



Antigliadin antibody testing for coeliac disease in children under 3 years of age is unhelpful

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verruca vulgaris or seborrheic keratosis.³⁻⁵ Investigation of its association with human papillomavirus has also been studied.⁶ Of importance is recognition of IFK as a benign epithelial neoplasm that can occur on the face and eyelids of the elderly and not to confuse it with malignancy. This case is unusual with the presence of sebaceous-like areas in an IFK. Basaloid cells may be follicular in origin or related to sebaceous gland units. However, the presence of mature sebocytes in association with a hair follicle is unexpected. Further, given the lack of sebaceous glands and no reports of mature sebocytes in IFK, we believe the basaloid cells admixed with mature sebocytes are not follicular in origin and represent true sebaceous differentiation. To our knowledge, this is the first reported case.

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Cutaneous actinomycosis: the great mimicker

Actinomycosis is an indolent, suppurative and chronic granulomatous infection caused by a Gram-positive organism that was initially thought to be a fungus.^{1,2} Actinomycosis is rare with estimated incidence of one case per institution per year, with male predominance.³ Precipitating factors of cervicofacial infection are related to dental and maxillofacial trauma. We describe an interesting case of facial actinomycosis that was misdiagnosed as sebaceous cyst and revealed later by histopathological findings of the tissue biopsy.

A 19-year-old healthy adolescent presented with a swelling on the chin that intermittently inflamed with pus discharge for 4 years. There was no exposure to

tuberculosis infection and no prior facial or dental trauma. The swelling was soft, non-tender, non-fluctuant and well defined measuring 1×2 cm. There was a central punctum with no skin erosion or fistula. Systemic examinations were unremarkable. It was excised for aesthetic reasons. Histopathological finding was reported as actinomycosis (fig 1). Haematological investigations and imaging were unremarkable. Although the swelling recurred 2 months later, he was successfully treated with 4 weeks of intravenous ampicillin followed by 6 months of oral antibiotic.

Actinomycosis was first described in 1877 by Bollinger as the cause of "lumpy jaw" in cattle.¹ The micro-organisms are of facultative anaerobic or microaerophilic Gram-positive bacteria classified under the genus *Actinomyces*.¹ Prompt diagnosis is difficult because of paucity of the clinical symptoms. It is thus designated as the "great masquerader" of the head and neck.³

Actinomyces is strictly endogenous to the host, residing in the oral cavity, or genitourinary or gastrointestinal tract. Breakdown of skin barrier caused by trauma may play a role in its pathogenesis.⁴

Clinical presentation includes insidious onset of constitutional symptoms such as fever, anorexia, malaise, weight loss and night sweats. Death due to actinomycosis is extremely rare.⁵

Histological examination shows the typical appearance of a sulphur granule in actinomycosis. The sulphur granule alone is not pathognomic, and diagnosis can be convincingly made with microbiological staining.^{6,7} A newer technique using fluorescein-isothiocyanate-labelled species-specific antiserum to stain the specimen is more simple and cost effective.⁸ Imaging modalities help to define the mass limits and extension for surgery.^{9,10}

Therapy with penicillin for 3 months is the mainstay of treatment.^{5,11} Alternatives are erythromycin, clindamycin, sulfona-

mide, tetracycline, lincomycin and amoxicillin.^{10,12,13} However, the duration of treatment remains an area of frequent debate. A good response after 3 months of therapy has been reported.^{14,15}

Actinomycosis remains a diagnostic challenge. Fortunately, infection in humans has become rare because of improvements in oral hygiene and effectiveness of antibiotic therapy.

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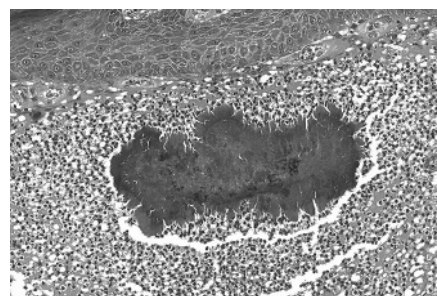


Figure 1 Skin biopsy. This section shows skin lined with keratinising stratified squamous epithelium with a nodule composed of a dense mixed inflammatory cells infiltrate composed of neutrophils, plasma cells and lymphocytes. A group of filamentous bacteria forms a "sulphur granule" with peripheral Hoepli-Splendore reaction. The bacterial colony stains positive for Gram, periodic acid-Schiff and Grocott stain.

Antigliadin antibody testing for coeliac disease in children under 3 years of age is unhelpful

It has been our practice to perform immunoglobulin (Ig)A anti-tissue transglutaminase

(tTG), IgA/IgG antiendomysial (EMA) and IgA/IgG antigliadin (AGA) antibody tests for children under 3 years of age being investigated for coeliac disease. This was based on data showing that EMA may be negative in children. In a study of 277 children under 2 years of age who had biopsy-proven untreated coeliac disease, 88% were EMA positive, 100% were IgG-AGA positive, and 84% were IgA-AGA positive. Eleven per cent of patients were positive for AGA only (though 25% of these were positive for IgG-AGA only).¹ The overall AGA specificity is poor, especially that of IgG-AGA.² Importantly, over a third of AGA-positive young children became spontaneously negative over the following 3 years.³

Data on using AGA alongside recombinant human tTG-based tests are limited and study sizes are small. Equivalent sensitivity of tTG and EMA has been shown with AGA in 27 children with untreated coeliac disease (mean age 5.0 years),⁴ and a study of 30 children (median age 2 years; range 8 months to 12 years) showed superior sensitivity of tTG (93%) over EMA (90%) and AGA (60%/93% for IgA/IgG).² Day *et al* analysed 36 antibody-positive samples (IgA-EMA and/or IgG/IgA-AGA) in children aged 6 months to 15 years. Seven had biopsy-proven coeliac disease, of which two were positive by AGA (IgA and IgG) only.⁵

We therefore audited our use of AGA in children to determine if it added any value to the protocol.

The results of AGA tests performed between 1 January 2006 and 23 September 2007 in children under 3 years of age without a previous diagnosis of coeliac disease were collected. Until February 2007, all samples had IgG-EMA, IgA-EMA, IgG-AGA and IgA-AGA tests performed. From February 2007 IgA-tTG was performed in addition to the above on all samples.

All AGA-positive samples without other serological evidence of coeliac disease were identified. Case notes were retrieved for these patients and the diagnoses were established. Specific checks of histopathology records to 31 December 2008 were made to identify those that had had a duodenal biopsy performed.

One hundred and sixty-seven AGA tests were performed in children under 3 years of age, of which 24 had results above the 99.5 percentile of normal (2 IgA only; 18 IgG only; 4 IgA and IgG). Sixteen of these patients had no other serological evidence of coeliac disease (2 were positive for IgA-AGA only, and 14 for IgG-AGA only). Only 1 of these 16 children (with an established diagnosis of primary hypogammaglobulinaemia) went on to have a duodenal biopsy, which was normal. These 16 children with no serological evidence of coeliac disease apart from raised AGA were followed up for a median of 23 months (range 17–36 months). None had a final diagnosis of coeliac disease. Most were being investigated for poor weight gain that

resolved on follow-up. Three had food allergy, one had fetal alcohol syndrome, one had irritable bowel syndrome, and one had type 1 diabetes. In all the other cases a failure to thrive resolved on follow-up and the patients were discharged, including one patient who underwent a trial gluten-free diet and reintroduction to no effect.

If gliadin testing had not been offered, no diagnoses of coeliac disease would have been missed during the 21 month period. Based on the results of our audit, it appears that all AGA-positive results in the presence of negative tTG/EMA were false positives. It could be argued that the failure to identify any patient with coeliac disease in the group was due to lack of confidence in the AGA assay with a resultant failure to perform a biopsy. However, all of these patients had a clear final diagnosis or resolution of the problems that precipitated investigations for coeliac disease. Though coeliac disease was not specifically excluded by biopsy, the follow-up period and clinical outcomes were sufficient to make this diagnosis unlikely.

There are few studies of the role of AGA in screening programmes for young children in parallel with human recombinant tTG-based assays. The published literature shows that a small number of young children with early coeliac disease are positive for AGA only. However, this must be balanced against the large number of false-positive AGA results seen in this group of patients.

These data support the view that AGA testing of children under the age of 3 years being investigated for coeliac disease is not justified. In our cohort, the use of only tTG and/or EMA in these children would have reduced the false-positive rate without affecting the detection rate.

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BOOK REVIEW

The Washington manual of surgical pathology

Edited by Peter A. Humphrey, Louis P. Dehner, John D. Pfeifer. Published by Lippincott Williams & Wilkins, 2008, pp 784, paperback, \$59.95.

The Washington manual of surgical pathology has been edited by a team from the Washington University School of Medicine and is meant to be the surgical pathologist's equivalent of the much older and famous *Washington manual of medical therapeutics*. The book has a range of contributors, from senior professors to fellows in the Lauren V. Ackerman Laboratory of that centre. Despite the multiauthorship, the style of most of the chapters is uniform and of a very high standard; I have found the book immensely useful over the past two months in daily practice. I have kept it next to my microscope and used it numerous times, either to clarify small doubts or for bigger diagnostic problems.

Most of the book deals with the practical aspects of the art and science of surgical pathology. Thus, all chapters begin with a recap of about a page on the anatomy and histology of the organ, in order to lay the foundation for pathology. There is little on aetiology, mechanisms of disease or pathogenesis. Yet this is not entirely ignored; in the section on histology in the chapter on the larynx, for instance, the reader is reminded that Reinke's space has few capillaries and no lymphatics and that this is probably the reason that very few T1 glottic carcinomas have nodal metastases. The types of specimens received—biopsy and different types of resections—are discussed with reference to what sections to submit and why. An example is the statement in the section on testicular tumours, that additional sections must be taken if the histological tumour type does not correlate with the serum tumour markers—but with the additional counsel that such correlation may not always be perfect because metastatic deposits may contain different elements from the primary tumour.

Doubts I have recently looked up and clarified include colonic biopsy in graft-versus-host disease (GVHD) (where I learnt that immunohistochemical staining for cytomegalovirus should always be done in biopsies showing apoptosis and crypt damage, the diagnostic feature of GVHD). The chapters on the placenta and most of the male genitourinary system were particularly well written. Because of space constraints, however—remember, this is a manual, not a textbook—some lesions have