



# Influenza follicles and their buds as early diagnostic markers of influenza: typical images

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## Influenza follicles and their buds as early diagnostic markers of influenza: typical images

An article by Dr Kenzaka<sup>1</sup> in the 'Images in medicine' section of the *Postgraduate Medical Journal* reported that influenza follicles are noted in ATLAS SAKUMA.<sup>2</sup> However, there is no reference to influenza follicles in Chapter VII: Influenza of ATLAS SAKUMA. It instead refers to lymph follicles, and their typical cases are presented in Chapter I: Adenovirus. Furthermore, in Case 11 of Chapter VII: Influenza, lymph follicles that were suspected to be due to adenovirus infection were presented. Miyamoto and Watanabe<sup>3</sup> were the first in the world to report posterior pharyngeal wall follicles in influenza and named them influenza follicles. The statistical data and the morphological classification of influenza follicles reported by Kenzaka were all drawn from Miyamoto and Watanabe.<sup>3</sup> Moreover, the mean duration between the onset and

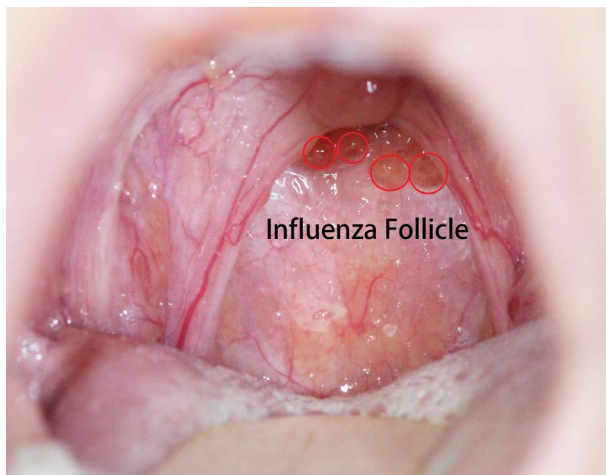
evaluation of novel influenza infections, as reported by Miyamoto and Watanabe,<sup>3</sup> was erroneously cited, as underlined in the following sentence: 'The sensitivity and specificity of influenza follicles observed  $7.8 \pm 5.3$  h (range, 3–20 h; median, 5 h) after onset were 95.4% and 98.4%, respectively, for the seasonal influenza diagnosis'.

Kenzaka claims that ATLAS SAKUMA<sup>2</sup> is available only in Japanese, with no English translation. However, Sakuma published an English translation<sup>4</sup> in 2008, where pharyngeal observations in influenza infections were noted as follows: 'the manifestations of oral cavity, fauces and pharynx are not severe, and usually only slight redness and slight swelling are observed'. It is truly regrettable that Sakuma's contribution through the English-translated work is not duly acknowledged. Also, two corrections are needed in the citation listed as Reference 2 by Kenzaka: (i) the referenced ATLAS SAKUMA in Japanese should be the second edition and (ii) the name of the publisher should be Maruzen Planet.<sup>2</sup> Kenzaka presents an image of a patient's

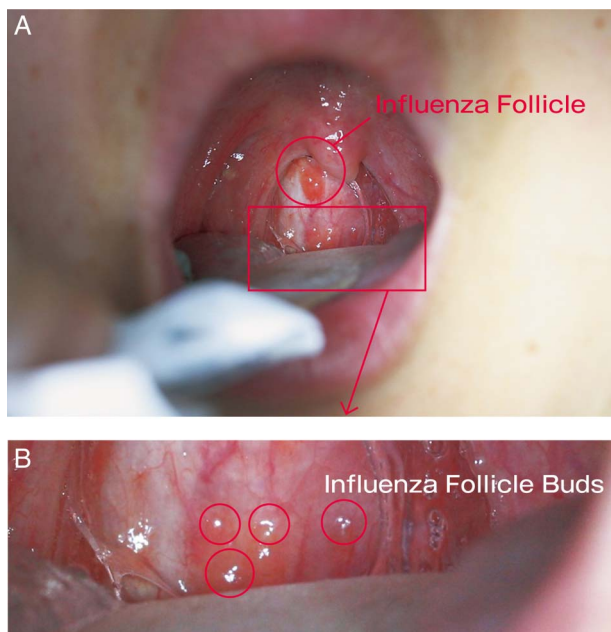
pharynx with influenza follicles and describes the morphology of the influenza follicles to be Yamada/Fukutomi classification type II gastric polypoid lesions, as described by Miyamoto and Watanabe<sup>3</sup> in *General Medicine*. According to the morphological classification of influenza follicles by Miyamoto and Watanabe, the lymph follicles of the posterior pharyngeal wall presented by Kenzaka are Yamada/Fukutomi classification type I gastric polypoid lesions; as such, they do not correspond to the definitive influenza follicles characterised by Miyamoto and Watanabe. These erroneous references and mischaracterisation of influenza follicles need to be corrected to avoid misunderstandings.

Among 419 patients diagnosed with seasonal influenza between 2003 and 2009, influenza follicles were identified with sensitivity of 94.5% and specificity of 98.4% regardless of the types of influenza (A/H3N2, A/H1N3, and B).<sup>3</sup> and the morphology of influenza follicles did not vary by the strains. Lymph follicles observed in upper respiratory inflammations such as adenovirus or enterovirus infection<sup>2</sup> are polymorphic and larger in size rather than hemispheric small (2–4 mm in diameter) follicles appearing in influenza infection, and influenza follicles are same in size for each patient. So, different sizes of influenza follicles observed in the same patient at the same time is a rare occurrence. Influenza follicles will be observed with or without associated severe lower airway disease.

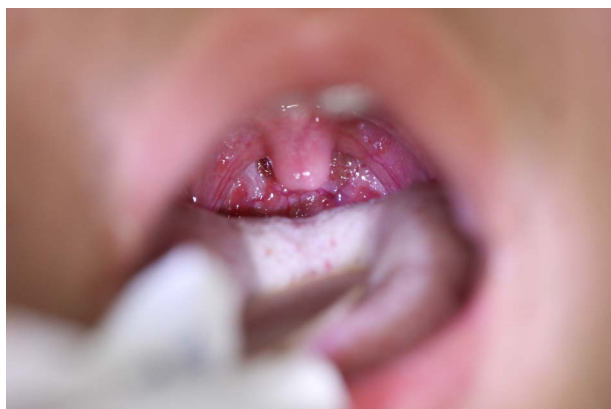
A typical case of influenza follicles is shown in figure 1. Miyamoto and Watanabe also discovered the presence of smaller influenza follicles that can be seen during an earlier phase than the definitive follicles of influenza infection, and they named them influenza follicle buds<sup>5</sup> (figure 2). This discovery may allow the diagnosis of influenza as early as 1 hour after fever onset, thereby enabling very early diagnosis of influenza and the identification of the pathophysiological expression of influenza follicles.



**Figure 1** A typical image of a definitive influenza follicle according to Miyamoto and Watanabe's<sup>2</sup> morphological classification of influenza follicles. In this case, the influenza follicles are aggregated in the upper part of the posterior pharyngeal wall; however, the location of the aggregation has no effect on the diagnosis.



**Figure 2** (A) A very rare case where influenza follicles and influenza follicle buds are observed together. Influenza follicle buds are shown inside the red rectangle. (B) A magnification of the image.



**Figure 3** A typical image of influenza follicle buds.<sup>4</sup>

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