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CASE REPORT
Heart failure

Autosomal dominant polycystic kidney disease and pericardial effusion: coincidence? I think not! Case report and review of the literature

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Background Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary disease causing chronic renal failure, with a high incidence of extra-renal manifestations including pericardial effusion.

Case summary We present the case of a 41-year-old female, known for ADPKD, who presented to our emergency department with epigastric pain radiating to the interscapular area. Blood exams showed moderate increase in inflammatory markers. Echocardiography revealed a circumferential pericardial effusion of 10 mm. She was put under treatment with colchicine therapy (1 mg b.i.d.) based on a presumptive diagnosis of acute pericarditis with pericardial effusion. She was hospitalized due to increase in pericardial effusion, underwent pericardial drainage, and started prednisone therapy with rapid recovery. We started a close follow-up on a monthly basis, with progressive decrease in pericardial effusion and progressive amelioration in symptoms, although the patient continued to report mild asthenia.

Discussion Pericardial effusion and ADPKD are conditions that both require an interdisciplinary discussion for optimal patient care that avoids neglecting pivotal symptoms and avoidable invasive examinations.

Keywords Pericardial effusion • Differential diagnoses • Polycystic kidney disease • Follow-up • Case report

ESC curriculum 6.6 Pericardial disease • 2.2 Echocardiography • 2.3 Cardiac magnetic resonance • 6.3 Heart failure with preserved ejection fraction

Learning points

- In patients with ADPKD, considering the high prevalence of extra-renal manifestations, multidisciplinary care can speed up the diagnosis of possible complications due to extra-renal manifestations.
- The long-term evolution of chronic pericardial effusion in patients with ADPKD is presently unknown, especially with respect to the risk of evolution into constrictive pericarditis, and therefore, a regular follow-up is mandatory.

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Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary disease causing chronic renal failure, with an incidence of 1:400–1000 live births.[1,2] Overall, it causes 4% of end-stage renal disease with dialysis in 5–10% of patients.[3] It is a systemic disorder with cysts in the kidneys and extra-renal manifestations, such as cysts in the liver, pancreas, and seminal vesicle, cerebral and aorta aneurysms, colonic diverticula, abdominal wall and inguinal hernia, and cardiac valve disease.[4–6] In the literature, some authors have reported an increased occurrence of pericardial effusion in patients with ADPKD. A retrospective analysis conducted at Mayo Clinic showed a larger prevalence of pericardial effusion in asymptomatic patients with ADPKD, suggesting a previous unknown extra-renal cardiac presentation of ADPKD.[1]

Case presentation

We present the case of a 41-year-old female with a known history of ADPKD, who presented to our emergency department with epigastric pain radiating to the interscapular area. At the cardiological auscultation, there was no friction rub and the thoracic pain did not worsen with inspiration or supine position. We completed the physical exam with abdominal examination in the context of epigastric pain; Murphy and Blumberg's signs were negative, and there were no signs of peritonism with normal peristalsis at auscultation. The temperature was always afebrile, as we reported in *Table 1*; at the time of admission, the body temperature was 36.7°C, the pressure values were 110/88 mmHg, the cardiac frequency was 63 b.p.m., and the SO_2 was 99% without oxygen therapy.

Table 1 **Summary of key clinical events,laboratory data, imaging test and therapies**

Month	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul
	Pericardiocentesis			MRI						
TTE controls	4	4	4	4	2	1	1			1
Pericardial effusion of the right cavities (mm)	30	0	13	20	28	22	18	20		16
Hospitalization	3 days									
Laboratory Testing	a			b						
Creatinine (44-80 µmol/L)	107	112	107	110	95	100	97			101
GFR (> 60 mL/min/1.73 m2)	57	55	58	56	67	62	65			61
CRP (< 5 mg/L)	30	< 1	< 1	< 1	< 1	< 1	< 1			< 1
NT-pro-BNP (< 623 ng/L)	240	408	470	190						
Symptoms and signs	Afebrile									
	Dyspnoea									
	Palpitations									
		Asthenia								
Therapy	NSAID + Pantoprazole									
	Colchicine									
			Corticosteroid							

a) **(Negative)** ANA, ANCA, ENA, anti-DNA, FR, C3 and C4 negative; SARS-Cov2 negative; INF-gamma quantiferon
b) **(Negative)** HIV, HCV, HBV, HEV, C. burnetii, Chlam. trach., Chlam. pneum., Leptospira PCR, Epstein-Barr virus IgM, M.pneumoniae

Electrocardiogram (ECG) was within normal limits, blood exams revealed a moderate increase in inflammatory markers, while myocardial enzymes were negative (C-reactive protein 30 mg/L, high-sensitive troponin-T 6 ng/L). Echocardiography revealed normal left ventricular ejection fraction, no relevant valve disease, but circumferential pericardial effusion of 10 mm. She was put under treatment with colchicine therapy (1 mg b.i.d.) based on a presumptive diagnosis of acute pericarditis with pericardial effusion. Initially, we abstained from introducing non-steroidal anti-inflammatory drugs (NSAIDs) due to relative contraindication in the presence of ADPKD.

Two days later, she returned to our attention reporting asthenia, palpitations, and dyspnoea on exertion. She was haemodynamically stable. Electrocardiogram showed normal sinus rhythm with low QRS complex voltages. Lab results were unremarkable. Echocardiography confirmed the presence of pericardial effusion (*Figure 1*), reaching 3 cm along right ventricle cavities, not haemodynamically relevant, but with an increase in size compared with the previous examination, which necessitated the hospitalization of the patient. We completed the diagnostic work-up ruling out an autoimmune aetiology (antibody panels comprehensive for ANA, ANCA, ENA, anti-DNA, FR, C3, and C4 were negative); SARS-CoV-2 nasopharyngeal swabs were also negative. We performed an initial work-up during the index hospitalization, with viral respiratory polymerase chain reaction (PCR) testing, blood cultures, and tuberculosis testing by means of IFN-gamma (QuantiFERON, Ag Tb1 and 2), which were negative. Thyroid function was normal (TSH 3.36 mU/L, fT3 5 pmol/L, fT4 15 pmol/L, PTH 6.5 pmol/L, anti-TPO < 10 U/mL, and anti-thyreoglobulin 12.5 U/mL) so that we could exclude also hypothyroidism as the cause of pericardial effusion. We then proceeded to pericardiocentesis with drainage of 300 mL of serous transudate, without malignant cells or bacterial growth. Due to the symptomatic clinical picture, we introduced an anti-inflammatory therapy with low-dose NSAIDs, for better management of the symptoms. The evolution was then favourable, with a regression in symptoms and a decrease in the size of the pericardial effusion. The patient was discharged home, with the indication to continue colchicine at 0.5 mg once per day for at least 3 months in association with low-dose NSAIDs.

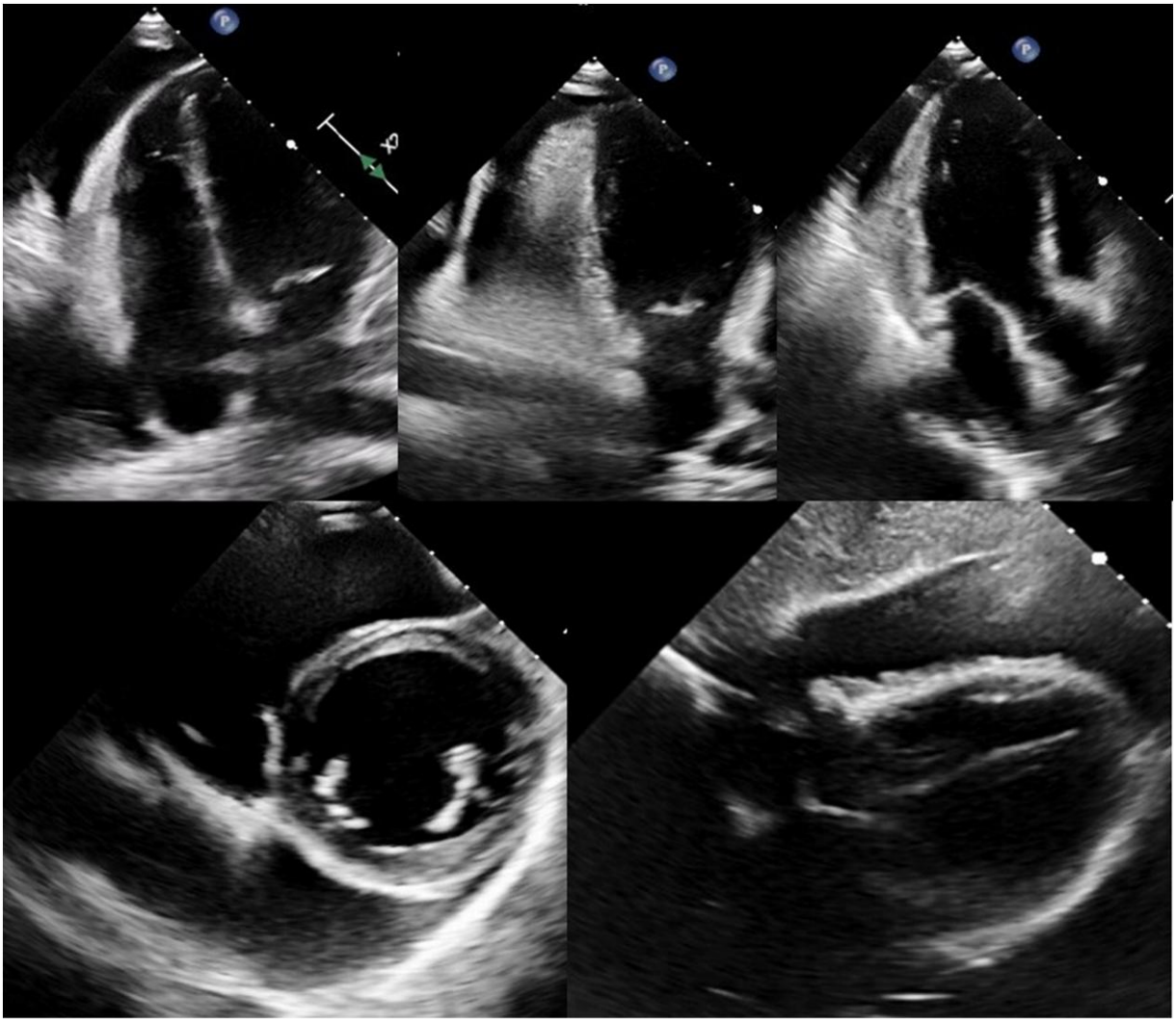

Figure 1 Initial echocardiography (line above: apical four-, two-, and three-chamber views; line below, parasternal short axis at papillary muscle level and subcostal view) showing relevant circumferential pericardial effusion, partly organized.

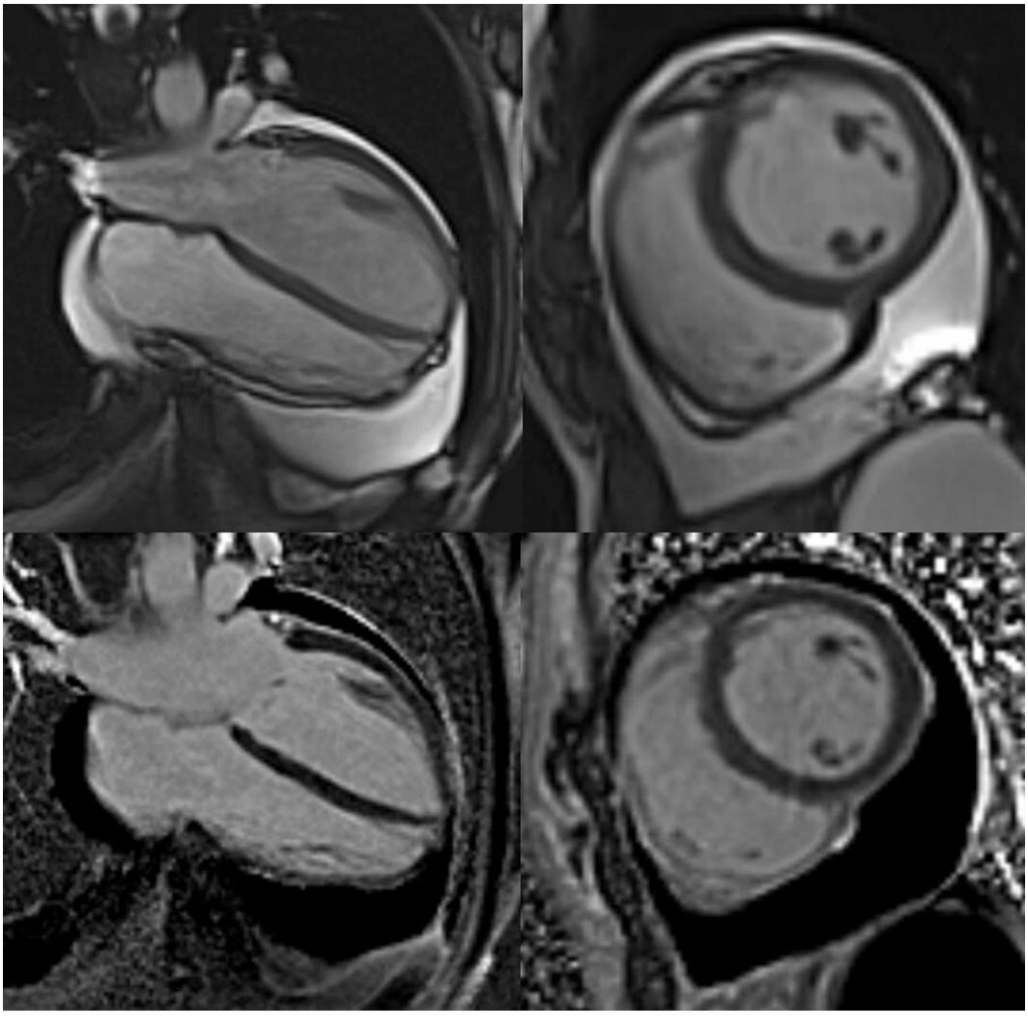

Figure 2 Cardiac magnetic resonance imaging at 4-month follow-up. In the first line, cine-steady-state free precession images (in four-chamber and mid short-axis views, respectively) show moderate residual pericardial effusion. In the line below, T_1 phase-sensitive inversion recovery late gadolinium enhancement acquisitions confirm the presence of pericardial fluid without significant pericardial thickening or contrast enhancement.

A close follow-up on a monthly basis was planned, during which the patient did not report any episodes of chest pain, although continued to present mild dyspnoea and asthenia. After 1 month, although the patient was stable, given our diagnosis of pericarditis and the ultrasound results with the persistence of pericardial effusion, we further increased the posology of ibuprofen at 600 mg t.i.d. At the 2-month follow-up appointment, a progressive increase in the effusion was observed, the patient reported transient worsening of asthenia, and we therefore introduced corticosteroid therapy (prednisone 25 mg once a day), together with colchicine. We extended the work-up during the follow-up, with an extensive panel of viral serologies taken ~2 months after the initial symptoms, so that we could exclude false negatives due to very early testing. The microbiological agents tested by serologies included HIV, HBV, HAV, HEV, *Coxiella burnetii*, *Chlamydia trachomatis*, *Chlamydia pneumoniae*, EBV, adenovirus, parvovirus B19, *Borrelia burgdorferi*, *Treponema pallidum*, *Leptospira*, and PCR for enterovirus. On the following follow-up, at 3 months, the clinical picture had improved, and we could start a reduction of prednisone. We also performed a cardiac magnetic reosonance imaing (MRI) (05.01.2023, *Figure 2*), which confirmed a significant circumferential pericardial effusion (maximum 22 mm at diaphragm level), but no signs of haemodynamic compromise. Moreover, there were no signs of ventricular interdependence, and the pericardium had not thickened; there was no pericardial hyper-signal in T_2-weighted short-tau inversion recovery sequence and no pericardial contrast in late gadolinium enhancement sequences. At the further follow-ups, we noticed a persistence of pericardial effusion, not haemodynamically relevant, at the level of the right cavities. In subsequent follow-up echocardiograms, there were no relevant signs of constrictive pericarditis, such as septal bounce, higher values of medial e'-wave at tissue Doppler imaging (TDI) compared to lateral e' (annulus reversus), or significant respiratory variation of mitral or tricuspid E-wave at pulsed wave-Doppler.

The therapy with the corticosteroid was then stopped (total duration of therapy: <2 months), and colchicine was stopped after a total of 6 months. In the meanwhile, the renal function was stable, and we constantly monitored that inflammatory and cardiac biomarkers remained within normal limits (troponin T-hs and NT-pro-BNP). *Table 1* summarizes the clinical and instrumental follow-up carried

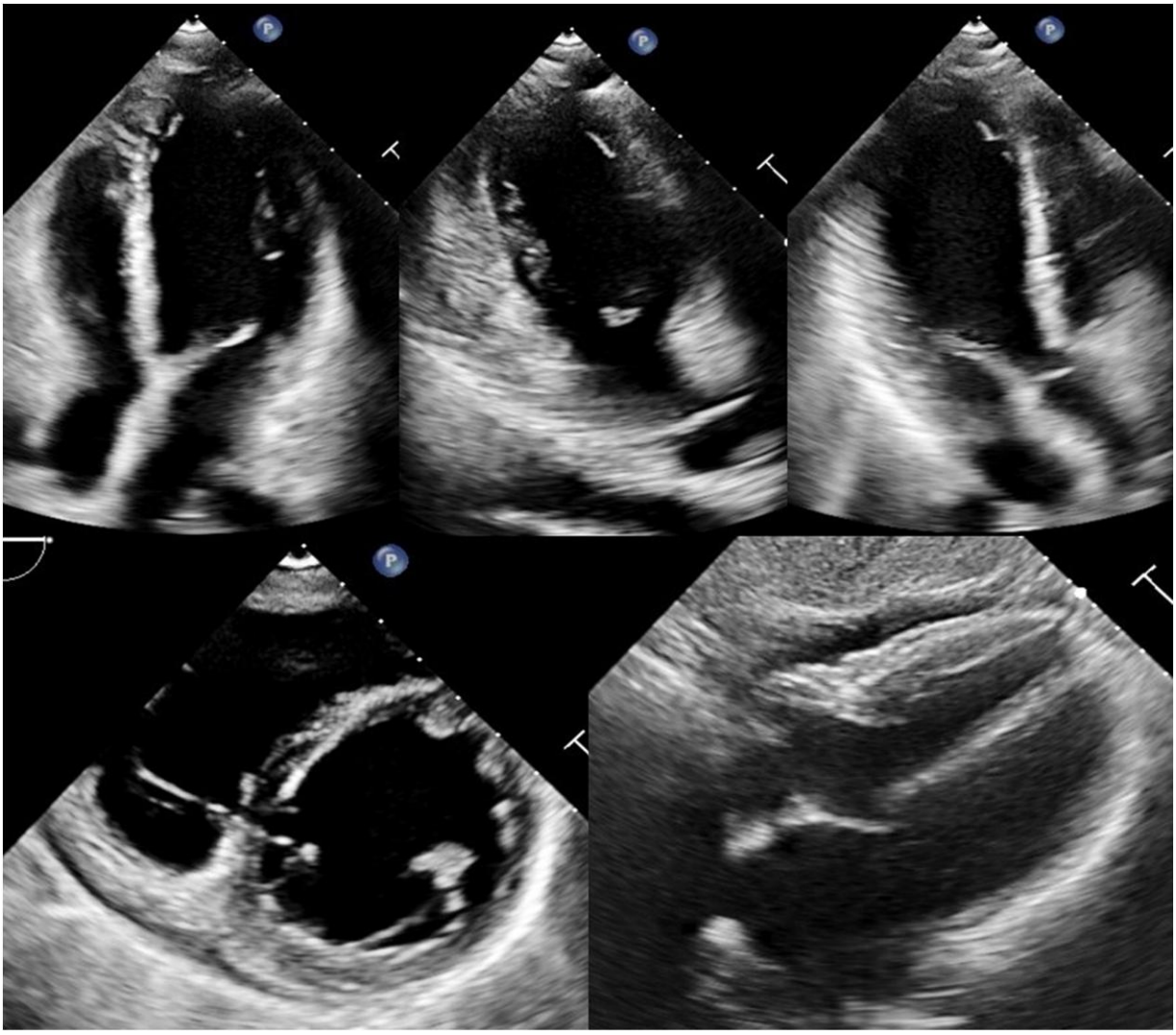

Figure 3 Echocardiography at 8-month follow-up (line above: apical four-, two-, and three-chamber views; line below, parasternal short axis at papillary muscle level and subcostal view) showing mild residual pericardial effusion.

out. At the last follow-up, the patient was clinically asymptomatic, and we observed a small reduction in the extent of pericardial effusion (*Figure 3*). However, the long-term evolution of chronic pericardial effusion in patients with ADPKD is presently unknown, especially with respect to the risk of evolution into constrictive pericarditis, and we have therefore planned a regular follow-up with repeated echocardiography and MRI to detect early signs of thickening of pericardium.

Discussion

Some cases of pericardial effusion in patients with ADPKD are reported in literature.[7,8] In most cases, patients were asymptomatic with no specific therapy needed.[9] Our patient was symptomatic for chest pain upon the first presentations, with a high suspicion of pericarditis. Our diagnostic work-up excluded other causes of pericardial effusion, such as infectious and autoimmune. Due to the symptoms of chest pain, we introduced a specific therapy for pericarditis, without recurrence of pain during the follow-up period, however with persistence of pericardial effusion in a patient who was mildly symptomatic for dyspnoea and asthenia. We suspected then that ADPKD could explain the persistent pericardial effusion despite the prolonged, specific therapy.

The case of the patient presented here was, in fact, atypical in several respects. The clinical presentation was strongly suspicious for pericarditis, for which a careful differential diagnosis was performed and led us to therefore assume this link with ADPDK. Indeed, without the symptomatology complained of by the patient, the team would have opted for a wait-and-see strategy. Ultrasound follow-up, improvement with introduced therapy, and literature search prompted us to proceed with more aggressive therapy given the young patient's symptoms.

At presentation, during the index hospitalization, the patient was suffering from acute pericarditis, and she was very symptomatic (epigastric pain, asthenia, palpitations, and dyspnoea on exertion), and for this reason, she received anti-inflammatory non-steroidal drugs and colchicine. NSAIDs were rapidly diminished and stopped as soon as the clinical

picture improved. Colchicine was continued at low, weight-adjusted doses to improve the response to medical therapy and mainly to prevent recurrence, as suggested by the current ESC guidelines. During the early follow-up, when the diagnostic work-up was not yet completed and was not completely clear the association between ADPKD and pericardial effusion, she reported worsening of general conditions, she was very anxious and demanding on medical care, and we noticed progression of the pericardial effusion. For these reasons, we started an empiric treatment with low-dose corticosteroids (maximum 25 mg/day), which helped to control the symptoms and which were tapered off soon after the improvement (tapering was done carefully to avoid both recurrent activity of the underlying disease and possible cortisol deficiency resulting from hypothalamic–pituitary–adrenal axis suppression during the period of steroid therapy).

The pathophysiology of pericardial effusion in ADPKD is still unknown. Different theories have been proposed. The most accepted suggests a link to mutations in PKD1 gene, with abnormal distensibility of connective tissue and an increased extracellular volume, which lead to an abnormal distensibility and impaired recoil of connective tissue and a consequent unusual distension of the parietal pericardium.[8–10]

Conclusion

In patients with ADPKD, considering the high prevalence of extra-renal manifestations, multidisciplinary care can speed up the diagnosis of possible complications due to extra-renal manifestations. Aetiology of pericardial effusion can be a challenge for clinicians. In our case, the presence of chest pain suggestive of pericardial effusion could not exempt the team from introducing specific treatment for pericarditis to avoid further possible complications. In our patient, the pericardial effusion was not compromising the haemodynamic status, but doctors were concerned not to overlook the painful presentation and potential risk of complications, the reason why we did not hesitate to introduce a specific therapy.

Indeed, the management was quite challenging. The patient presented with a clinical picture of acute pericarditis, and for this reason, she was put on colchicine. We initially abstained from NSAIDs due to concerns of possible deterioration of renal function, but we introduced them when she was symptomatic and we stopped them as soon as the clinical picture improved. During the follow-up, the patient presented worsening of asthenia and an increase in pericardial effusion, and for this reason, we introduced low-dose corticosteroid therapy, with a progressive reduction and rapid discontinuation of the treatment once the clinical and instrumental picture had improved. We continued colchicine for 6 months, mainly to prevent recurrences of pericarditis. Until now, the patient is asymptomatic, and the pericardial effusion is mild and stable; she is not receiving any therapy. The stability of the clinical picture, the progressive amelioration of symptoms, and the absence of biological and clinical indices of complications, thus considering the possible link with ADPKD and the data in the literature ruling out complications or the need for further invasive investigations, led us to choose a strategy of regular follow-ups with clinical examination and imaging by echocardiography.

Pericardial effusion and ADPKD are conditions that both require an interdisciplinary discussion for optimal patient care, which avoids neglecting pivotal symptoms or leads to protracted and sometimes avoidable invasive examinations.

Lead author biography

I am an internal medicine and cardiology specialist, working at Istituto Cardiocentro Ticino, Lugano, Switzerland. I have a strong interest in clinical cardiology and heart failure. This work is dedicated to Loredana, Marco, and Laura, my lighthouse in the dark.

Consent: The authors confirm that written consent for submission and publication of this case report, including the images and associated text, has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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Data availability

We state that, upon reasonable request, all data and software codes on which the conclusions of the paper rely are available to readers.

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