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CASE REPORT
Heart failure

High-output heart failure associated with primary plasma cell leukaemia due to arteriovenous shunting: a case report

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Background Primary plasma cell leukaemia is rarely associated with high-output heart failure, and the underlying mechanism is not well understood. We encountered a rare case of high-output heart failure caused by primary plasma cell leukaemia. Its underlying mechanism was clarified through imaging studies.

Case summary A 49-year-old man with no specific medical history was admitted to our hospital because of heart failure that did not improve with diuretic therapy. His condition was diagnosed as high-output heart failure and primary plasma cell leukaemia after admission. Extensive bone involvement in primary plasma cell leukaemia and arteriovenous shunts in the same lesion were suspected after various imaging studies. The first cycle of chemotherapy with bortezomib, adriamycin, and dexamethasone led to remission of primary plasma cell leukaemia and improved heart failure symptoms. The patient received further chemotherapy in addition to autologous peripheral blood stem cell transplantation and maintenance therapy and had no recurrence of pPCL or heart failure for 1 year to date.

Discussion Primary plasma cell leukaemia can be associated with high-output heart failure, which is caused by arteriovenous shunting at the lesion site with diffuse bone involvement. Imaging studies may lead to the early diagnosis of aetiology and treatment of patients with high-output heart failure associated with primary plasma cell leukaemia.

Keywords High-output heart failure • Primary plasma cell leukaemia • Bone involvement • Arteriovenous shunt • Case report

Learning points

- Primary plasma cell leukaemia (pPCL) can be the aetiology of high-output heart failure (HOHF).
- Abnormal peripheral blood findings associated with pPCL may not appear until heart failure progression.
- Primary plasma cell leukaemia can cause HOHF through arteriovenous shunting at the lesion site with diffuse bone involvement.

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Introduction

High-output heart failure (HOHF) is characterized by increased cardiac output, decreased systemic vascular resistance, and reduced arterial-venous oxygenation gradient. The pathogenesis varies according to the aetiologies, including obesity, arterio-venous shunts, or liver disease.[1] Primary plasma cell leukaemia (pPCL) is a rare but aggressive form of myeloma.[2,3] However, pPCL is rarely associated with HOHF, and the underlying mechanism is not well understood. Herein, we encountered a rare case of HOHF caused by pPCL that helped clarify its underlying mechanism.

Timeline

Day 0	**Dyspnoea on exertion appeared.**
Day 9	Diuretic therapy was initiated based on the diagnosis of heart failure [brain natriuretic peptide (BNP) 195.5 pg/mL].
Day 19	Admitted to our hospital due to worsening heart failure. Right heart catheterization revealed high-output heart failure (BNP 399.7 pg/mL).
Day 20	First detection of atypical lymphocytes in peripheral blood.
Day 25	Angiography and blood sampling in the iliac region
Day 28	Diagnosis of primary plasma cell leukaemia
Day 30	Magnetic resonance imaging of the pelvic lesion (BNP 571.3 pg/mL)
Day 34	Chemotherapy was initiated at a specialized hospital.
Day 51	Completed the first course of chemotherapy and heart failure symptoms improved markedly (BNP 29.6 pg/mL).
Day 368	Remained stable with no recurrence of primary plasma cell leukaemia or heart failure symptoms (BNP <5.8 pg/mL)

Case presentation

A 49-year-old Asian man with no significant medical history presented to our hospital with a chief complaint of dyspnoea on exertion that had appeared approximately 10 days before presentation. Vital signs were normal, except tachycardia; further, S3 heart sounds were heard upon auscultation, and his lower legs were warm with mild oedema. Blood test results indicated mild anaemia, elevated creatinine level, and elevated brain natriuretic peptide level (195.5 pg/mL; normal range 0.0–18.4 pg/mL) (*Table 1*), and radiography showed mild cardiomegaly and bilateral pleural effusions. An electrocardiogram showed sinus tachycardia with a heart rate of 100 b.p.m., and echocardiography revealed left ventricular hyperkinesis (ejection fraction 73%) and enlargement of the inferior vena cava (IVC), but without evidence of diastolic dysfunction or structural abnormalities (*Video 1*). Diuretics were started on suspicion of heart failure. On the 19th day after symptom onset, he was admitted to our hospital because of worsening heart failure despite increased urine output.

Right heart catheterization performed on the day of admission showed a marked increase in cardiac output (cardiac index: 9.7 L/min/min^2) and a marked decrease in systemic vascular resistance (6.4 WU) (*Table 2*). The patient was diagnosed with HOHF. Oxygen saturation test showed no evidence of intracardiac shunting. However, blood oxygen saturation in both the superior vena cava and IVC was high (85.8% and 84.8%, respectively). No findings of hyperthyroidism, severe anaemia, sepsis, vitamin B1 deficiency, or obesity were observed on investigating the cause of the high-output state. Although diuretics were administered, heart failure and organ damage continued to progress, and systemic vascular resistance measured by Swan–Ganz catheter continued to decrease despite the administration of noradrenaline and vasopressin. Arteriography and blood gas tests of the iliac region were performed to investigate the presence of extracardiac shunts. Immediately after applying the contrast agent (iopamidol) from the iliac artery onwards, the ilium, sacrum, pubis, femoral neck, and femur on the same side absorbed it, and the iliac vein and IVC were immediately perfused with iopamidol (*Video 2*). In addition, there was a significant O_2 step-up between the common femoral vein and common iliac vein on both sides (*Table 3*).

Atypical lymphocytes were detected in the peripheral blood for the first time on the day after admission (Day 20), and their count continued to increase thereafter (*Table 1*). After additional tests, including bone marrow biopsy and flow cytometry, 4 weeks after symptom onset, the patient's condition was diagnosed as pPCL. Magnetic resonance imaging (MRI) of the pelvic lesion showed extensive bone involvement of tumour cells (*Figure 1*). Therefore, we considered that the diffuse bone involvement of pPCL caused the formation of giant arteriovenous shunts, which led to a hyperdynamic state due to decreased systemic vascular resistance.

After transfer to a specialized hospital for pPCL treatment, chemotherapy with bortezomib, adriamycin, and dexamethasone was administered. After one cycle of chemotherapy, the patient revealed a complete response, and heart failure symptoms and organ failure improved markedly (*Table 1*). He was treated with further chemotherapy, autologous peripheral blood stem cell transplantation, and maintenance therapy and had no recurrence of pPCL or heart failure for 1 year to date.

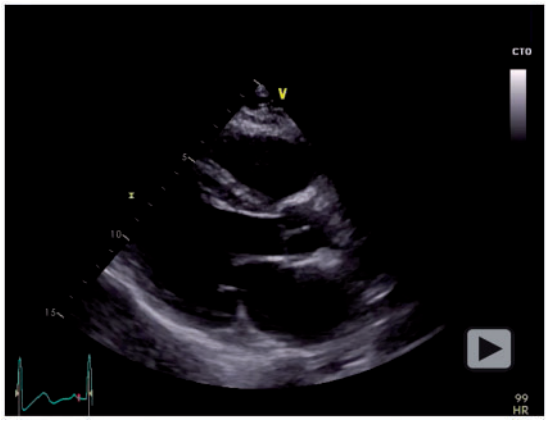
Discussion

The present report shows that HOHF can occur with pPCL as an aetiology, and the underlying mechanism involves arteriovenous shunting at the lesion site with diffuse bone involvement. In our case, the clinical course of heart failure and pPCL was consistent, suggesting that pPCL was the aetiology of HOHF. Even if blood cell abnormalities are not apparent in the early stages of HOHF, haematologic diseases such as pPCL cannot be ruled out. The prognosis for pPCL is poor,[2,3] and treatment should be administered promptly after diagnosis. The number of cases of HOHF associated with pPCL remains small since it was first reported in 1985.[4,5]

Table 1 Laboratory measurements

	Reference	Day 9[a]	Day 19[b]	Day 20	Day 22	Day 24	Day 26	Day 30	Day 51[c]
WBC (×109/L)	3.3–9.0	6.8	7.1	6.8	7.7	11.2	13.2	23.6	1.2
A-Ly (%)	0.0	0	0	0.5	3.5	11.0	34.5	60.0	0
Hb (g/dL)	13.5–17.5	11.1	10.4	10.2	9.7	9.5	8.9	8.5	9.6
PLT (×109/L)	140–340	138	82	81	71	83	55	27	51
ALB (g/dL)	4.1–5.1	4.5	4.5	4.4	4.4	4.5	4.5	4.3	3.2
AST (U/L)	10–40	19	30	28	37	50	203	330	69
ALT (U/L)	5–45	19	29	27	27	28	112	214	180
LDH (U/L)	124–222	253	308	309	347	460	936	1800	309
T-bil (mg/dL)	0.2–1.2	1.1	2.8	3.5	3.7	4.2	4.4	5.9	2.3
UA (mg/dL)	3.8–7.0	9.7	12.5	14.4	14.9	17.4	18.7	21.2	2.4
BUN (mg/dL)	8.0–20.0	19.6	27.2	31.8	44.6	57.8	76.0	97.4	14.3
Cre (mg/dL)	0.6–1.0	1.4	2.1	2.3	2.8	3.7	3.0	2.1	0.7
Ca (md/dL)	8.8–10.1			9.8		10.1	9.6	9.1	7.9
BNP (pg/mL)	0.0–18.4	195.5	399.7					571.3	29.6

ALB, albumin; ALT, alanine aminotransferase; A-Ly, atypical lymphocyte count; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; BUN, blood urea nitrogen; Ca, calcium; Cre, creatinine; Hb, haemoglobin; LDH, lactate dehydrogenase; PLT, platelet count; T-bil, total bilirubin; UA, uric acid; WBC, white blood cell count.
[a]first visit day.
[b]Admission day.
[c]At the end of the first cycle of chemotherapy.



Video 1 Echocardiography revealed left ventricular hyperkinesis without evidence of diastolic dysfunction or structural abnormalities.

Table 2 Right heart catheterization data on admission (Day 19)

	Pressure (mmHg)	Oxygen saturation (%)
Right heart catheterization data		
Superior vena cava	21	85.8
Inferior vena cava	22	84.8
Right atrium	23	85.1
Right ventricle (s/d/e)	53/18/25	83.5
Pulmonary artery (s/d/m)	47/27/38	83.7
Pulmonary artery wedge (m)	21	94.9
Atrial oxygen saturation		94.9
Calculated measurements		
Cardiac output/Cardiac index	16.5 L/min	9.7 L/min/m^2
Systemic vascular resistance	6.4 WU	
Qp/Qs	1.0	

d, diastolic; e, end-diastolic; m, mean; s, systolic.

The underlying mechanism reported in this report was based on the results of angiography and blood sampling in the iliac region and pelvic MRI findings, which coincided with the site of bone involvement and shunt location. Notably, probably because of the presence of relatively less bone marrow, the femoral heads and greater trochanters showed less evidence of tumour involvement in both imaging studies. In addition, the results of right heart catheterization on admission showed high oxygen saturation not only in the IVC, but also in the superior vena cava, suggesting that shunting occurred in the upper limb bones and skull. Chaoui *et al.*[5] hypothesized that a humoral factor that dilated peripheral vessels was involved in the mechanism of HOHF caused by pPCL. However, in our case, the systemic vascular resistance shown by the Swan–Ganz catheter continued to decrease even with the use of vasoconstrictors. This is consistent with the fact that the underlying mechanism of HOHF involves shunting and not vasodilation. In addition, in our case, the entire iliac bone was contrasted immediately after contrast in the iliac artery, and the iliac vein was contrasted promptly thereafter. This may indicate that the formation of numerous microneovessels from the artery to the entire bone is involved in establishing the shunt. In addition, the shunt was expected to be reversible and to disappear rapidly with pPCL treatment since the patient's heart failure

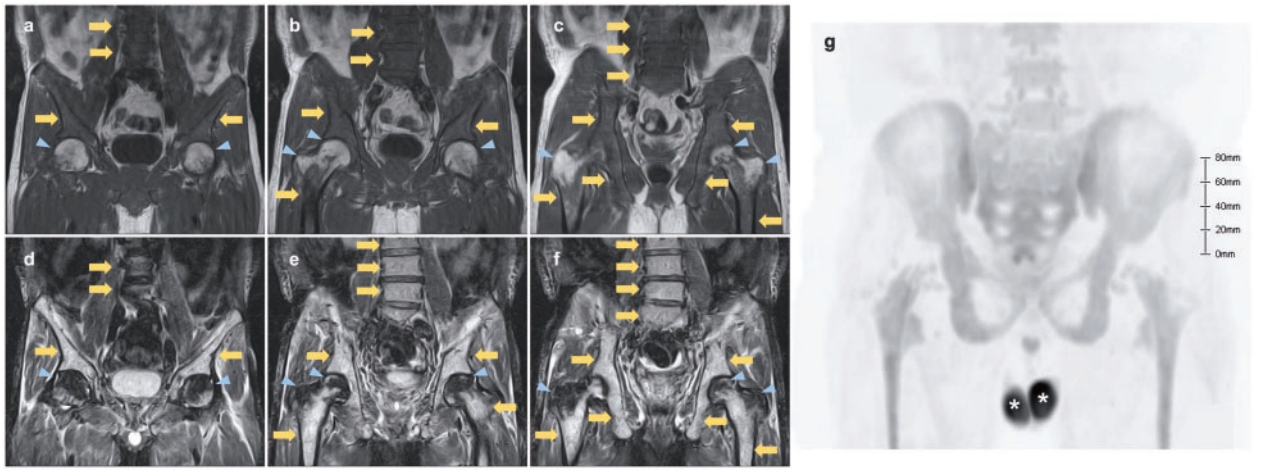
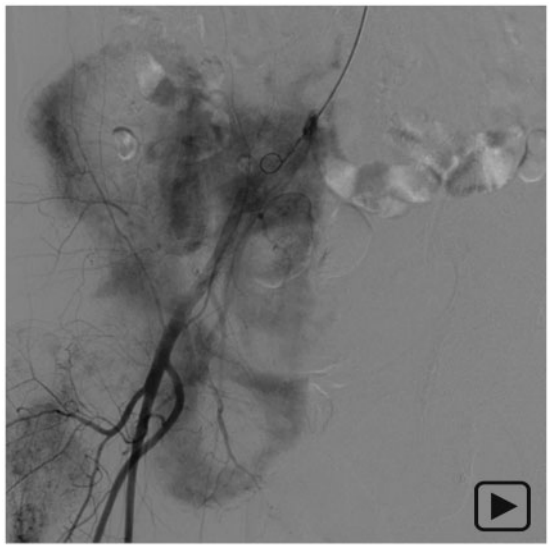


Figure 1 Coronal pelvic magnetic resonance imaging revealed the vertebral bodies of lumbar, sacrum, bilateral ilium, pubis, ischium, and femurs (yellow arrows), showing a homogeneous low signal intensity on T1-weighted images (*A–C*) and high signal intensity on short TI inversion recovery (*D–F*). They showed high signal intensity on diffusion-weighted whole-body imaging with a background body signal (*G*). Bilateral femoral heads and greater trochanters (blue arrowheads) did not show the same findings (*A–G*). *testes.



Video 2 Immediately after contrast injection in the right iliac artery, the ilium, sacrum, pubis, ischium, femoral neck, and femur, excluding the femur head and greater trochanter on the same side, were contrasted, followed by the right iliac vein and inferior vena cava. Similar findings were observed on the left side.

Table 3 Oxygen saturation in the veins of the lower body on Day 25

	Oxygen saturation (%)
Right radial artery (reference)	83.7
Inferior vena cava distal to the renal vein	64.8
Left side	
Common iliac vein	64.4
Common femoral vein	43.2
Right side	
Common iliac vein	59.8
Common femoral vein	47.9

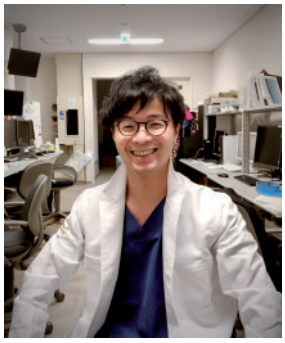
symptoms improved rapidly after only one cycle of chemotherapy for pPCL. One study investigated the presence and location of shunts using scintigraphy in 11 patients with multiple myeloma complicated by HOHF.[6] Their results showed that all patients had femoral involvement and a corresponding arteriovenous shunt and that the shunt volume positively correlated with cardiac output. pPCL, an analogous disease of multiple myeloma, may have a similar mechanism.

To the best of our knowledge, this is the first report on the underlying mechanism of HOHF caused by pPCL. Given this mechanism, MRI, scintigraphy, and arteriography may be helpful in diagnosing patients with HOHF having an unclear aetiology to determine the presence of shunts. It is difficult to suspect pPCL until peripheral blood abnormalities become apparent. However, if a patient has heart failure, the shunts should have already been formed, and non-invasive imaging tests may prove the presence of shunts at an early stage. If the presence of shunts can be demonstrated, early advanced testing, such as bone marrow biopsy, may lead to the earlier diagnosis and treatment of pPCL. A key limitation of our case report is that it lacked imaging data that could be used to check for disappearing bone involvement and shunts after the resolution of heart failure symptoms.

In conclusion, HOHF can occur with pPCL through arteriovenous shunting at the lesion of diffuse bone involvement. In patients with HOHF, whose aetiology is not clear on routine examination, pPCL may be the aetiology even if abnormal blood-cell findings

are not initially evident. If the aetiology is unclear, imaging studies can reveal the presence of shunts, which may help early diagnosis and treatment.

Lead author biography



Yuta Sudo was born in 1985 in Tokyo, Japan. He studied cardiovascular medicine at the Kameda Medical Centre and Yokosuka Kyosai Hospital. He specializes in cardiovascular care and has extensive knowledge about heart failure and cardiac implantable electronic devices.

Supplementary data

Supplementary material is available at *European Heart Journal—Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

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

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References

1. Reddy YNV, Melenovsky V, Redfield MM, Nishimura RA, Borlaug BA. High-output heart failure: a 15-year experience. *J Am Coll Cardiol* 2016;**68**:473–482.
2. Mina R, D'Agostino M, Cerrato C, Gay F, Palumbo A. Plasma cell leukemia: update on biology and therapy. *Leuk Lymphoma* 2017;**58**:1538–1547.
3. Tuazon SA, Holmberg LA, Nadeem O, Richardson PG. A clinical perspective on plasma cell leukemia; current status and future directions. *Blood Cancer J* 2021;**11**:23.
4. Tamir R, Lewin RF, Inbal A, Heller I, Theodor E. High-output cardiac failure as a presenting symptom of plasma cell leukemia. *Isr J Med Sci* 1985;**21**:679–682.
5. Chaoui D, Gallet B, Genet P, Mbungani B, Al Jijakli A, Arakelyan N et al. High-output cardiac failure revealing primary plasma cell leukemia. *Case Rep Hematol* 2013;**2013**:504612.
6. Inanir S, Haznedar R, Atavci S, Unlü M. Arteriovenous shunting in patients with multiple myeloma and high-output failure. *J Nucl Med* 1998;**39**:1–3.