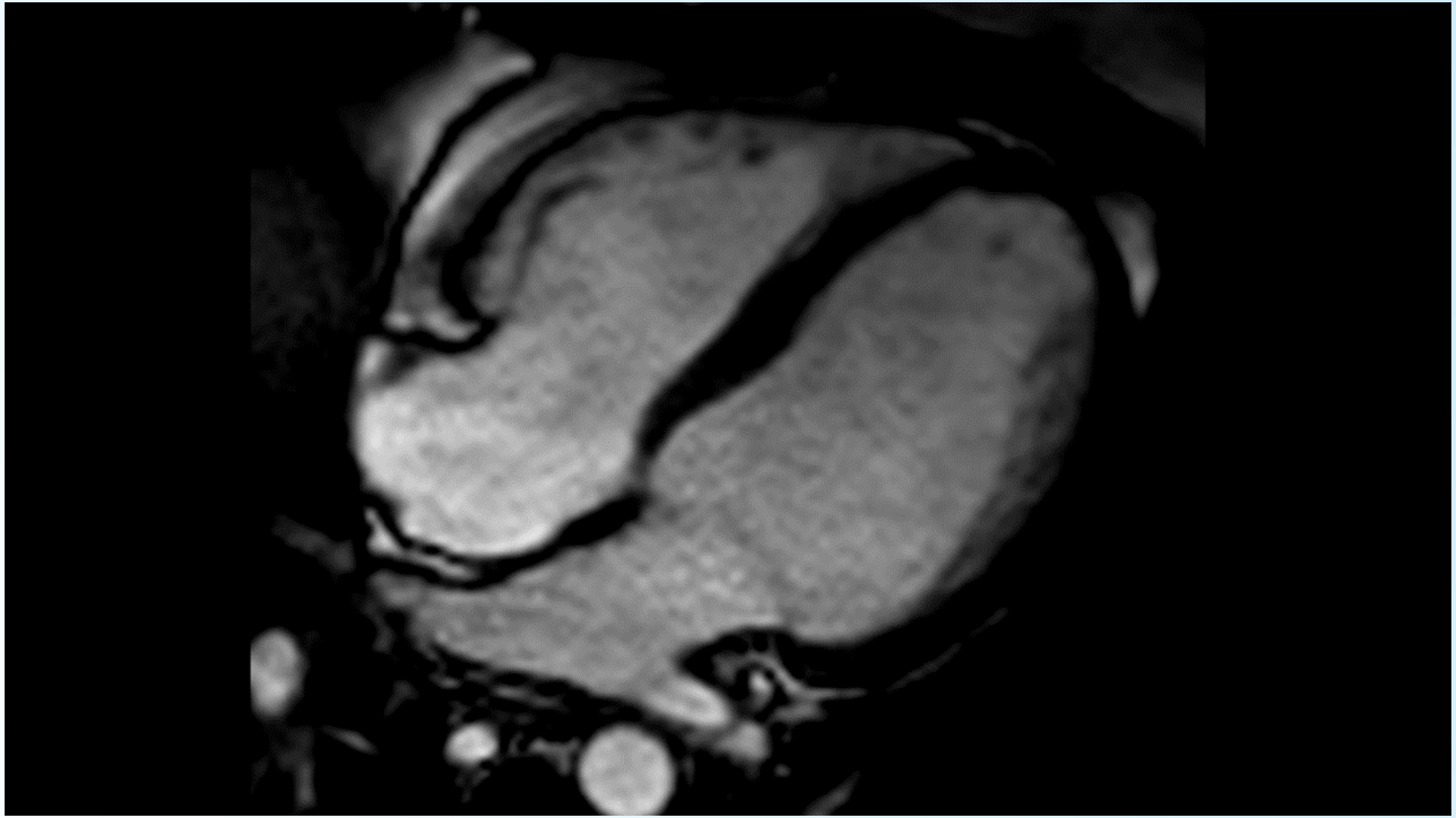


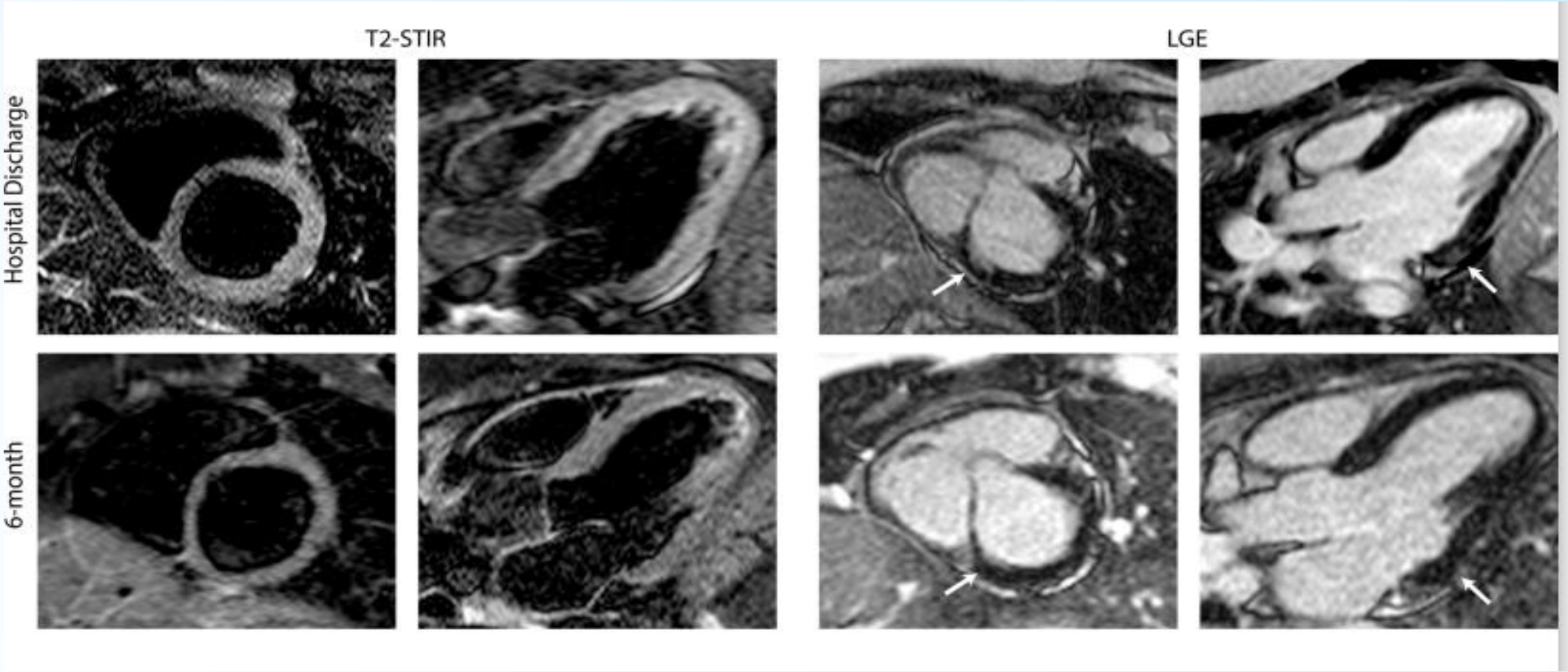
Controllo 6 mesi

C



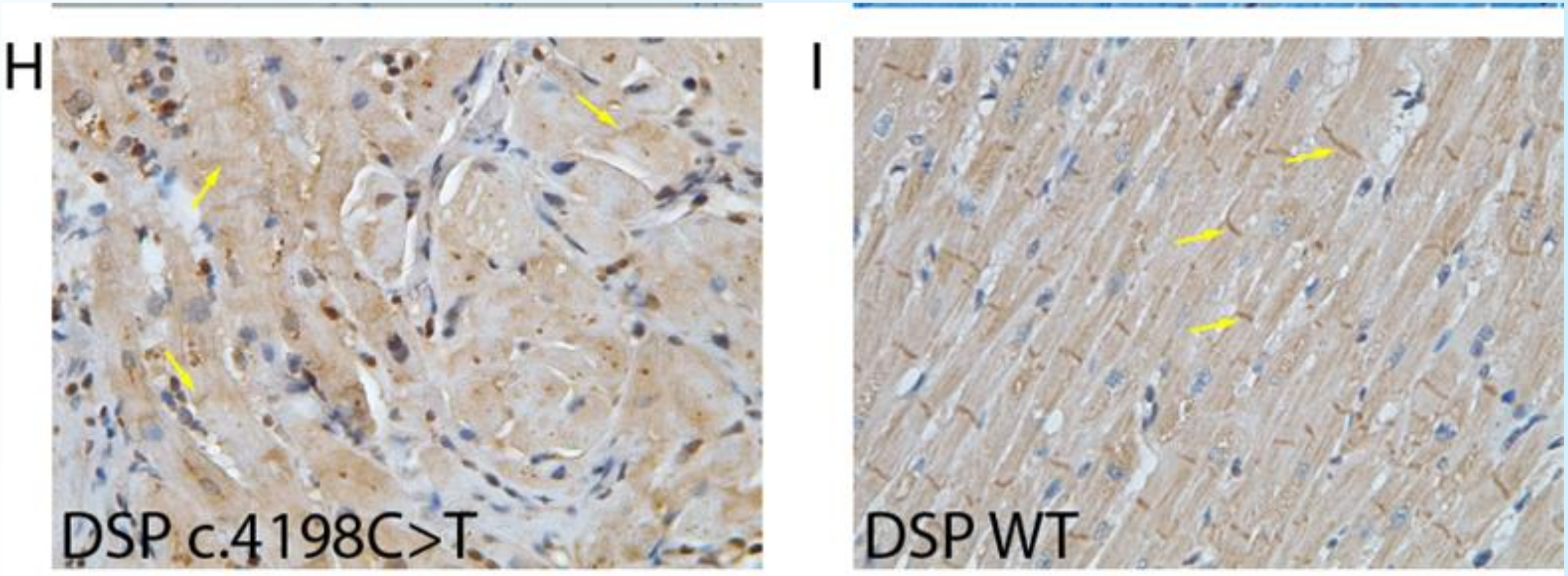
Pre-discharge cardiac magnetic resonance imaging (CMR) showed normal biventricular geometry and contractility (LVEF 74%)




T2-STIR
LGE
Hospital Discharge
6-month

	Admission	Discharge	6-month follow-up
WBC (10^3/uL) (n.v. 4.50-11) **Neutrophils (%)**	47.93 94.4	11.41 55.6	10.61 59
Creatinine (mg/dL, n.v. 0.6-1.1)	1.5	0.5	0.6
ALT (U/L, n.v. 0-34) **AST (U/L, n.v. 10-49)**	280 266	26 71	32 66
Ferritin (ng/mL, 30-400) **hsCRP (mg/dL, n.v. < 1)**	4325 27.3	2403 < 0.4	210 4*
NT-proBNP (pg/mL, n.v. 0-125) **hsTnI (pg/mL, n.v. 40.8-115.1)**	53000 568	251 38	/ < 2.5

Because of the unusual clinical presentation the patient underwent DNA sequencing for 174 common cardiomyopathy-causing genes with next generation sequencing detecting **pathogenic heterozygous variant in the form of nonsense mutation c.4198C>T (p.Arg1400*) for desmoplakin (DSP) gene**.



DSP is a fundamental structural protein for anchoring intermediate filaments to desmosomes in cardiomyocytes, which ensures normal force transmission.

DSP mutations, in fact, can lead to development of a rare and distinct cardiomyopathy, characterized by recurrent myocarditis (that can be the first sign of this disease), fibrosis and ventricular dysfunction (mainly of the left ventricle) which can facilitate the onset of ventricular arrhythmias.

We hypothesize that the presence of an unknown DSP mutation has promoted the unusual presentation of AOSD as fulminant myocarditis