obstructive embolism of the main pulmonary artery; a defective artificial valve; tamponade; a gross tension pneumothorax; and severe subvalvular obstruction as in pulmonary infundibular shutdown.

If one of the abovementioned conditions is present, permanent brain damage may ensue despite correctly executed cardiac massage and artificial ventilation. Failure of resuscitation will only become apparent when no signs of brain activity can be elicited and then it could be too late. The capnograph may give proof of ineffective cardiac massage at a stage when signs of brain activity are still present and other measures can be instituted at a much earlier stage, as was demonstrated in case 1. Here the surgeon was informed that the massage was ineffective at a stage where the pupils of the patient were still small. In case 2, signs of cardiovascular failure occurred only after CO₂ content of alveolar gases dropped to zero. The reason why it occurred at that late stage might be ascribed to the fact that the patient was cooled down to 30°C by surface cooling. In case 3, the surgeon could also have been warned at an early stage of impending cardiovascular failure.

It is felt that much can be gained and lives can be saved if capnography is used routinely in the care of the critically ill patient.

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Familial Waldenström’s Macroglobulinaemia

A Case Report

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SUMMARY

A patient with Waldenström’s macroglobulinaemia, whose father died of the same condition, is presented. The literature on familial occurrence of paraproteinaemia is briefly reviewed.


The finding of a familial incidence of paraproteinaemia is most unusual, but it is known to occur both in Waldenström’s macroglobulinaemia and in multiple myeloma. A patient with Waldenström’s macroglobulinaemia, whose father died of the same illness, is presented.

CASE REPORT

The father of our patient was born in 1892 and was first seen in December 1961 because of general malaise, irritability, loss of appetite and loss of weight. He had a previous history of pulmonary tuberculosis, malaria, Malta fever and a tendency to bony fractures, of which he had had several. He was found to be anaemic and his liver and spleen were palpable 3 cm and 2 cm below the costal margin, respectively. His ESR was constantly in the region of 130 mm/h (Westergren). He was found to have a total protein of 10.2 g/100 ml, with 7.6 g/100 ml globulin. There was no Bence Jones protein, and radiological examination and study of bone marrow aspirate were negative. He was referred to Germany where he was seen by Professor L. Heilmeyer in July 1962. Investi-
gations confirmed monoclonal gammopathy, and ultra-
centrifugal analysis showed a marked increase in macro-
globulins. Biopsy specimens of marrow, liver, and spleen
revealed infiltration by the plasmacytoid lymphocytes
which are seen in Waldenström's macroglobulinaemia.
He was treated with steroids and received transfusion as
required. In 1966 a splenectomy was performed, which
showed infiltration characteristic of Waldenström's
macroglobulinaemia. The patient died shortly thereafter,
but the cause of death is unknown.

His son, born in 1929, was first seen in November
1975 because of complaints of generalized muscle ache,
malaise and lack of energy. He had had a thyroidectomy
in 1960 and was on replacement therapy. Examination
was entirely negative. Laboratory studies revealed normal
thyroid function and a normal peripheral blood count.
The ESR, however, was elevated at 40 mm h (Wester-
gren). Chemical investigation of serum showed normal
renal and liver function, normal calcium levels, and an
elevated total protein of 9.4 g/100 ml of which 4.9 g/100
ml was globulin. The monoclonal gammopathy was due
to IgM, which had a concentration of 2.73 g/100 ml. IgG
and IgA levels were within normal limits. Bone marrow
aspirate and trephine biopsy specimens appeared normal.
It was decided to observe him at monthly intervals. Some
3 months later he was overtly depressed; treatment with a
tricyclic antidepressant cleared all his symptoms, including
those present at first. Eight months later, while still on
antidepressant therapy, he again complained of stiffness
of muscles and general lack of energy. Physical examina-
tion was entirely negative, but bone marrow biopsy
demonstrated areas of infiltration by plasmacytoid lym-
phocytes. Repeat bilateral bone marrow aspirates and
trephine biopsies confirmed the abnormal cellular infiltrate
and, in view of this, therapy with chlorambucil and pred-
nisone was commenced.

DISCUSSION

The first well-documented case of multiple myeloma
which occurred in a family appears to be that reported by
Mandema and Wildervanck, followed by reports from
Nadeau et al. and Herrell et al. Waldenström's macro-
globulinaemia in 2 brothers was documented by Massari et al.
in 1962.

Seligmann et al. studied the sera of 216 close relatives
of 65 patients with Waldenström's macroglobulinaemia. An IgM-type 'M-component' was found in 8 of the 216 relatives, 6 of whom were apparently healthy. Typical Waldenström's macroglobulinaemia occurred in 2 siblings in each of 2 families.

Spengler et al. reviewed the available literature and
found only 21 families with a familial incidence of
paraproteinaemia and added 2 patients of their own. Of
these 4, 1 patient's maternal aunt had died of myeloma,
and 2 patients each had an affected sister — 1 with an
asymptomatic IgG and 1 with an asymptomatic IgM par-
paraprotein. The 4th patient had Waldenström's macro-
globulinaemia and his daughter showed an IgM para-
protein.

The familial association demonstrated is clearly signi-
cant, and the incidence of elevated IgM levels, as reflected
in electrophoretic 'spikes' in relatives of patients with
Waldenström's macroglobulinaemia, is much higher than
in the population at large. The incidence of elevated
immunoglobulin levels in a random sample of the adult
population of Sweden was less than 1%., and only 8% of
the spikes on electrophoresisgrams were of the IgM
class. Seligmann et al. found no IgG or IgA spikes in the
relatives of their patients with Waldenström's macro-
globulinaemia.

The brother reported by Massari et al. appeared to
have macroglobulins of a very similar, if not identical,
structure. Their mother had no clinical symptoms, but
her serum contained elevated levels of γ-1-macroglobulin.
The authors felt that the disease might be inherited,
becoming manifest only in the homozygous state.

Seligmann et al. on the other hand, found that in
different affected family members, the biochemical and
antigenic structures of the paraprotein were never identi-
cal. Of great interest is one family in which the asympto-
matic mother's serum contained a single electrophoretic
IgM spike with two distinct types of macroglobulin. One
possessed individual antigenic specificity similar, if not
identical, to the macroglobulin of the son, while the other
shared the individual specific antigens of the macro-
globulin of the other son.

It has been postulated that environmental factors may
be of importance, but the evidence for this is uncon-
vincing. Transmission by sex-linked inheritance and by
autosomal inheritance has been suggested. Although no
definite mode of inheritance has been formulated, it
seems highly probable that a genetically determined
immunological abnormality exists, perhaps requiring the
influence of non-hereditary factors.

At present it is uncertain as to what proportion of
asymptomatic patients with monoclonal spikes will de-
velop the malignant process. There is no good correlation
between the level of the paraprotein spike and the pla-
smacytoid-lymphocyte infiltration of the marrow. It is
difficult to define the early stages of Waldenström's
disease, hence our policy in this case has been to do
marrow aspirates and trephine biopsies approximately
every 6 months and to examine the patient clinically every
month. In view of the fact that 'benign monoclonal gam-
mopathies' of the IgM type do exist, a paraprotein spike
in an asymptomatic patient is insufficient reason to com-
ence therapy, even when there is a family history of
Waldenström's macroglobulinaemia.

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