The Journal of Laryngology and Otology
January 1993, Vol. **107**, pp. 51–53

Fatal massive upper respiratory tract haemorrhage: an unusual complication of localized amyloidosis of the larynx

Louis Tsun-Cheung Chow, M.R.C. Path., F.R.C.P.A.,* Wing-hing Chow, M.R.C.P.,** Bobby Shui-fung Shum, D.M.J.† (Hong Kong)

Abstract
Localized amyloidosis of the larynx is usually described as a non-bleeding lesion. We report a patient with localized laryngeal amyloidosis who developed a massive upper respiratory tract haemorrhage and died. This potentially fatal complication of localized amyloidosis of the larynx merits recognition as the disease could be controlled in most instances by surgical excision of the amyloid deposit.

Key words: Amyloidosis; Larynx; Haemorrhage; Upper respiratory tract.

Introduction

Tumour-like, organ-limited amyloidosis is a relatively rare but well recognized condition. It is characterized by the deposition of amyloid confined to a particular site or organ, with resulting symptoms and signs. It is usually not accompanied by plasma cell dyscrasia and not followed by systemic disease. The common sites of involvement include the respiratory tract (Simpson *et al.*, 1984), skin (Brownstein and Helwig, 1970) and the urinary bladder (Fujihara and Glenner, 1981). In the respiratory tract, localized amyloidosis is most common in the larynx where the deposits are almost always concentrated to the ventricular folds (Michaels and Hyams, 1979).

In this paper, we describe a patient with localized amyloidosis of the larynx presenting with massive upper respiratory tract haemorrhage who died. To our knowledge, this complication of localized laryngeal amyloidosis has not been reported.

Case report

A 38-year-old salesman attended his private doctor with a three week history of malaise, runny nose, sore throat, dry cough and hoarseness of voice. The onset was insidious and there was no associated fever or weight loss. His past health had been good. Physical examination was unremarkable apart from a congested oropharynx. There was no abnormal lymphadenopathy. The clinical diagnosis was upper respiratory tract infection with acute laryngitis and a course of antibiotic was prescribed. Two days later, however, the patient had massive haemoptysis in the middle of the night. He complained of difficulty in breathing and died shortly afterwards before he could be transferred to the district hospital.

Pathological findings

On post-mortem examination, the significant findings were in the respiratory tract. The entire laryngeal mucosa showed diffuse thickening, and this was particularly prominent in the ventricular folds. In addition, an area of mucosal ulceration, 2 × 1 cm, was seen in the anterior wall, just beneath the vocal folds (Fig. 1). The floor of the ulcer was covered by blood clot, and the surrounding mucosa was congested and haemorrhagic. The trachea appeared unremarkable. However, blood clots were seen in its lumen and the entire bronchopulmonary tree was filled with fresh blood. Both lungs were congested and their cut surfaces were haemorrhagic.

Cut section of the larynx revealed deposition of pale yellow firm substance in its mucosa, responsible for the diffuse thickening (Fig. 1). This substance gave a blue reaction with iodine and sulphuric acid. Microscopically, it consisted of homog-

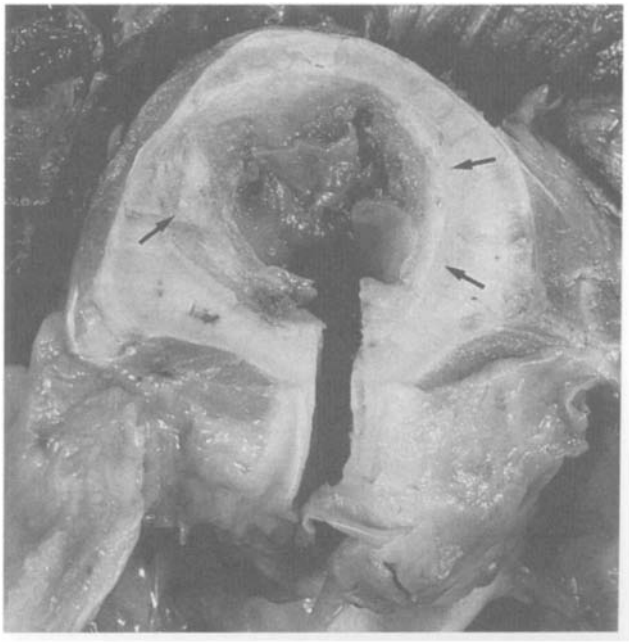

Fig. 1
Cut section of the larynx viewed obliquely and posteriorly from below, revealing mucosal deposits of amyloid as pale yellow firm substance (arrows). An area of mucosal ulceration is seen.

From the Institute of Pathology,* Queen Elizabeth Hospital, Hong Kong, the Department of Medicine,** Grantham Hospital, Aberdeen, Hong Kong and the Forensic Pathology Service,† Department of Health, Hong Kong.
Accepted for publication: 8 August 1992.

eneous eosinophilic material extensively deposited in the subepithelial lamina propria of the entire larynx, with focal ossification (Fig. 2a). It exhibited metachromasia with crystal violet stain. With congo red, it stained orange and demonstrated apple green birefingence with polarized light examination (Fig. 2b), indicating that it was amyloid. The congophilia was resistant to pre-treatment with potassium permanganate. There was widespread loss of seromucinous glands, with only residual ducts surrounded and compressed by amyloid (Fig. 3). In particular, heavy deposits of amyloid were seen around the blood vessels, many of which appeared ectatic (Fig. 3). In the area of ulceration, the covering epithelium was eroded, exposing the underlying amyloid which was covered by blood clot and fibrin.

Focal subepithelial deposits of amyloid were seen only in the initial two centimetres of the trachea, the rest of the trachea and bronchopulmonary tree were free from involvement. The other organs were unremarkable with no amyloid deposition. Examination of the bone marrow showed no evidence of plasma cell dyscrasia.

Discussion

The larynx is one of the commonest sites of involvement in localized amyloidosis (McAlpine and Fuller, 1964). According to New (1919), cases of localized laryngeal amyloidosis might be classified into two main categories, the nodular and the diffuse infiltrative types. The nodular or 'tumour-forming' type consists of discrete masses of amyloid deposit in the larynx, usually in the vestibule, less frequently in the ventricular and vocal folds or subglottis. It may be sessile or pedunculated, and is often multiple. It is more dangerous because of its potential risk of causing acute respiratory obstruction. In the diffuse infiltrative type, extensive subepithelial deposits of amyloid are seen in the larynx, starting usually at the glottis and extending downward by contiguity to the tracheobronchial tree for a variable extent. It may result in progressive stenosis of the airways. Both types may occur in all regions of the respiratory tract and many cases have been described in which both types were present (McAlpine and Fuller, 1964).

Our patient showed the typical pathological features of the diffuse infiltrative type of localized amyloidosis of the larynx. Extensive subepithelial deposits of amyloid were seen in the entire laryngeal mucosa, being most abundant in the ventricular folds (Fig. 2a). Moreover, the resistance of the congophilia of the amyloid to pre-treatment with potassium permanganate suggests that the amyloid is derived from an immunoglobulin light chain (Wright *et al.*, 1977; Van Fijswijk and Van Heusden, 1979), a finding supported by previous workers (Westermark *et al.*, 1982).

The clinical presentation of our patient, however, is unique. Localized amyloidosis of the larynx has been regarded as a non-bleeding lesion and its overlying mucosa is usually intact (Stark and New, 1949; McAlpine and Fuller, 1964; Michaels and Hyams, 1979). In contrast, our patient had a massive haemorrhage from his laryngeal lesion, and an area of mucosal ulceration was identified (Fig. 1). He suffocated to death by the large amount of blood flooding into his bronchopulmonary tree. This complication of localized laryngeal amyloidosis should not be surprising as haemorrhage is a well recognized complication in amyloidosis involving other organs (Yood *et al.*, 1983), including the stomach (Macmanus and Okies, 1976; Bjornsson *et al.*, 1987) and the tracheobronchial tree (Shaheen *et al.*, 1975). In

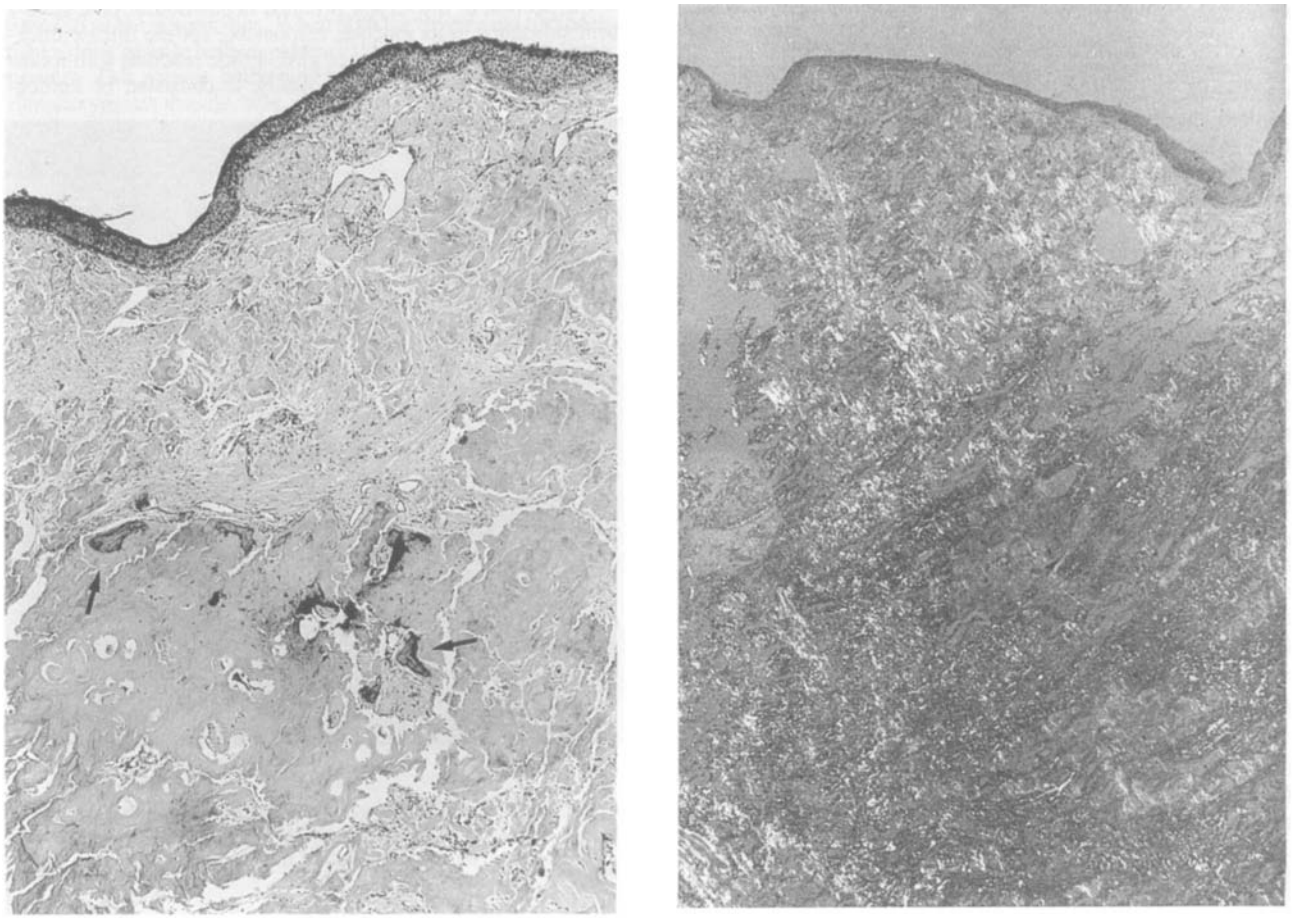

Fig. 2

a. In the lamina propria are extensive subepithelial deposits of amyloid, with focal ossification (arrows). H&E, ×12.5.

b. After staining with congo red, the amyloid exhibits apple green birefringence on polarized light examination. Congo red, ×12.5.

https://doi.org/10.1017/S0022215100122145 Published online by Cambridge University Press

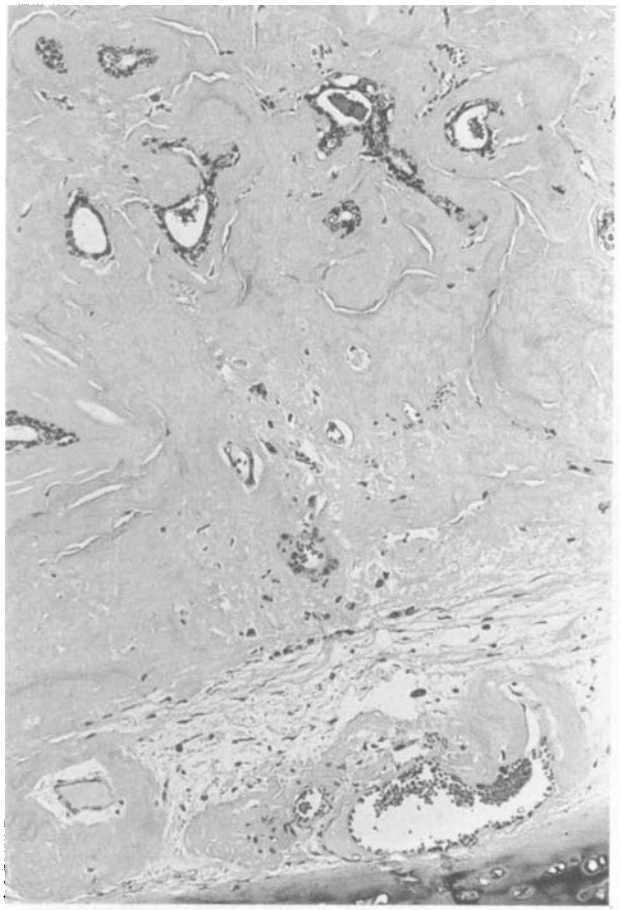

Fig. 3

There is widespread loss of seromucinous glands, with only residual ducts surrounded by amyloid. Heavy deposits of amyloid are seen around the blood vessels, one of which appears ectatic. H&E, ×50.

particular, cerebral amyloid angiopathy has recently been implicated as an important cause of intracerebral haemorrhage in the elderly (Gilles *et al.*, 1984; Cosgrove *et al.*, 1985; Mandybur, 1986). The bleeding was thought to be related to amyloid infiltration of blood vessels with consequent increased vascular fragility (Mandybur, 1986). In our patient, heavy deposits of amyloid were seen around the blood vessels, many of which assumed an irregular contour and appeared ectatic (Fig. 3). This would presumably result in increased fragility and decreased contractility, predisposing to massive haemorrhage. Furthermore, as our patient was suffering from an episode of upper respiratory tract infection, the mucosal inflammation, coupled with the elevated airway pressure secondary to repeated coughing, might have resulted in the mucosal ulceration and initiation of haemorrhage.

In conclusion, massive haemorrhage as a potentially fatal complication of localized amyloidosis of the larynx merits recognition since the disease could be controlled in most instances by surgical excision of the amyloid deposit.

Acknowledgement

We thank Miss Cindy L. K. Lau for her expert secretarial assistance.

References

Bjornsson, S., Johannsson, J. H., Sigurjonsson, F. (1987) Localized primary amyloidosis of the stomach presenting with gastric haemorrhage. *Acta Medica Scandinavica*, **221:** 115–119.

Brownstein, M. H., Helwig, E. B. (1970) The cutaneous amyloidosis. I. Localized forms. *Archives of Dermatology*, **102:** 8–19.

Cosgrove, G. R., Leblanc, R., Meagher-Villemure, K. , Ethier, R. (1985) Cerebral amyloid angiopathy. *Neurology*, **35:** 625–631.

Fujihara, S., Glenner, G. G. (1981) Primary localized amyloidosis of the genitourinary tract. Immunohistochemical study on 11 cases. *Laboratory Investigation*, **44:** 55–60.

Gilles, C., Brucher, J. M., Khoubesserian, P., Vanderhaeghen, J. J. (1984) Cerebral amyloid angiopathy as a cause of multiple intracerebral hemorrhages. *Neurology*, **34:** 730–735.

Macmanus, Q., Okies, J. E. (1976) Amyloidosis of the stomach: report of an unusual case and review of the literature. *American Surgeon*, **42:** 607–610.

Mandybur, T. I. (1986) Cerebral amyloid angiopathy: The vascular pathology and complications. *Journal of Neuropathology and Experimental Neurology*, **45:** 79–90.

McAlpine, J. C., Fuller, A. P. (1964) Localized laryngeal amyloidosis. A report of a case with a review of the literature. *Journal of Laryngology and Otology*, **78:** 296–314.

Michaels, L., Hyams, V. J. (1979) Amyloid in localized deposits and plasmacytomas of the respiratory tract. *Journal of Pathology*, **128:** 29–38.

New, G. B. (1919) Amyloid tumours of the upper air passages. *Laryngoscope*, **29:** 327–341.

Shaheen, N. A., Salman, S. D., Nassar, V. H. (1975) Fatal bronchopulmonary hemorrhage due to unrecognized amyloidosis. *Archives of Otolaryngology*, **101:** 259–261.

Simpson II, G. T., Skinner, M., Strong, M. S., Cohen, A. S. (1984) Localized amyloidosis of the head and neck and upper aerodigestive and lower respiratory tracts. *Annals of Otology, Rhinology and Laryngology*, **93:** 374–379.

Stark, D. B., New, G. B. (1949) Amyloid tumors of larynx, trachea or bronchi; report of 15 cases. *Annals of Otology, Rhinology and Laryngology*, **58:** 117–134.

Van Fijswijk, M. H., Van Heusden, C. W. (1979) The potassium permanganate method: A reliable method for differentiating amyloid AA from other forms of amyloid in routine laboratory practice. *American Journal of Pathology*, **97:** 43–58.

Westermark, P., Sletten, K., Pitkanen, P., Natvig, J. B., Lindholm, C. E. (1982) Localized laryngeal amyloidosis: partial characterization of an amyloid fibril protein AL. *Molecular Immunology*, **19:** 447–450.

Wright, J. R., Calkins, E., Humphrey, R. L. (1977) Potassium permanganate reaction in amyloidosis: A histologic method to assist in differentiating forms of this disease. *Laboratory Investigation*, **36:** 274–281.

Yood, R. A., Skinner, M., Rubinow, A., Talarico, L., Cohen, A. S. (1983) Bleeding manifestations in 100 patients with amyloidosis. *Journal of the American Medical Association*, **249:** 1322–1324.

Address for correspondence:
Dr Louis T. C. Chow,
Institute of Pathology,
Queen Elizabeth Hospital,
Wylie Road,
Kowloon,
Hong Kong.
Fax: (852)-385-2455