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Intravascular Papillary Endothelial Hyperplasia in the Skin and Subcutaneous Tissue

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Summary. Twenty-four cases of Intravascular Papillary Endothelial Hyperplasia (IPEH) have been studied. IPEH comprises approximately 2% of benign and malignant vascular tumours of the skin and subcutaneous tissue. This peculiar tumour-like process lacks specific clinical characteristics and its diagnosis must be based on microscopic examination. Histologically it is characterised by a papillary proliferation of endothelial cells forming vascular channels, commonly assocaited with thrombus and in some cases simulating angiosarcoma. – Follow-up of 10 cases indicates a benign clinical course.

Key words: Intravascular papillary endothelial hyperplasia – Skin and subcutaneous tissue – Benign condition – Diagnosis based on histology.

Introduction

Recently, attention has been focused on a peculiar tumour-like process of the skin and subcutaneous tissue described under different names: Intravascular papillary endothelial hyperplasia (Barr et al., 1978; ClearKin and Enzinger, 1976; Kreutner et al., 1978), intravascular endothelial proliferation (Cozzutto et al., 1979), intravascular angiomatosis (Salyer and Salyer, 1974), Masson's pseudoangiosarcoma (Kuo et al., 1976) and vegetant intravascular haemagioendothelioma (Amérigo et al., 1979). This benign lesion is characterised histologically by papillary endothelial proliferations confined within a vascular lumen and was first described by Masson (1923) as "hémangioendothéliome végétant intravasculaire" in haemorrhoidal veins. Similar papillary endothelial proliferations have been reported in thrombotic blood vessels (Navarro and Sánchez, 1977; Salyer and Salyer, 1975) and induced experimentally in animals by techniques including irradiation (Ardlie and Schwartz, 1968; Berry and Amérigo, unpublished observations).

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Several articles emphasise the danger of misdiagnosing angiosarcoma from superficial histological similarities (Barr et al., 1978; ClearKin and Enzinger, 1976; Cozzutto et al., 1979; Kuo et al., 1976; Salyer and Salyer, 1974; Salyer and Salyer, 1975) and, occasionally from a misleading clinical picture (Barr et al., 1978).

We have reviewed the vascular tumours of the skin and subcutaneous tissue in the files of a general hospital with the aim of studying the relative incidence, histological and clinical characteristics of this little known entity.

Material and Methods

All the surgical cases recorded as benign or malignant vascular tumours of the skin and subcutaneous tissue in the files of the Institute of Pathology of The London Hospital between 1909 and 1978 were reviewed (1217 cases). In reviewing these tumours we followed the classification of Johnson (1976) for vascular tumours of the skin and that of Stout and Lattes (1969) for the subcutaneous tissue. Twenty-four cases fulfilling the histological criteria of this tumour-like process were selected. In each case in our series the specimen was serially sectioned and routinely stained with haematoxylin and eosin. Masson's trichrome, Wilder's reticulin and Verhoeff van Gieson for elastic fibres were used in some cases. Clinical records were reviewed and where practicable the general practitioners were contacted for follow-up information.

Results

In the 24 cases there was a relative preponderance of female patients, with a ratio 2:1. The age at presentation ranged from 2 to 71 years. There was no preffered site for the lesion. The commonest site was the face (10 cases), followed by the hands and fingers (7), neck (2), and chest, leg, thigh, axilla and groin.

The most frequent clinical sign was the development of a recent swelling. The lesion commonly appeared as a tender or firm mass or nodule which was red or bluish in colour (Fig. 1). The duration of the lesion varied between 10 days and 20 years in the 14 cases where an adequate history was available. A history of preceding trauma was obtained in one patient who had a recurrence of the lesion. In one case multiple nodules were present. One of the patients was treated with radiotherapy several months before excision.

The most frequent clinical diagnosis made was haemangioma (10 patients), followed by naevus (4), epidermoid cyst (3), lipoma (3), granuloma pyogenicum, wart, glomus and facial lymph gland. No lesion was considered malignant before excision. The management in all the patients, was by local excision.

Follow-up information was obtained in 10 cases and ranged in duration from 1 to 53 years. Three patients presented with recurrences of the lesion (3, 12 and 18 months); after the second excision the lesion did not recur.

Pathological Features

The excised specimen was usually reported as a pseudo-encapsulated mass containing small spaces filled by haemorrhagic material. The size of the lesion

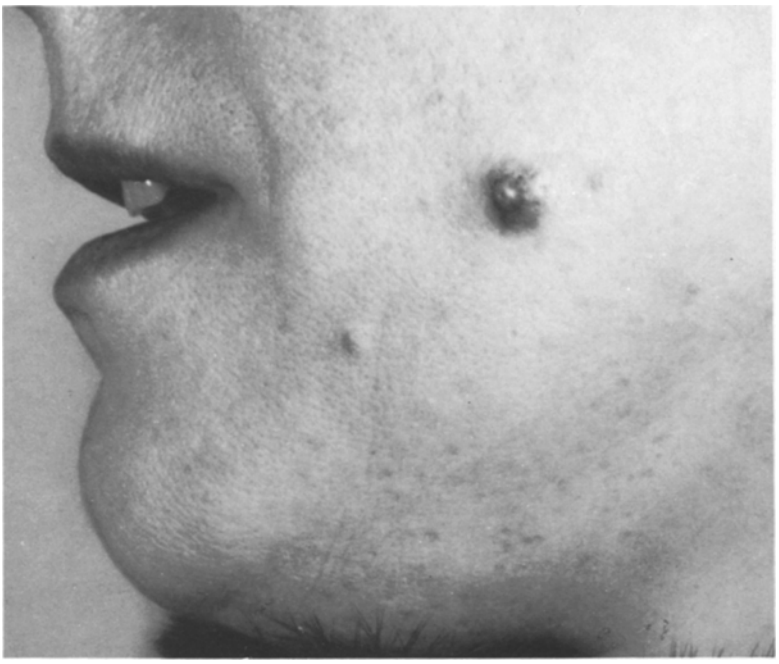

Fig. 1. Clinical appearance of intravascular papillary endothelial hyperplasia: prominent 0.6 cm soft nodule of left cheek in 37 year old woman

varied from 0.2 to 4 cm. Seventeen cases were located in the skin and seven in subcutaneous tissue, including muscle.

Seventeen cases were reported originally as haemangioma with organising thrombus; other histological diagnoses were haemangioma (4), papillary lymphangioma, angiokeratoma and serpentine aneurysm. None was reported as angiosarcoma.

Histologically the lesion presented two different patterns: a pure form, within a vascular space (6 cases) or a mixed form consisting of a focal change in cavernous haemangioma (14 cases), capillary haemangioma (2) and lymphangioma circumscriptum (2).

The microscopic features, exhibited by these 24 cases were similar: the most distinctive finding was a mass of papillary formations, covered by endothelial cells and confined within one or several vascular spaces (Fig. 2). These papillary structures gave rise to anastomosing vascular channels, of varying calibre, composed of a single layer of swollen endothelial cells around a dense hyalinized stroma, generally devoid of vessels although occasionally papillae centred by capillaries were seen (Figs. 3 and 4). Cellular pleomorphism, mitotic figures and solid areas were noted in some of the cases (Figs. 5 and 6), but necrosis of the papillary processes was never seen. Thrombus was commonly found in various stages of organization. This thrombus seemed to serve as a matrix for the development of the papillary endothelial proliferations (Fig. 7). Three

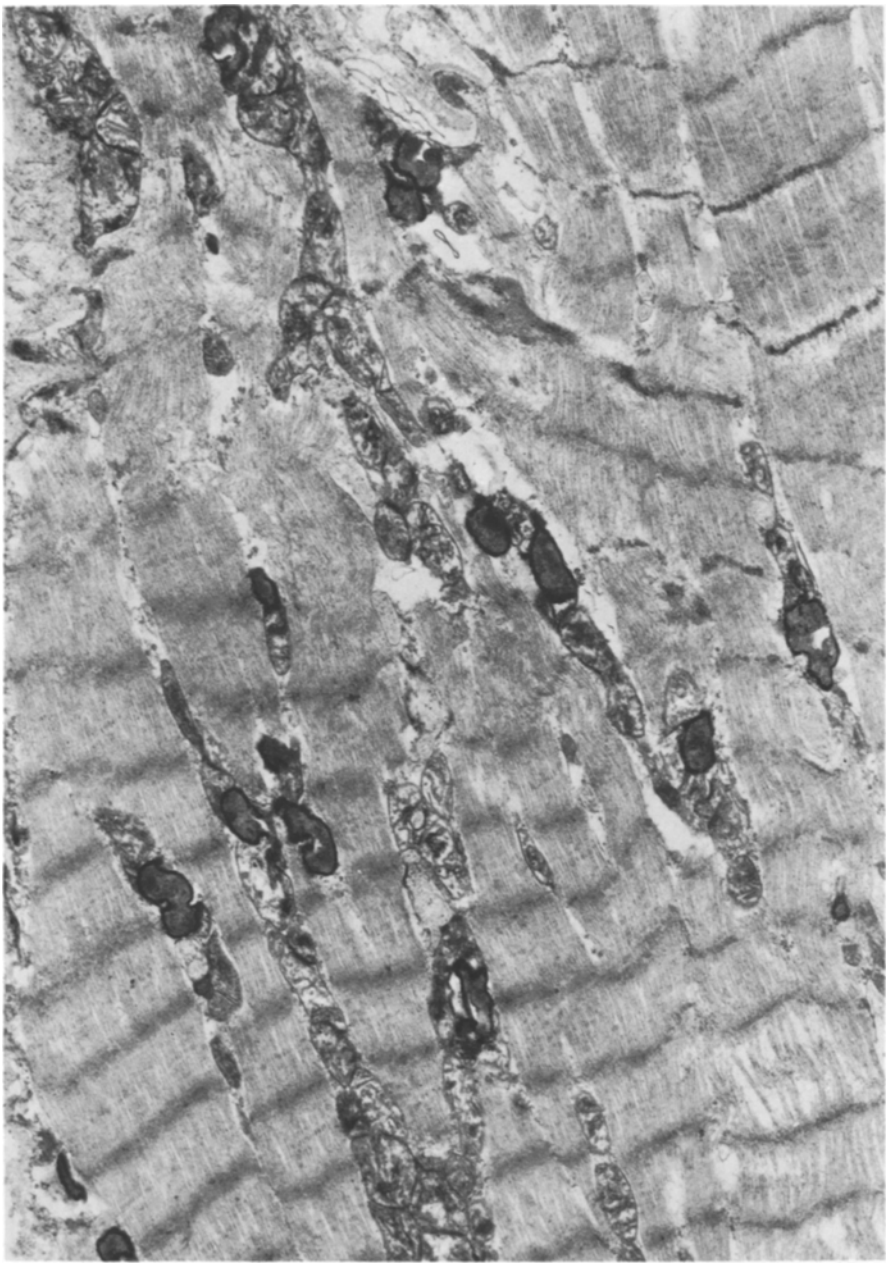

Fig. 2. Papillary proliferations confined within a dilated vascular space. H & E, ×15

Fig. 3. Vascular channels composed of hyalinized papillae, devoid of vessels and covered by a single layer of swollen endothelial cells. H & E, ×250

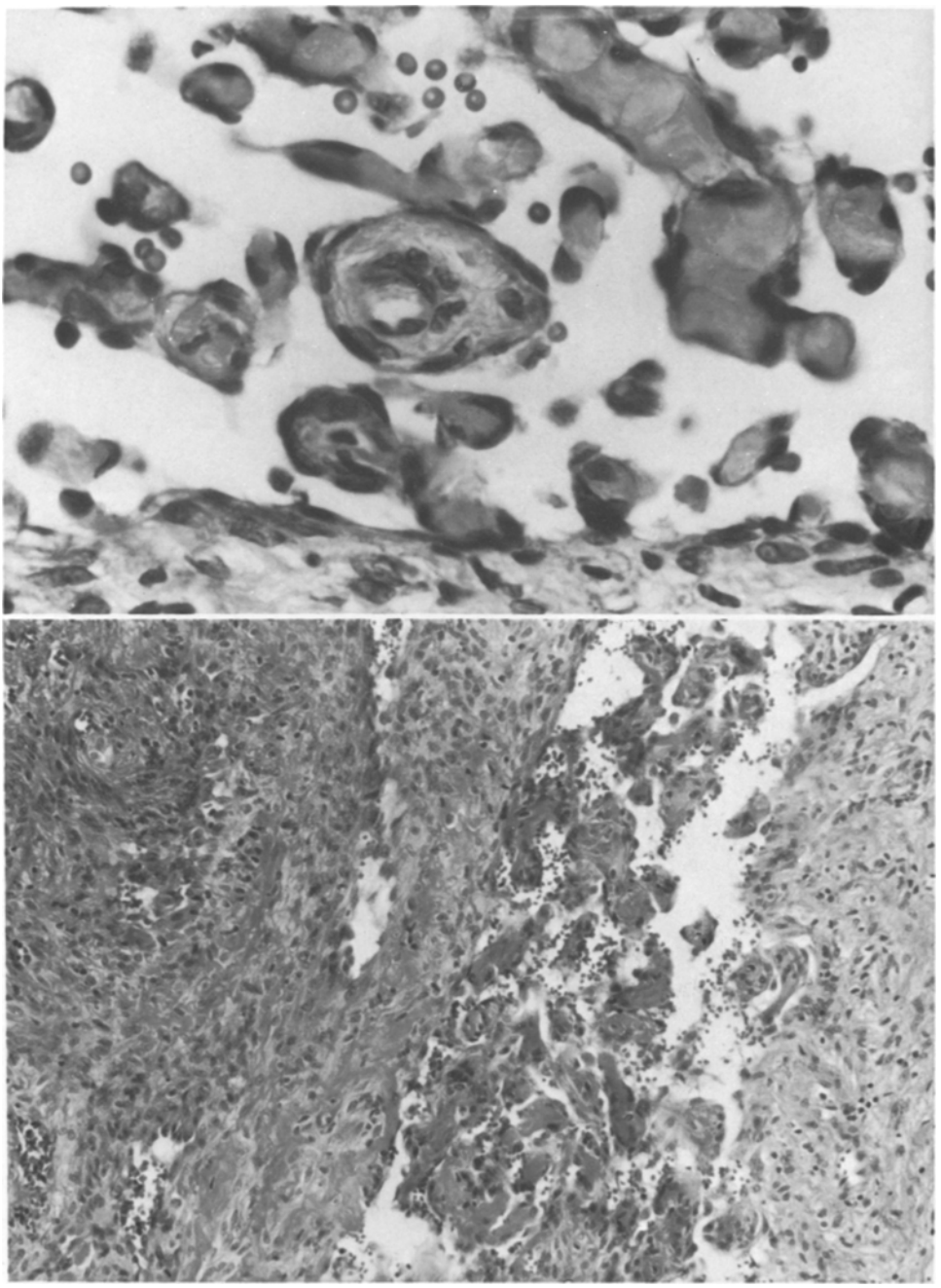

Fig. 4. Papillary structures originating from the endothelium and floating free in the vascular space are present. Occasionally, capillaries are seen in the centre of some papillae. H & E, × 1,000

Fig. 5. Papillary areas alternating with solid endothelial proliferations. H & E, × 100

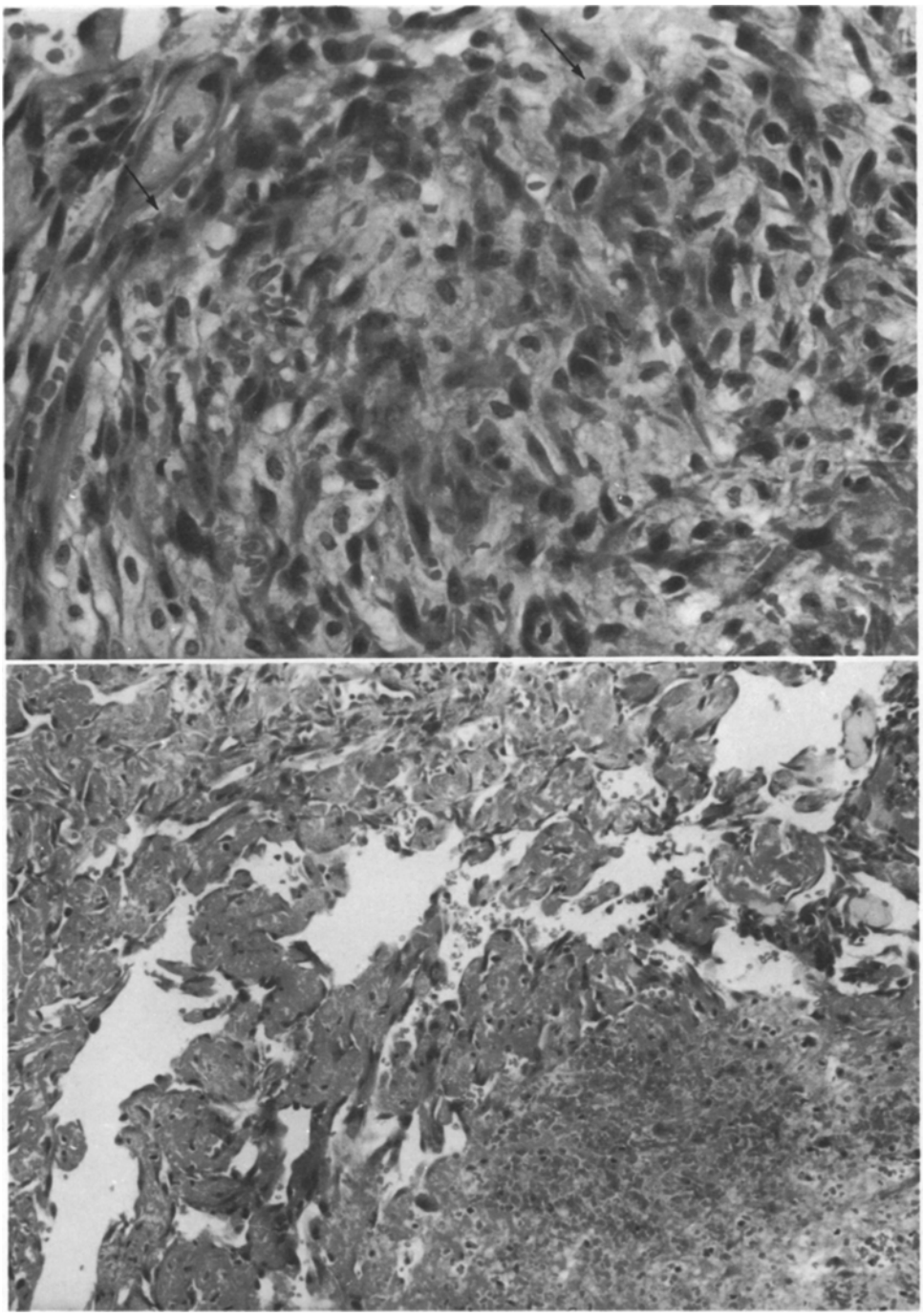

Fig. 6. Focal nuclear atypia and mitosis (*arrows*) are occasionally observed. H & E, ×1,000

Fig. 7. Hyalinized papillary stalks. Note transition from organizing thrombus in the right side of the field. H & E, ×250

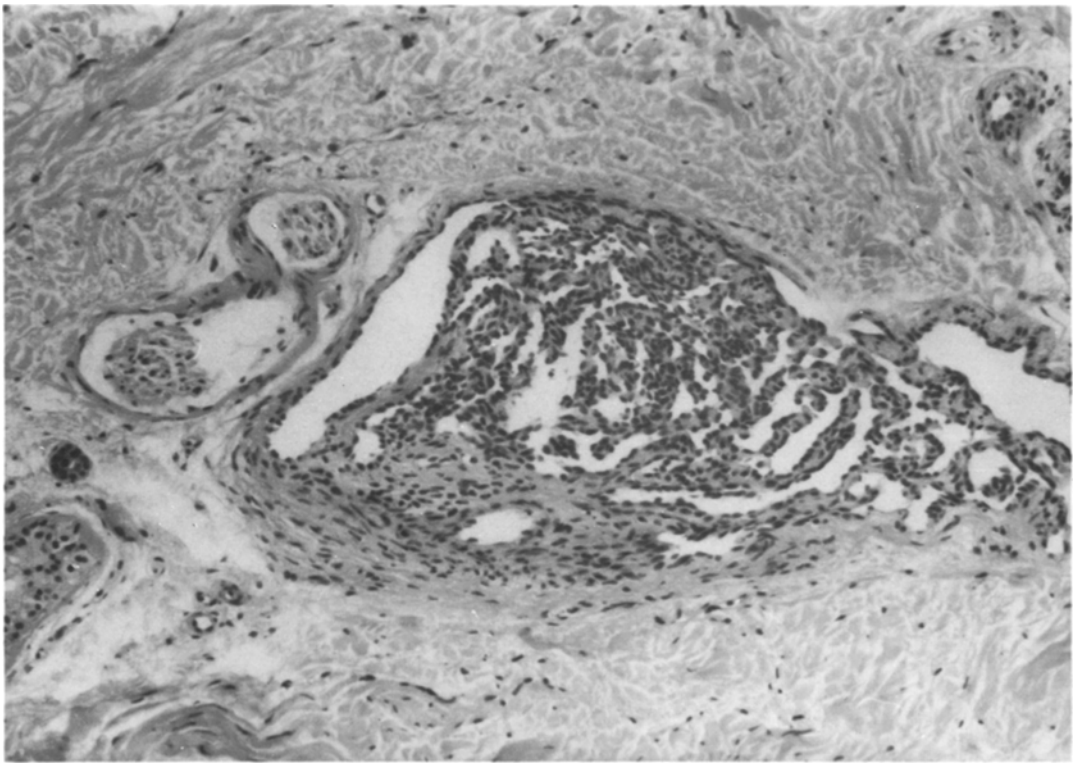

Fig. 8. Anastomosing vascular fronds not associated with thrombus constituting a focal change in a lymphangioma circumscriptum. H & E, ×100

cases showed no evidence of thrombotic phenomena and one of these, which constituted a focal change in a lymphangioma circumscriptum, appeared to be identical histologically with the case originally described by Masson (Fig. 8). The other two cases where thrombi were not seen were mixed forms constituting a focal change in a lymphangioma circumscriptum and cavernous haemangioma, respectively. Haemosiderin deposition was encountered both inside and outside the vascular spaces, principally in the less papillary areas and in the surrounding connective tissue. Inflammatory cells were scanty and only occasional lymphocytes and macrophages were identified in some of the cases.

In two of the three recurrent cases, papillary proliferations were present in the first specimen. In the third case papillary formations appeared in the recurrent lesion 18 months later; this patient had a history of preceding trauma before the first excision. In the patient with multiple nodules only one of these showed the singular histology of IPEH; the other two nodules presented the usual microscopic features of a cavernous haemangioma.

Discussion

In a previous paper (Amérigo et al., 1979) we have called this entity vegetant intravascular haemangioendothelioma; however here we refer to it as intravascu-

lar papillary endothelial hyperplasia (IPEH). This is the most frequently used name in the English literature (Barr et al., 1978; ClearKin and Enzinger, 1976; Kreutner et al., 1978; Navarro and Sánchez, 1977), is more descriptive and less confusing than haemangioendothelioma (Civatte and Harter, 1967; Fievez and Hamels, 1977; Masson, 1923) or Masson's pseudoangiosarcoma (Kuo et al., 1976). The number of reported cases of IPEH in the skin and subcutaneous tissue is 80 (Amérigo et al., 1979; Barr et al., 1978; Civatte and Harter, 1967; ClearKin and Enzinger, 1976; Cozzutto et al., 1979; Fievez and Hamels, 1977; Kreutner et al., 1978; Kuo and Gómez, 1979; Kuo et al., 1976) not including three of the eleven cases reported by Warner and Wilson-Jones (1968) as "pyogenic granuloma recurring with multiple satellitosis" and also two cases described by Dupont and Lachapelle (1964) as angiomatous growths in the lumina of angiomas taken from a patient with Maffucci-Kast syndrome, which are, judging from their histological descriptions and illustrations, probably IPEH developing as a focal change in pyogenic granuloma and haemangioma respectively. Moreover, one case of angioendothelioma reported by Gold (1970) and later referred to by Wilson-Jones (1976) as "acquired progressive lymphangioma" seems to be an IPEH developing in a lymphangioma very similar to the cases reported by Kuo and Gómez (1979) and two of the cases presented in this article. None of these cases of IPEH developing in lymphangioma showed evidence of thrombotic phenomena as would be expected.

Our study shows that IPEH is not uncommon, representing approximately 2% of 1,217 cases of benign and malignant vascular tumours of the skin and subcutaneous tissue.

Several papers point out that angiosarcoma is a potential differential diagnosis (Barr et al., 1978; ClearKin and Enzinger, 1976; Cozzutto et al., 1979; Salyer and Salyer, 1974; Salyer and Salyer, 1975), but we feel that these authors have overemphasized this point. In the articles that we have reviewed only one clinical diagnosis of a malignant tumour (squamous carcinoma) was made (Amérigo et al., 1979); four lesions were originally diagnosed as haemangiosarcoma (Cozzutto et al., 1979; Kuo et al., 1976). We believe that the clinical presentation of cutaneous angiosarcoma (large and extensive lesion, usually with smaller outlying nodules, necrosis and ulceration, commonly affecting the elderly), the gross characteristics (non-circumscribed and infiltrating mass) and histological features (presence of necrosis, the extension of the tumour outside the vascular space, evidence of more than two layers of endothelial cells in the papillary formations, abundant cellular pleomorphism and mitosis) are findings which readily differentiate it from IPEH. We consider that the most difficult differential diagnosis is from the controversial condition described by Rosai and Akerman (1974) as intravenous atypical vascular proliferation; however, in this process the endothelial proliferation is solid rather than papillary, is not so closely associated with thrombus, may extend into the vessel wall (Cozzutto et al., 1979) and is interpreted by some authors (Kuo et al., 1976; Rosai and Akerman, 1974) as a morphological variant of angiolymphoid hyperplasia with eosinophilia (Meheregan and Shapiro, 1971). Moreover, a rare condition referred to by Wilson-Jones (1976) as "acquired tufted angioma" seems to have a histology similar to IPEH. There are, nevertheless, important differences;

in the illustrations shown by the author thrombi are not present and the endothelial proliferations are formed by uncannalized capillaries. Vascular tumours reported as malignant endovascular papillary angioendotheliomas (Dabska, 1969; de Dulanto and Armijo-Moreno, 1973; Hazard, 1954) are variants of angiosarcoma presenting in children and showing a florid papillary growth, infiltration of the stroma and a tendency to metastasize to regional lymph nodes.

The nature of IPEH is still a matter of speculation, although the general opinion is that it is a reactive process and not a true neoplasia. It seems probable that IPEH results from organization of a thrombus (Amérigo et al., 1979; Barr et al., 1978; ClearKin and Enzinger, 1976; Cozzutto et al., 1979; Salyer and Salyer, 1974; Salyer and Salyer, 1975). Nevertheless, we agree with Kuo et al. (1976) that in some instances IPEH may be regarded as a primary event, principally in those lesions where thrombi are not seen and the unique histological finding is anastomosing vascular fronds growing within a vascular space either as a solitary lesion or as a focal change in a benign vascular tumour.

Despite the incomplete follow-up of our series (10 cases) IPEH certainly seems to be a benign lesion. Follow-up of some larger series (ClearKin and Enzinger, 1976; Kuo et al., 1976) showed no evidence of metastasis. Nevertheless, IPEH may recur if it arises in a primary vascular lesion which may itself recur.

The diagnosis of this condition must be based on microscopic examination since IPEH lacks specific clinical findings.

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