



**Warren Weightman**

MBBS, FRACP, FACD, is Director of Dermatology, The Queen Elizabeth Hospital, Woodville, South Australia.

**Patrick J Phillips**

MBBS, MA(Oxon), FRACP, MRACMA, GDipHlthEcon(UNE), is Senior Director, Department of Endocrinology, The Queen Elizabeth Hospital, South Australia. patrick.phillips@nwhs.sa.gov.au

# Pigmented and thickened axillary folds

Andrew, 45 years of age, presents with a 12 month history of dark, thickened skin in both axillae. He is concerned about the appearance and would like to know how to treat it. He is moderately obese, with a body mass index (BMI) of 31.2 kg (BMI = weight [kg] ÷ height<sup>2</sup> [m<sup>2</sup>]) but is otherwise well and on no medication. There is no family history of any similar skin disorder.



## Question 1

What is your initial diagnosis and where else would you examine clinically?

## Question 2

What associations are there with this disorder and what investigations would you undertake?

## Question 3

What treatment would you consider?

## Answer 1

The most likely diagnosis is acanthosis nigricans (AN). Key clinical features are pigmented areas (macules through to patches and plaques) which may be 'velvety' and usually symmetrical. The axilla is the most common site but you would examine the posterior and lateral neck, groins and other flexures such as submammary folds and umbilicus. Rarely palms, soles and mucous membranes can be affected.

In early cases, causes of hyperpigmentation such as drug induced or postinflammatory need to be considered. In later cases where there is significant thickening, pigmented seborrhoeic, keratoses or skin tags should be considered.

## Answer 2

There is no gender difference in incidence. An American study<sup>1</sup> showed that the prevalence of AN was highest in black people (13.3%), then Hispanic (5.5%), and lowest in white people (5%). There is an inherited form (irregularly autosomal dominant) which usually presents in childhood and often becomes more severe after puberty.

The most common association is with insulin resistance, which occurs in all types of AN. Insulin resistance is seen often with obesity, diabetes mellitus and polycystic ovarian disease. Insulin growth factor (IGF-1) receptors are present in skin keratinocytes and are stimulated by high levels of insulin. In malignant AN, transforming growth factor-alpha (TGF-alpha) works through amplification of epidermal growth factor receptors.

Acanthosis nigricans is also associated with syndromes that share a relative tissue resistance to insulin. These include: Praeder-Willi syndrome, Crouzon syndrome and Seip-Lawrence syndrome. Drugs such as nicotinic acid, fusidic acid and oral contraceptives can induce these changes.

Acanthosis nigricans can be associated with malignancy, particularly an adenocarcinoma. In these cases there is usually rapid progression and more extensive involvement. The palms and soles are frequently thickened and the nails may be brittle or ridged. The mucous membranes are involved in at least 50% of cases and warty, papillomatous thickening around the eyes and lips may be a presenting symptom. There is often severe itching and irritation. The onset of AN may precede the diagnosis of the malignancy. Reported malignancies include: gastric, bladder, kidney, bile duct, thyroid, lymphoma, oesophagus, bronchus and rectum.

Investigations are directed to associated causes and include fasting blood glucose and consideration of the presence of polycystic ovary syndrome. If a malignancy is suspected then investigations should aim to identify the type, site and stage of the malignancy and potential treatment.

## Answer 3

In cases associated with obesity, the most effective treatment is weight loss. The thickness and velvety texture resolve slowly. The pigmentation will fade but may not clear completely. Any underlying disorder should also be treated and if a malignancy is found and removed, there is often good improvement. Unfortunately any malignancy is often advanced at the time of diagnosis. Topical treatment includes tretinoin cream or keratolytics such as salicylic acid 5–10% in aqueous cream or a glycolic acid cream.

Conflict of interest: none declared.

## Reference

1. LaFleur L, Wernli B, Allen PS, Wild RA. Acanthosis nigricans. *Skin & Aging* 2006;14:50–7.

**afp** CORRESPONDENCE email: [afp@racgp.org.au](mailto:afp@racgp.org.au)