Sudden death of a patient with primary hypereosinophilia, colon tumours, and pulmonary emboli

K Uemura, M Nakajima, N Yamauchi, M Fukayama, K Yoshida

A 33 year old man was admitted to hospital six days after the onset of abdominal pain. There was hypereosinophilia, but the cause could not be identified (primary hypereosinophilia). The hypereosinophilia, high C reactive protein concentration, and gastrointestinal symptoms were alleviated by corticosteroid treatment. Unexpectedly, after this apparent recovery, he was found dead on the 27th day after admission. Necropsy disclosed two solid tumours primarily composed of eosinophils in the ascending and transverse colon. The cause of the sudden death was pulmonary artery emboli, derived from a thrombus in the left iliac vein.

Hypereosinophilia (HE) is caused either by parasite infection, allergic diseases, drugs (secondary HE), or unknown causes (primary HE). The lung, skin, intestine, and peripheral nerves are affected by allergic vasculitis and granulation in some patients with HE. Most of these patients respond to corticosteroid or immunosuppressive treatment. However, patients with HE sometimes die suddenly of myocarditis, eosinophilic endomyocardial fibrosis (Loeffler’s endomyocarditis), myocardial dysfunction (congestive heart failure), or thrombotic hypertrophic mitral-tricuspid valve disease. It was previously reported that hypercoagulation as a result of HE causes biventricular apical mitral-tricuspid valve disease. It was previously reported that hypercoagulation as a result of HE causes biventricular apical mitral-tricuspid valve disease.

DISCUSSION

This is the first report of an eosinophil derived solid tumour in any organ, including the intestine. The tumour was distinct from eosinophilic enteritis. During hospitalisation, the gastric and intestinal infiltration of eosinophils was confirmed by biopsy. However, at necropsy neither eosinophilic infiltration nor inflammation was evident in the colon and small intestine, probably because of the steroid treatment. The cells in the tumours had few eosinophilic granules, suggesting their immaturity. The immature eosinophils were also seen in the bone marrow during hospitalisation. Although sudden death as a result of eosinophilic myocarditis has been reported, we found no eosinophilic infiltration. It is likely that the two tumours protruding into the intestinal cavity would have caused the obstructive intestinal ileus and the abdominal pain.

Abbreviations: HE, hypereosinophilia
The patient died of pulmonary artery emboli, derived from deep iliac vein thrombosis. It has been suggested that eosinophils cause hypercoagulation, probably through invasive tissue damage and tissue factor exposure, as malignant tumours do. Consistent with this hypothesis, the four major proteins secreted from eosinophils—major basic protein, eosinophil derived neurotoxin, eosinophil cationic protein, and eosinophil peroxidase—are potent and non-specific cytotoxins. In addition, these four granule proteins may promote platelet activation and coagulation. For example, major basic protein and eosinophil peroxidase can release 5-hydroxytryptamine, a potent platelet activator. Eosinophil cationic protein accelerates coagulation through a factor XII dependent mechanism. Moreover, the four eosinophil derived proteins inhibit the anticoagulation activity of thrombomodulin on the endothelial and endocardial surface.

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Thrombosis can be caused by either of three factors: blood stasis, injury to a vein, or hypercoagulability. First, the patient was allowed to move relatively freely, in contrast to the absolute bed rest usual in patients with leg fracture,
major surgery, brain injury, or haemorrhage. The colon tumour could not have compressed the iliac vein. However, it is known that occasionally thrombosis can be caused in the left iliac vein by iliac artery compression, as in our case. There was neither deep vein injury in the lower extremities nor medical practices that can cause vessel injury. Accordingly, it is tempting to speculate that the intrinsic hypercoagulation resulting from hypereosinophilia contributed to the extensive left iliac vein thrombosis under relatively light bed rest.

In conclusion, we present the first case of the primary hypereosinophilic syndrome with colon solid tumours and sudden death caused by pulmonary emboli. It remains to be elucidated how hypereosinophilia leads to the development of a tumour.

Authors’ affiliations
K Uemura, M Nakajima, K Yoshida, Department of Forensic Medicine, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan
N Yamauchi, M Fukayama, Department of Human and Diagnostic Pathology, Graduate School of Medicine, University of Tokyo

Correspondence to: Dr K Uemura, Department of Forensic Medicine, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan; kuemura@m.u-tokyo.ac.jp

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