DISCUSSION

The presence of pseudo-pseudohypercalcaemia in association with Waldenström's macroglobulinaemia had resulted in an erroneous provisional diagnosis of primary hyperparathyroidism. In patients with Waldenström's macroglobulinaemia, genuine hypercalcaemia is rare^{1,2} and pseudohypercalcaemia is even rarer.^{3,4} Indeed, there were only two case reports of pseudohypercalcaemia in Waldenström's macroglobulinaemia due to either calcium binding to the IgM paraprotein³ or paraprotein interference in the calcium Arsenazo III method.⁴ The findings for this patient are consistent with the notion of IgM paraprotein interference with the calcium Arsenazo III method and the consequent pseudo-pseudohypercalcaemia.⁴ The mechanism of the interference is likely to be increased turbidity produced by paraprotein interaction with the acidic medium of the calcium Arsenazo III reagent and not with the alkaline CPC method.⁴

It is possible that if the pseudo-pseudohypercalcaemia had not been recognised, this patient would have had an unnecessary neck exploration, since persistent hypercalcaemia (as in this case) is an indication for parathyroid surgery irrespective of symptoms or complications of primary hyperparathyroidism.⁵

CONCLUSION

We report a case of apparent primary hyperparathyroidism due to pseudo-pseudohypercalcaemia in association with Waldenström's macroglobulinaemia.

We conclude that it is important to identify patients with falsely elevated serum calcium levels in patients with paraproteinaemias to prevent unnecessary investigations, erroneous diagnosis and potentially inappropriate treatment.

Since pseudo-pseudohypercalcaemia in association with Waldenström's macroglobulinaemia may be multifactorial in origin, we suggest that apparent hypercalcaemia in these

patients should be confirmed by measurement of plasma ionised calcium with or without urinary calcium excretion.

Authors' affiliations

A Elfatih, Department of Clinical Biochemistry, Whipps Cross University Hospital, Leytonstone, London, UK

N R Anderson, Department of Clinical Biochemistry, George Elliott Hospital, Nuneaton, UK

M N Fahie-Wilson, Department of Clinical Biochemistry, Southend Hospital, Prittlewell Chase, Westcliffe-on Sea, UK

R Gama, Department of Clinical Chemistry, New Cross Hospital, Wolverhampton, UK; Department of Research Institute, Healthcare Sciences, Wolverhampton University, Wolverhampton, UK

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Informed consent was obtained from the patient described in this report.

Correspondence to: Dr A Elfatih, Department of Clinical Biochemistry, Whipps Cross University Hospital, Leytonstone, London E11 1NR, UK; abubaker.elfatih@whippsx.nhs.uk

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A distinctive vulval fibroma of so-called prepubertal type in a postmenopausal patient

O O Ajibona, C J Richards, Q Davies

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The case of a 65-year-old female patient who has had a large right vulval mass for over 30 years is reported here. The mass was excised, but the hypocellular mesenchymal tumour was difficult to classify histologically. On further specialist assessment, it was found to be identical to the recently recognised distinctive prepubertal vulval fibroma. These are very rarely reported in children, and till now, has never been reported in an adult.

CASE REPORT

A 65-year-old postmenopausal woman was referred with a painless vulval swelling that the patient had had for over 30 years. It had gradually increased in size over the past few years, causing discomfort during sexual intercourse and when riding a bicycle. It also caused an embarrassing bulge in her leotard as she taught yoga. She remained fit and healthy. There was no previous medical history of note. Examination revealed a 9 cm × 5 cm × 5 cm soft, non-tender, non-reducible right vulval mass with normal skin fully mobile over it. It was partially fixed to underlying structures (fig 1).

MRI of the pelvis and perineum revealed a diffuse abnormality causing enlargement of the right side of the vulva and perineum extending from the infrapubic region to the anal margin. There was extensive signal change within the perineal fat. No discrete mass was seen and no lymphadenopathy was detected.

An initial incisional biopsy suggested that the unusual vulval mass was a benign smooth muscle hamartoma without atypia or malignancy. Surgical excision of the mass was performed with excellent cosmetic results followed by further histological assessment. This showed that the lesion was composed of bland fibroblastic cells associated with abundant stromal collagen, which seemed to be infiltrating and replacing large parts of the submucosal tissue, entrapping nerves, vessels and adipose tissue and extensively disrupting normal pre-existing smooth muscle (fig 2). The cellularity was increased above the appearances, normal at this site. The individual spindle cells had pale distinct cytoplasm with bland nuclei and no conspicuous mitotic activity. Immunostains showed CD34 positivity whereas S-100 protein and smooth muscle actin were negative. The tumour stained oestrogen and progesterone receptor negative. As the lesion was difficult to classify, a specialist histological opinion was sought.

Figure 1 Vulval mass with scar of previous incisional biopsy.

Morphologically, this lesion was considered to be identical to a distinctive vulval fibroma of so-called prepubertal type.

DISCUSSION

This represents the first report in the literature of a distinctive vulval fibroma of the prepubertal type in an adult. Moreover, our patient was postmenopausal. This mesenchymal tumour has only recently been recognised by Iwasa and Fletcher¹ who analysed a series of 11 prepubertal girls with an age range of 4–12 years. As in their series, the tumour was hypocellular and poorly margined consisting of bland spindle-shaped cells and stromal collagen. There was diffuse infiltration between pre-existing local tissues such as neural and smooth muscle. Cytological atypia and mitotic hyperactivity were absent. The tumour stained for CD34 but not for S-100 or smooth muscle actin.

The main differential diagnosis is with a desmoplastic fibroblastoma or collagenous fibroma, but this usually forms a discrete mass with more distinctive larger stellate fibroblastic cells and does not stain for CD34.^{2,3} The other differential diagnosis included a number of mesenchymal and tumour-like lesions, the most important of which was aggressive angiofibroma. This tumour shares some histological features with vulval fibroma but, unlike the latter, has a diffusely myxoid stroma with delicate collagen fibrils and perivascular smooth muscle proliferation. Vulval fibroma, by contrast, contains short bundles of thick, wavy collagen, myxoid change is not so diffuse and there is no perivascular smooth muscle proliferation. The cells of aggressive angiofibroma are immunoreactive for desmin whereas those of vulval fibroma are not. Cytogenetics can be used to differentiate the two, but this is not widely available and routine histological and immunohistochemical examinations can differentiate between the two in most cases.⁴

Other differential diagnosis included angiofibroblastoma, cellular angiofibroma, fibroepithelial stromal polyp, neurofibroma and desmoplastic fibroblastoma. Angiofibroblastoma is a benign well-circumscribed vulval tumour with a thin fibrous tissue capsule, variable cellularity, prominent thin-walled blood vessels and desmin positive tumour cells grouped around vessels. Cellular angiofibroma is a relatively well-demarcated tumour, which is invariably more cellular than vulvar fibroma and often

Figure 2 Bland fibroblastic cells and collagen infiltrating muscle and adipose tissue of the vulva (magnification $\times 300$).

contains adipocytes towards the periphery of the tumour. The vessels are more numerous and usually hyalinised. Neurofibroma occurs rarely as a solitary lesion at this site. Although, the stroma can appear similar to vulval fibroma the spindle cells are tapered with wavy, buckled nuclei and show consistent S-100 immunoreactivity. Fibroepithelial stromal polyps can rarely have a myxoid stroma and contain stellate-shaped spindle cells with multinucleate cells, which extend to the base of the epithelium. The lesional cells are oestrogen and progesterone receptor positive.

Although non-aggressive, prepubertal vulval fibromas have been shown to recur with incomplete excision. A complete surgical excision was desirable in this patient but this was technically impossible because of the extent of the tumour and the desired cosmetic results. Since our patient had a slow-growing benign tumour re-excision is unlikely to be required in this 65-year-old. The patient had been counselled appropriately before surgery and was made aware of the possibility of recurrence. She remains well about 20 months after surgery with no sign of recurrence of the lesion. She remains under biannual surveillance.

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Authors' affiliations

O O Ajibona, Q Davies, Department of Obstetrics and Gynaecology, University Hospitals of Leicester, Leicester, UK

C J Richards, Department of Histopathology, University Hospitals of Leicester, Leicester, UK

Competing interests: None declared.

Correspondence to: Miss O O Ajibona MRCOG, Department of Obstetrics and Gynaecology, Leicester Royal Infirmary, Infirmary Square, Leicester LE1 5WW, UK; funmi.ajibona@swbh.nhs.uk

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