A 29-year-old woman presented in February 2010 with acute-onset severe chest pain. This radiated to the left shoulder and was associated with breathlessness. She was afebrile, her saturations were 100% on air, and her clinical examination was entirely normal. An electrocardiogram showed diffuse 2- to 3-mm ST-segment elevation. At presentation, troponin I was elevated at 2.4 ng/mL (normal <0.1 ng/mL). Full blood count, chest radiograph, arterial blood gas, and bedside echocardiogram were unremarkable. She was diagnosed with myopericarditis and discharged from the accident and emergency department with nonsteroidal anti-inflammatories.

Two days later, she returned with worsening chest pain and was admitted for investigation. She had a full blood count, and urea and electrolytes were within the normal range. Troponin I was significantly elevated at 15.2 ng/mL, C-reactive protein was >160 mg/L (normal <10 mg/L), and D-dimer was >20 000 μg/L (normal 0 to 500 μg/L). Her electrocardiogram showed further widespread ST elevation, and repeat bedside echocardiogram demonstrated a mass at the left ventricular apex, with apical hypokinesis (Figure 1 and online-only Data Supplement Movie I). A cardiac magnetic resonance scan revealed apical scarring consistent with a small myocardial infarct, with adherent apical thrombus in both the left and right ventricles (Figures 2 and 3 and online-only Data Supplement Movies II and III).

Coronary angiography showed no evidence of coronary artery disease. To exclude paradoxical embolism, a bubble echocardiogram was performed, which was normal. In view of her intracardiac thrombus, therapeutic dose low-molecular-weight heparin was commenced.

Over the 3 days after admission, she developed an isolated neutropenia, with her neutrophil count dropping to 0.92×10⁹/L (2.0 to 7.0×10⁹/L). In addition to her elevated D-dimer at presentation, she further developed evidence of a coagulopathy, with a prolonged prothrombin time (17.0 seconds, NR 12.0 to 15.5 seconds), activated partial thromboplastin time (39.1 seconds, NR 24 to 34 seconds) and low fibrinogen (1.4 g/L, NR 1.5 to 4.0). These results were consistent with disseminated intravascular coagulation.
Examination of her peripheral blood film showed abnormal, granular, bilobed promyelocytes. A bone marrow aspirate was performed and demonstrated a diffuse infiltration of these abnormal promyelocytes, consistent with a diagnosis of acute promyelocytic leukemia (APL). She was started on all-trans retinoic acid (ATRA) and idarubicin chemotherapy according to an established protocol for management of APL. Her coagulopathy was corrected with fresh frozen plasma and cryoprecipitate.

The diagnosis of APL was confirmed by molecular analysis, which showed a rare molecular variant (Signal Transducer and Activator of Transcription 5 beta - Retinoic Acid Receptor Alpha) rather than the typical ProMyelocytic Leukemia - Retinoic Acid Receptor Alpha fusion that occurs in \( \approx 95\% \) of cases. After completing 1 cycle of ATRA and idarubicin chemotherapy, the patient was in clinical, morphological, and cytogenetic remission.

Signal Transducer and Activator of Transcription 5 beta - Retinoic Acid Receptor Alpha APL was first described in 1998, with only a handful of cases reported since. Clinical characterization remains poor, but it has previously been shown to be unresponsive to ATRA. On this basis, the patient was subsequently changed to standard chemotherapy for acute myeloid leukemia.

A follow-up cardiac magnetic resonance imaging scan at 2 months showed dramatic reduction (although not complete resolution) in the thrombus size (Figure 4 and online-only Data Supplement Movie IV). The follow-up cardiac magnetic resonance imaging scan also showed a drop in ejection fraction from 71% to 45%, probably because of anthracycline chemotherapy. The patient has since had further chemotherapy and remains in remission to date.

**Discussion**

APL accounts for 10% to 15% of cases of acute myeloid leukemia; patients characteristically present with pancytopenia and a coagulopathy, which may manifest as hemorrhage or thrombosis. Although bleeding is more common, accounting for the majority of the early mortality, \( \approx 10\% \) of patients with APL have evidence of thrombosis at presentation.

We hypothesize that our patient’s myocardial infarct occurred because of in situ coronary artery thrombosis, previ-
ously reported as a rare presenting feature of APL. To our knowledge, this is the first report of intracardiac thrombus complicating acute myocardial infarction in APL. Other types of arterial thrombosis have been reported, including ischemic stroke and acute limb ischemia.

Complex pathophysiology underlies the paradox of bleeding and thrombosis in APL. There is disseminated activation of the coagulation cascade, with release of potent procoagulant factors from leukemia cells, including tissue factor, cancer procoagulant, and prothrombotic cytokines. Tissue factor binds with factor VII whereas cancer procoagulant activates factor X, both acting to promote thrombosis.

A critical component of the initial management of APL is blood product support, to correct the coagulopathy, and initiation of ATRA. Management of thrombosis in APL is without strong evidence base, but in the absence of bleeding, low–molecular-weight heparin may be of benefit by offsetting pathological activation of factor Xa by leukemia cells.

In this case, myocardial ischemia resolved after initiation of low–molecular-weight heparin, but percutaneous coronary intervention has previously been described for coronary artery thrombosis in APL. Low–molecular-weight heparin was continued beyond the acute phase to reduce the risk of extension or embolization of the intracardiac thrombus.

APL should be considered as a rare cause of myocardial infarction. Management of thrombosis in APL is complicated by the risk of life-threatening hemorrhage. For patients presenting with a thrombotic episode, prompt recognition of the underlying leukemia and initiation of appropriate therapy are key to reducing overall morbidity and mortality. In this case, cardiac magnetic resonance imaging aided both diagnosis and assessment of response to treatment of the intracardiac thrombus.

Acknowledgments

The authors acknowledge the contributions of Jelena Jovanovic (Department of Medical and Molecular Genetics, King’s College London, UK), Dr Paresh Vyas, Dr Anna Schuh, and the Cytogenetics Team (Churchill Hospital, Oxford, UK).

Sources of Funding

Dr Peniket and Dr Myerson are supported by the Oxford NIHR Biomedical Research Centre. Professor Grimwade is funded by Leukaemia and Lymphoma Research. Dr Herring is a Clinical Lecturer in Cardiovascular Medicine at Oxford University and is supported by the British Heart Foundation.

Disclosures

None.

References

Myocardial Infarction With Intracardiac Thrombosis as the Presentation of Acute Promyelocytic Leukemia: Diagnosis and Follow-Up by Cardiac Magnetic Resonance Imaging
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Circulation. 2011;123:e370-e372
doi: 10.1161/CIRCULATIONAHA.110.986208
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/123/10/e370

Data Supplement (unedited) at:
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