ESC European Society of Cardiology

European Heart Journal - Case Reports (2023) **7**, 1–4
https://doi.org/10.1093/ehjcr/ytad487

CASE REPORT
Inherited cardiac conditions/cardiomyopathies

An unusual concomitance of acute heart failure: prolactinoma in a patient with left ventricular dysfunction—a case report

Wataru Saito[1†], Makoto Idouji[1], Kimitaka Shibue[2], and Shinya Ito [1*†]

[1]Cardiovascular Centre, Medical Research Institute Kitano Hospital, PIIF Tazuke-Kofukai, 2-4-20, Ogimachi, Kita-ku, Osaka 530-8480, Japan; and [2]Department of Diabetes and Endocrinology, Medical Research Institute Kitano Hospital, PIIF Tazuke-Kofukai, Osaka, Japan

Received 27 March 2023; revised 19 September 2023; accepted 2 October 2023; online publish-ahead-of-print 4 October 2023

Background Heart failure concomitant with prolactinoma is extremely rare.

Case summary We present the case of a 29-year-old man who had acute decompensated heart failure concomitant with visual loss in his right eye. Transthoracic echocardiography indicated severely decreased left ventricular (LV) function. A massive tumour on the sella turcica was detected by brain computed tomography. The findings of the laboratory tests showed hyperprolactinaemia with hypopituitarism, and the antigen test for coronavirus disease 2019 was positive as an incidental finding. Medication for heart failure and cabergoline therapy were started immediately. His LV function significantly improved, and he had no symptoms after a year.

Discussion Prolactinoma in men, which can cause visual loss and hypopituitarism, is frequently substantial when diagnosed. The cardiac manifestation of prolactinoma is uncommon. It is believed that a major contributing component to the pathogenesis of peripartum cardiomyopathy is hyperprolactinaemia. Hyperprolactinaemia may cause endothelial damage and cardiomyocyte dysfunction, eventually resulting in LV dysfunction. The success of LV reverse remodelling may be significantly impacted by heart failure and hormone treatments. Heart failure and endocrine therapy should be administered concurrently to patients who have prolactinoma and congestive heart failure.

Keywords Congestive heart failure • Prolactinoma • Hyperprolactinaemia • Cardiac magnetic resonance imaging • Case report

ESC curriculum 6.5 Cardiomyopathy • 2.3 Cardiac magnetic resonance • 6.2 Heart failure with reduced ejection fraction

Learning points

- Heart failure with reduced ejection fraction concomitant with hyperprolactinaemia should be treated immediately with endocrine therapy, which is a dopamine agonist.
- It should be noted that prolactinoma can affect left ventricular ejection fraction due to hyperprolactinaemia.

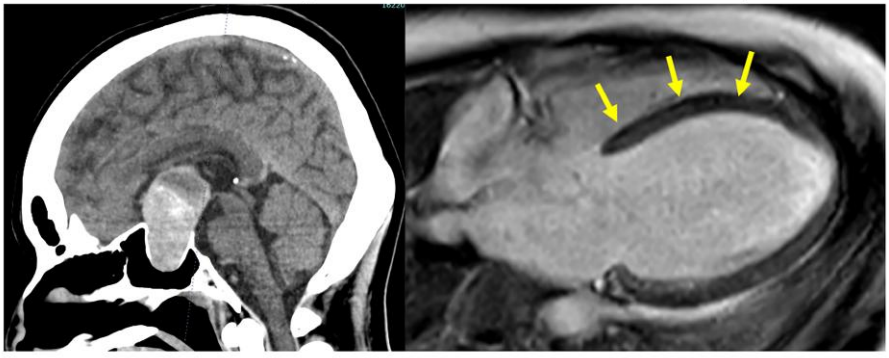
* Corresponding author. Tel: +81 6 6361 0588, Fax: +81 6 6366 0588, Email: blad.wunderbar@gmail.com
† These two authors contributed equally to this work.
Handling Editor: Valentina Rossi
Peer-reviewers: Henrike Aenne Katrin Hillmann; Deborah Belfort
Compliance Editor: Lavanya Athithan

Introduction

Prolactinoma is the most common pituitary tumour accounting for 40% of all pituitary tumours.[1] It is well known that hypersecretion of prolactin causes infertility and gonadal dysfunction. However, the association between hyperprolactinaemia and heart failure is not well comprehended. We present the case of a patient with heart failure concomitant with giant prolactinoma.

Summary figure

Heart failure with reduced ejection fraction concomitant with macroprolactinoma



Optimal medial therapy for heart failure and macroprolactinoma is a key element of therapeutic approach

Case presentation

A 29-year-old man with a previous history of seizures was referred to our hospital. For over a year, shortness of breath with exertion had been steadily worsening. Additionally, he reported visual loss in his right eye, and vision test revealed loss of light perception in the right eye. He had no familial history of cardiac or sudden cardiac death. A physical examination revealed bilateral pitting oedema on the feet. The electrocardiogram showed a regular sinus rhythm without ischaemic signs and left ventricular (LV) hypertrophy. Chest X-ray revealed marked cardiomegaly. Blood test showed significant elevation of brain natriuretic peptide level [900 pg/mL (normal <18.4 pg/mL)]. White blood cell counts were 7300/μL (normal 3300–8600/μL), haemoglobin levels were 15.6 g/dL (normal 13.7–16.8 g/dL), platelet count was 276 000/μL (normal 158 000–348 000/μL), creatinine level was 1.44 mg/dL (normal 0.6–1.1 mg/dL), and blood urea nitrogen level was 13.9 mg/dL (normal 8.0–20.0 mg/dL). Positive result of the coronavirus disease of 2019 (COVID-19) was incidentally detected. Transthoracic echocardiography (TTE) revealed an LV ejection fraction (LVEF) of 23% with no regional wall motion abnormality. Left ventricular end-diastolic diameter was 68 mm. No asymmetric LV hypertrophy was found (thickness of the interventricular septum, 9 mm; thickness of the posterior wall, 11 mm). Brain computed tomography indicated a giant tumour ($30 \times 29 \times 53$ mm^3) on the sella turcica (*Figure 1*).

Clinical presentation and echocardiographic parameters resulted in the diagnosis of non-ischaemic congestive heart failure, which might be linked to a pituitary tumour. Prolactin level was 5729 ng/mL (normal 4.29–13.69 ng/mL), thyroid stimulating hormone level was 9.879 μIU/mL (normal 0.61–4.23 μIU/mL), free thyroxine level was 0.63 ng/dL (normal 0.70–1.48 ng/dL), adrenocorticotropic hormone level was 14.1 pg/mL (normal 7.2–63.3 pg/mL), cortisol level was 3.4 μg/dL (normal 3.7–19.4 μg/dL), luteinizing hormone level was 0.63 mIU/mL (normal 2.2–8.4 mIU/mL), and follicle-stimulating hormone level was 0.75 mIU/L (normal 1.8–12.0 mIU/mL). Pituitary magnetic resonance imaging revealed a giant tumour ($30 \times 28 \times 48$ mm^3) with suprasellar extension and bilateral optic chiasmal compression. In light of the aforementioned findings, the diagnosis of prolactinoma with hypopituitarism diagnosis was made.

Dobutamine continuous infusion (1 γ) and furosemide injection were administered to the patient. Hydrocortisone (100 mg/day) was administered intravenously, followed by oral medications in order to treat panhypopituitarism. With heart failure status compensated, the first-line therapy for heart failure with decreased ejection fraction, referred to as 'fantastic four',[2] was initiated. Cabergoline was started for hyperprolactinaemia on Day 6. On Day 9, levothyroxine (50 μg/day) was started for hypothyroidism. Cardiac magnetic resonance imaging revealed linear mid-wall late gadolinium enhancement in almost all segments (*Figure 2*). No high-intensity finding suggesting myocardial oedema was detected in the T2-weighted image. Coronary computed tomography scan revealed no critical stenosis. The patient's LVEF on TTE was improved at the end of 1 month (31%), as measured by the modified Simpson method. One year following admission, the patient was free of symptoms. As the prolactine level dramatially decreased, TTE demonstrated further improved LVEF (47%), as measured by the modified Simpson method (*Figure 3*). Follow-up brain magnetic resonance imaging revealed the residual tumour, but the size of the tumour diminished over time.

Discussion

Prolactinoma is a benign neoplasm accounting for ~40% of all pituitary tumours.[1] The symptoms frequently linked to macroprolactinoma can be categorized based on their underlying causes. High amounts of circulating prolactin can cause various disorders, including hypogonadism, amenorrhoea, infertility, and galactorrhoea. Additionally, mechanical compression resulting from the extracellular expansion of the tumour, which is typically seen in macroprolactinoma

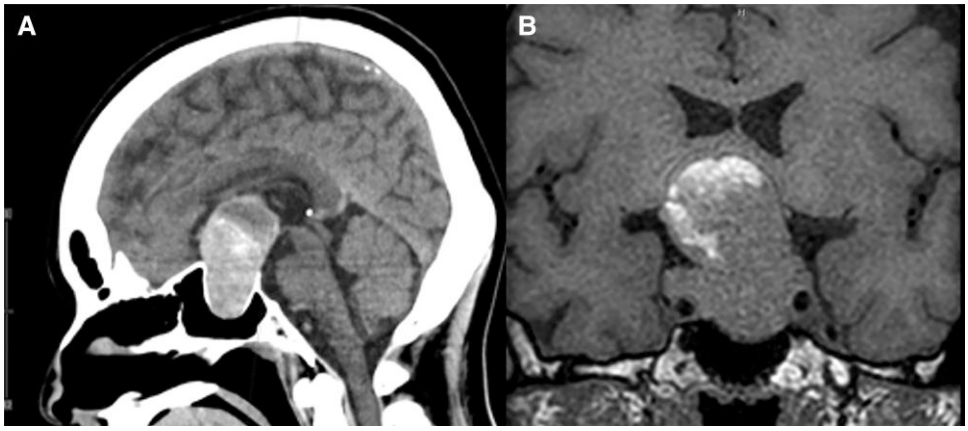


Figure 1 (*A*) Brain computed tomography scan on Day 1 revealed a giant tumour on the sella turcica. (*B*) Contrast brain magnetic resonance imaging on Day 13 indicated heterogeneous high intensity with the suprasellar extension on T1-weighted image.

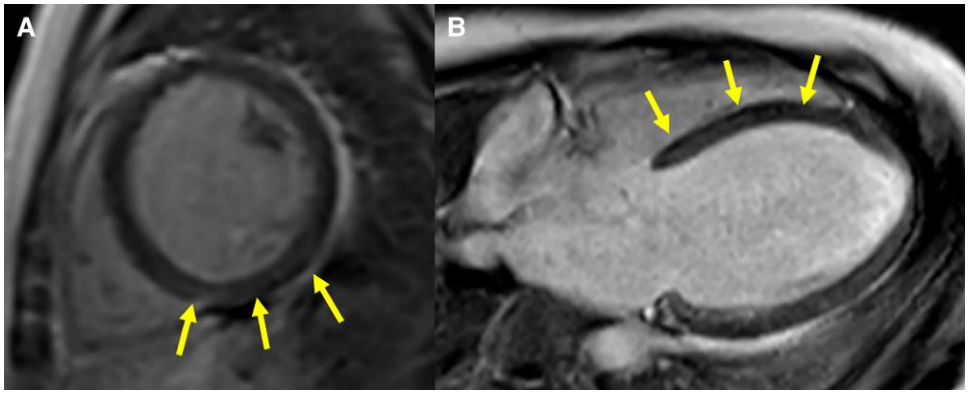


Figure 2 (*A* and *B*) Cardiac magnetic resonance image of the axial and long axis on Day 8 revealed linear late gadolinium enhancement in the mid-segments (arrows).

(>1 cm) or giant prolactinoma (>4 cm), frequently causes visual field abnormalities and headaches. In fact, >70% of patients diagnosed with giant prolactinoma had some form of visual abnormalities.[3] A dopamine agonist is the basic treatment for all forms of prolactinoma. Comprehension of the cardiac effects of prolactinoma is limited. Dopamine agonist therapy, however, could affect the amelioration of lower LVEF. Although the exact mechanism remains unknown, this correlation shows that hyperprolactinaemia may be linked to congestive heart failure.

Peripartum cardiomyopathy (PPCM) is a form of heart failure resulting from pregnancy concomitant with lower LVEF.[4] It has been suggested that high prolactin levels may function critically in PPCM pathophysiology. Recent research suggests that although full-length prolactin increased inflammation in PPCM, cleaved 16 kDa prolactin causes endothelial damage and consequent cardiomyocyte dysfunction.[5] In patients with PPCM, prolactin inhibition using bromocriptine, a dopamine-D2-receptor agonist, was associated with a high rate of LV function recovery in patients with PPCM.[6] The combination of genetic predisposition,[7] vascular inflammation, and hyperprolactinaemia was considered to cause PPCM.

Generally, hyperprolactinaemia does not seem to exhibit a direct effect on LV function, and limited reports suggest an association between them. Toulis *et al.*[8] reported that men with prolactinoma have increased risk for incident cardiovascular disease even after treatment with dopamine agonists. Hyperprolactinaemia might result in a predisposition to atherosclerotic disorders by promoting metabolic diseases, such as increasing insulin resistance and elevated LDL cholesterol.[9] The association between prolactinoma and LV dysfunction has seldom been reported. Therefore, our case could be associated with the two-hit theory.[10] According to this theory, a small (16 kDa) fragment of prolactin that is produced in response to oxidative stress can cause vascular endothelial dysfunction. A combination of hyperprolactinaemia, inflammation, or genetic factors might affect the aetiology of this illness.

Additionally, COVID-19 infection could be a predisposing factor for heart failure aggravation. Oxidative stress, or excessive amount of reactive oxygen species, is caused by COVID-19. Reactive oxygen species directly changes proteins involved in excitation–contraction coupling to disrupt contractile dysfunction.[11] The patient's COVID-19 antigen test result was positive at admission. This might affect the exacerbation of

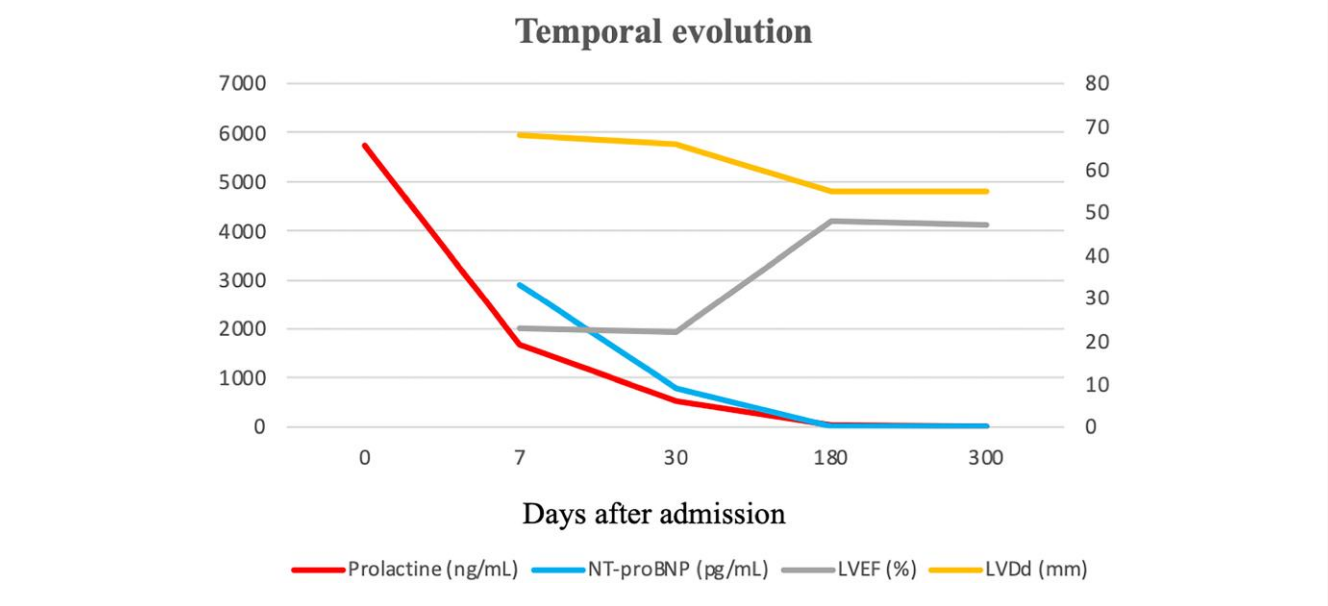


Figure 3 Temporal evolution of prolactin level, N-terminal probrain natriuretic peptide (NT-proBNP) level, left ventricular diastolic diameter, and left ventricular ejection fraction from admission to after discharge.

congestive heart failure. In our case, prolactinoma with congestive heart failure was a rare first presentation.

Patient's perspective

The patient was satisfied with the relief of symptoms owing to the recovery of left ventricular function with heart failure concomitant with prolactinoma.

Conclusion

Patients with congestive heart failure concomitant with prolactinoma should undergo endocrine and heart failure therapies simultaneously. Successful treatment of uncommon diseases requires a multidisciplinary approach.

Lead author biography

Dr Wataru Saito graduated from Osaka City University and started his career in Medical Research Institute Kitano Hospital, PIIF Tazuke-Kofukai, Osaka, Japan. He is a general cardiology physician.

Consent: Following COPE guidelines, the patient's informed consent has been obtained for the submission and publication of this report, including photos and related data.

Conflict of interest: None declared.

Funding: None declared.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

References

1. Schlechte JA. Prolactinoma. *N Engl J Med* 2003;**349**:2035–2041.
2. Bauersachs J. Heart failure drug treatment: the fantastic four. *Eur Heart J* 2021;**42**:681–683.
3. Shibue K, Yamakawa M, Nishida N, Hamasaki A. Resolution of visual field defect in macroprolactinoma after treatment with cabergoline. *Cureus* 2022;**14**:e25548.
4. Sliwa K, Petrie MC, Hilfiker-Kleiner D, Mebazaa A, Jackson A, Johnson MR, *et al.* Long-term prognosis, subsequent pregnancy, contraception and overall management of peripartum cardiomyopathy: practical guidance paper from the Heart Failure Association of the European Society of Cardiology Study Group on Peripartum Cardiomyopathy. *Eur J Heart Fail* 2018;**20**:951–962.
5. Hilfiker-Kleiner D, Sliwa K. Pathophysiology and epidemiology of peripartum cardiomyopathy. *Nat Rev Cardiol* 2014;**11**:364–370.
6. Hilfiker-Kleiner D, Haghikia A, Berliner D, Vogel-Claussen J, Schwab J, Franke A, *et al.* Bromocriptine for the treatment of peripartum cardiomyopathy: a multicentre randomized study. *Eur Heart J* 2017;**38**:2671–2679.
7. Ware JS, Li J, Mazaika E, Yasso CM, DeSouza T, Cappola TP, *et al.* Shared genetic predisposition in peripartum and dilated cardiomyopathies. *N Engl J Med* 2016;**374**:233–241.
8. Toulis KA, Robbins T, Reddy N, Balachandran K, Gokhale K, Wijesinghe H, *et al.* Males with prolactinoma are at increased risk of incident cardiovascular disease. *Clin Endocrinol (Oxf)* 2018;**88**:71–76.
9. Berinder K, Nystrom T, Hoybye C, Hall K, Hulting AL. Insulin sensitivity and lipid profile in prolactinoma patients before and after normalization of prolactin by dopamine agonist therapy. *Pituitary* 2011;**14**:199–207.
10. Huttner IG, Wang LW, Santiago CF, Horvat C, Johnson R, Cheng D, *et al.* A-Band titin truncation in zebrafish causes dilated cardiomyopathy and hemodynamic stress intolerance. *Circ Genom Precis Med* 2018;**11**:e002135.
11. Magadum A, Kishore R. Cardiovascular manifestations of COVID-19 infection. *Cells* 2020;**9**:2508.