9

Pregnancy Proteins As Tumor Markers

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1. INTRODUCTION

Human pregnancy proteins can be classified into three groups, "pregnancy-specific" (trophoblast-specific), "pregnancy-associated," and "fetal" (Table 1). This classification will, for convenience, be used here, although it is becoming increasingly apparent that the rigorous application of the term "pregnancy-specific" may be inadvisable. Pregnancy-specific proteins had been thought to be exclusively products of the trophoblast, but there is now evidence for the ectopic production of similar, if not identical, proteins by malignant nontrophoblastic tumors (Weintraub and Rosen, 1971; Braunstein et al., 1973), and recent work has also demonstrated the presence of SP1 in cultured fibroblasts (Rosen et al., 1978), although this may be an in vitro phenomenon.

The proteins chorionic gonadotropin and alphafetoprotein are described in earlier chapters. Of those proteins detailed in Table 1, it is our intention in this review to describe only those which are known to be ectopic products of nontrophoblastic tumors or which appear to have a relationship to tumor dissemination. These are:
2. PREGNANCY-SPECIFIC PROTEINS

2.1. PLACENTAL LACTOGEN (hPL)

2.1.1. Properties

This protein (which has also been referred to as chorionic somatomammotropin) was first identified and purified by Josimovich and MacLaren (1962), although a "prolactinlike substance" had been earlier identified in human placenta by Ito and Higashi (1961).

Placental lactogen is immunologically related to human growth hormone (Josimovich and MacLaren, 1962), and amino acid sequencing studies have shown 85% homology between the two proteins (Sherwood et al., 1971). Placental lactogen contains 190 amino acid residues and its molecular weight is 22,279 (Li et al., 1973).

A number of studies have demonstrated that hPL is a trophoblast product. Its concentration in retroplacental blood is greater than that in the peripheral maternal blood (Josimovich and MacLaren, 1962), and it has been localized in the cytoplasm of the syncytiotrophoblast using a fluorescent antibody technique (Sciarra et al., 1963).

Small amounts of hPL (150 ng/mg extract) have been detected by radioimmunoassay of extracts of normal testis (Payne and Ryan, 1972), although no hPL was detectable in sera from normal male subjects.

2.1.2. Placental Lactogen in Pregnancy

Detection of hPL in maternal serum is possible as early as 5 weeks after conception. The concentration rises continuously until about 34 weeks and then levels out. Serum hPL concentrations at term are of the order of 6–10 mg/L, but the range of normal values is wide and their distribution skewed (Letchworth, 1976).

The half-life of hPL in the circulation is short, being of the order of 12–25 minutes (Spellacy et al., 1966; Grumbach et al., 1968), and it has been found to vary from subject to subject (Pavlou et al., 1972).