Elastofibroma

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SYNOPSIS Three cases of elastofibroma are described and the literature is reviewed. It is suggested that they are non-neoplastic lesions resulting from trauma. Their staining reactions and the response of the elastic type fibres to enzyme digestion suggest that these fibres are either true elastin or very closely related to it.

Jarvi and Saxén (1961) described the first four cases of a connective tissue lesion which they named elastofibroma dorsi. Stemmermann and Stout (1962) added two cases and carried out a detailed investigation of the lesion's staining properties and its response to elastase digestion. Since then further case reports have appeared by Delvaux and Lester (1965), Marston and Wilson Jones (1965), Brown, Clearkin, Nakachi, and Bundick (1966), and Barr (1966). Three cases are added by us and the recorded cases are shown in Table I. It is likely that this condition is more frequent than the published records

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suggest. Stemmermann (1967) mentions having seen four cases since the publication of his paper in 1962 and Tighe, Clark, and Turvey (1968) have recently studied two more.

Whatever the true nature of the 'tumours' they have constant and unusual properties. With one exception (Barr, 1966) they have all been situated in the lower subscapular space deep to the rhomboids and latissimus dorsi. They present as a swelling which has been bilateral in two cases. In a third case with bilateral swellings one appeared four years after the other. They have varied in size from about 2 cm in diameter up to 11 cm. In some cases they

TABLE I
ELASTOFIBROMA

Case	Author	Age	Sex	Occupation	Size	Length of History	Follow-up	Suggested Aetiology
1-4	Jarvi & Saxen (1961)	All ages	Not stated	Not stated	Size of plum to size of hand	1-6 years	No recurrences or metastases	Friction between scapula and thorax
5	Stemmermann & Stout (1962)	66	F	Manual worker	5 cm in diameter	3 days	No recurrences or metastases	?Friction between scapula and thorax
6		70	F	Manual worker	Bilateral, 7 × 3 cm	4 years	No recurrences or metastases	—
7	Delvaux & Lester (1965)	62	M	Not stated	3 × 5 cm	4 weeks	No recurrences or metastases	—
8	Marston & Wilson Jones (1965)	55	F	Housewife	4 cm	6 months	No recurrences or metastases	—
9	Brown <i>et al.</i> (1966)	58	F	Manual labour	About 9 cm	6 months	No recurrences or metastases	—
10	Barr (1966)	45	F	Clerk	5 × 7 × 1.5 cm, 1960 right 7.5 × 2 cm, 1964 left	12 months 12 months	No recurrences or metastases	Elastotic degeneration of collagen after trauma and friction ?Enzymatic defect related to connective tissue metabolism
11	Barr (1966)	62	F	Not known	8 × 5.5 × 3 cm	3 months	No recurrences or metastases	—
12	Barr (1966)	75	M	Baker	Over greater trochanter, 8 × 5 × 3 cm	1 year	No recurrences or metastases	—
13	Mackenzie, Wilson, & Cooke (1968)	47	M	Electric engineer	8 × 6 cm	10 days	No recurrences or metastases	—
14	Mackenzie <i>et al.</i> (1968)	64	F	Housewife and domestic worker	7.5 cm, slightly tender, partly cystic	5 months	No recurrences or metastases	Traumatic origin Elastic type fibres very closely related to elastin
15	Mackenzie <i>et al.</i> (1968)	66	M	Retired chemist	2.5 × 1 × 1 cm	Incidental finding during oesophageal resection	Died post-operatively	—

were slightly painful and fixation to the rib cage has been noted. They occur in the older age groups and there is often a history of hard manual work. They have never been known to recur or metastasize and their histological appearances are constant and pathognomonic.

CASE REPORTS

CASE 1 The patient, a man aged 47, noticed a lump in the right scapular region 10 days before admission. It was painless, not tender, and there was no limitation of movement. Although there was a past history of pulmonary tuberculosis, the patient's health was good at the time of admission. At operation a firm mass 8 cm by 6 cm was found extending underneath the tip of the scapula. It was greyish white with fatty streaks and appeared to be infiltrating surrounding muscles (Fig. 1). The patient made an uneventful recovery and has remained well for nine months. He was an electrical engineer but was also a keen gardener, which involved some heavy manual work. The histology was typical of elastofibroma.

CASE 2 The patient, a woman aged 64, complained of a slightly tender lump in her back for five months. At operation a partly cystic swelling, 7.5 cm in diameter, attached to the ribs and rhomboid muscles was removed. Recovery was uneventful and she has remained well for three years. She was a housewife and professional domestic worker, and had done a lot of manual work. The histology was similar to case 1.

CASE 3 The patient, a man aged 66, underwent thoracotomy for resection of a carcinoma of the oesophagus.

FIG. 1. Operation specimen showing elastofibroma and adjacent muscle.

During the operation a mass, 2.5 cm by 1 cm, was removed from beneath the tip of the left scapula. He was a retired chemist and there was no history of manual work. The patient died postoperatively. The histology was again typical.

The specimen from case 1 was available for detailed study. Sections stained with haematoxylin and eosin and for elastic tissue were examined from the other two cases. The histology appeared identical in all three cases.

The diagnosis of elastofibroma can be made on haematoxylin and eosin sections alone although a confirmatory elastic stain is advisable. Haematoxylin and eosin sections show large amounts of relatively acellular collagen with scattered blood vessels and fatty tissue. Nucleated cells are mainly fibroblasts. Amongst the collagen are numerous branched and unbranched eosinophilic fibres seen in longitudinal and transverse section (Fig. 2). They measure up to about 250 μ in length and about 25 μ in diameter. It is these fibres which take up elastic stains. However, the precise appearances depended upon the stain used. The Verhoeff-van Gieson method showed a darkly staining central core covered by a thin envelope staining as collagen. These appearances are identical to those described by Stemmermann and Stout (1962). With Sheridan's method the whole fibre stained dark green. We consider the latter to be a more constant and reliable stain. Considerable variations were noted with the Verhoeff-van Gieson method depending on the degree of differentiation. With Sheridan's stain some of the fibres had clear-cut edges while others showed a serrated edge which, in longitudinal section, gave a coiled spring appearance (Figs. 3 and 4).

Tissue from the aorta of a young adult was used as a control for elastic tissue. The staining reactions were also carried out on five cases of severe senile elastosis (senile degeneration of collagen). One such case was used for digestion experiments.

A word of warning is necessary regarding terminology. Puchtler and Sweat (1964) have pointed out that the term 'elastic tissue' may have a different meaning for the chemist as opposed to the histologist. For the chemist elastic tissue must contain the protein elastin whereas the histologist uses the term for tissues which stain in a definite way with such stains as Sheridan or Verhoeff-van Gieson. The authors point out that stains of resorcin-fuchsin type are not specific for elastin and that, after acetylation, sulphation and phosphorylation, basement membranes, reticulin fibres, and collagen will take up the stain. In addition Gillman, Penn, Bronks, and Ronx (1955) noted differences in the staining reactions of true elastic fibres in arteries and in the dermis from 'elastotically degenerated' fibres

FIG. 2.

FIG. 4.

FIG. 3.

FIG. 2. *Pale fibres seen in longitudinal and transverse sections. Haematoxylin and eosin. $\times 540$.*

FIG. 3. *Fibres seen in longitudinal and transverse sections before digestion. Sheridan $\times 620$.*

FIG. 4. *Fibres showing partial digestion by pancreatic elastase after 15 minutes. Sheridan $\times 620$.*

from the same sources. They recommended toluidine blue, Mallory's PTAH, Ponceau 2R light green, and a modification of Mallory's triple stain as being particularly valuable. The results with these and other stains are shown in Table II, from which it will be seen that the fibres of elastofibroma resemble aortic elastic fibres and stain differently from the degenerate elastotic material with Mallory's triple stain and Ponceau 2R.

The chemical properties of elastin were reviewed by Partridge (1962) and particular emphasis was laid on the relative susceptibility of collagen and elastin to digestion by various proteolytic enzymes and on the effects of digestion on their staining reactions.

ENZYME EXPERIMENTS

In an attempt to identify the elastotic material in elastofibroma the effects of four enzyme systems were compared.

CRYSTALLINE PEPSIN This enzyme converts native collagen to material staining like elastin (Tunbridge, Tattersall, Hall, Astbury, and Reed, 1952), and also digests elastin (Fisher, Rosenthal, and Lancing, 1960). In this experiment 2 mg pepsin (Calbiochem, 3 × cryst. porcine, batch 72948) was used in 1 ml of 0.02N HCl, pH 1.6 w/v.

CRYSTALLINE TRYPSIN This enzyme digests denatured collagen but not native collagen or elastin; 0.1 mg trypsin (Calbiochem, essentially free of chymotrypsin,

batch 72451) in 1 ml of 0.05M sodium phosphate, pH 6.0 was used.

CRYSTALLINE PANCREATIC ELASTASE This enzyme readily attacks most denatured protein but not native collagen; 0.25 mg elastase (Sigma, 2 × cryst., porcine pancreas, batch 26B—0050) per 1 ml of 0.015M sodium borate, pH 9.0 was used.

ALUMINA-ADSORBED BACTERIAL ELASTASE This is said to be specific for elastin (Mandl and Cohen, 1960); 25 mg elastase (Calbiochem bacterial, batch 65526) was adsorbed with 200 mg alumina Cv gel (Sigma, aged, Batch 17B—8650) in 40 ml of distilled water, pH 7.6-8 adjusted with dilute ammonia, stood at 4°C for 18 hours and then centrifuged, for 10 minutes at 3,000 g. The supernatant was used as the enzyme preparation. According to Mandl and Cohen the protein concentration should have been approximately 0.06 mg/ml, but no protein determination was performed.

In all cases 20 μ frozen sections were incubated at 37°C in the enzyme or control solution for the specified time and then immediately washed three times by immersion in ice-cold buffer before processing. All buffers were prepared using a pH meter. The results obtained with case 1 are shown in Table III. Results with the control aortic tissue and with one case of senile elastosis are shown in Tables IV and V.

DISCUSSION

There are two main problems connected with elastofibroma, namely, the pathogenesis of the

TABLE II

STAINING REACTIONS OF ELASTOTIC TISSUE IN ELASTOFIBROMA, AORTIC CONTROL, AND FIVE CASES OF SENILE ELASTOSIS (S.E. 1-5)

	<i>Haematoxylin and Eosin</i>	<i>Toluidine Blue</i>	<i>Mallory's Triple stain</i>	<i>Mallory's PTAH</i>	<i>Sheridan</i>	<i>Ponceau 2R</i>	<i>Autofluorescence in Ultra-violet Light</i>
Elastofibroma	Pink	Colourless	Red	Orange (occasional dark blue or brown cores)	Dark green-black	Light red	Positive, pale yellow green
Aortic control	Pale pink	Pale blue-green	Red	Orange-red	Dark green-black	Light red	Positive, pale yellow green
S.E.1. to S.E.5.	Pale pink	Very pale blue	Pale blue	Orange	Dark green-black	Green or grey	Positive, pale yellow green

TABLE III

ELASTOFIBROMA

Exposure Time (min.)

	15	30	45	60	75	180	24 Hours
Pepsin in acid buffer	+	++	++	++	+++	+++	+++
Trypsin in alkaline buffer	—	—	—	—	—	—	—
Pancreatic elastase in dilute borate	+	++	+++	+++	+++	+++	+++
Bacterial elastase in dilute ammonia	—	—	—	—	—	++	+++
Enzyme-free acid buffer alone	—	—	—	—	—	—	—
Enzyme-free alkaline buffer alone	—	—	—	—	—	—	—
Enzyme-free dilute ammonia alone	—	—	—	—	—	—	—

+++ = Complete digestion
— = no digestion

TABLE IV

AORTIC CONTROL

	Exposure Time (min)						
	15	30	45	60	75	180	24 Hours
Pepsin in acid buffer	—	+	+	+	++	+++	+++
Trypsin in alkaline	—	—	—	—	—	—	—
Pancreatic elastase in dilute borate	+	++	+++	+++	+++	+++	+++
Bacterial elastase in dilute ammonia	—	—	—	—	—	++	+++
Enzyme-free acid buffer alone	—	—	—	—	—	—	—
Enzyme-free alkaline buffer alone	—	—	—	—	—	—	—
Enzyme-free dilute ammonia alone	—	—	—	—	—	—	—

TABLE V

	Exposure Time (min)			
	60	90	180	24 Hours
Pepsin in acid buffer	+++	+++	+++	+++
Trypsin in alkaline buffer	—	—	—	—
Pancreatic elastase	+++	+++	+++	+++
Bacterial elastase	++	++	++	+++
Enzyme free acid buffer only	—	—	—	—
Enzyme free alkaline buffer only	—	—	—	—
Enzyme free dilute ammonia only	—	—	—	—

lesion and the nature of the elastotic material contained in it.

The natural history of elastofibroma excludes a true neoplasm and points towards a reactive or degenerative process, as suggested by Stemmermann and Stout (1962) and Barr (1966). Tighe *et al.* (1968) studied two cases with the electron microscope and reached a similar conclusion. We have examined the subscapular area in routine necropsies during the last year, and the thoracic surgeons have looked for similar lesions during thoracotomies. No case of elastofibroma has been found. As indicated by Barr (1966), tissue from the subscapular space contains elastic fibres but they are fewer in number and different in appearance from the fibres of elastofibroma. The suggestion that these lesions are the result of trauma, while not very convincing, is the best that can be offered.

As far as the elastotic fibres are concerned opinion has been divided as to whether they are true elastic tissue (elastin) or allied to the degenerate elastotic material seen in senile elastosis.

As a means of settling this question classical histological staining techniques have two disadvantages. Denatured collagen and collagen breakdown products undergo physicochemical changes and acquire some of the staining properties of elastin (Ramachandran 1955; Rich and Crick, 1955). Secondly elastic fibres retain their structure after they have ceased to take up elastic stains (Partridge and Davis, 1955; Saxl, 1957). The enzyme experiments were used in an attempt to overcome these disadvantages. Pepsin was of particular interest,

since Tunbridge *et al.* (1952) by treating native collagen with pepsin, claim to have produced material which, in the electron microscope and in staining reactions, resembled the elastotic material seen in senile elastosis. We did not observe any increase in the amount of tissue taking up the Sheridan stain. In our hands pepsin brought about complete digestion of the elastotic material in all three materials with loss of affinity for Sheridan's stain. Both trypsin and pancreatic elastase have a high affinity for collagen breakdown products while elastin, consistent with its very low lysine and arginine content, is resistant to tryptic hydrolysis. Crystalline trypsin had virtually no effect on the tissues studied while both preparations of elastase digested all three. Although detailed amino acid analysis might clarify the position further, we feel that the results of enzyme digestion show that all the elastotic material examined contained elastin. It must also be stressed that there is no general agreement as to the precise nature of the elastotic material in senile elastosis. Using the electron microscope Tunbridge *et al.* (1952) and Niebauer and Stockinger (1965) believed that it came from collagen while Banfield and Brindley (1963), also using the electron microscope, thought that it came from elastin. Until this problem is solved it seems unwise to suggest that as far as the fibres in elastofibroma are concerned, a choice must be made between elastin and senile degeneration of collagen. The distinction may be quite unreal and histochemical stains and enzyme studies suggest that elastofibroma fibres are composed largely of elastin. From the practical point of view it is extremely important not to interpret the lack of encapsulation, the adherence to the rib cage, and the infiltration of surrounding tissues as indicating a malignant neoplasm. Local excision is adequate treatment for this condition.

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